

## BOETHICS, BIOSAFETY AND BIOSECURITY

### Science, ethics and values

What is science? Professor John Ziman of the Imperial College of Science and Technology, London, one of the most influential writers on the practice of science points out that definitions given by professional scientists, historians of science, philosophers of science, and representatives of other related disciplines tend to emphasize different aspects of the subject, often with quite different policy implications. Science is derived from a *Latin* term “*Scio*” that means observation and theoretical form, observation and experiment. Science is an investigation of the universe by a set of methodologies. In science progress is made by scientific methods. This is a Step-wise, not a single activity, not a value free. Ethics is associated with science. Here issues arise from scientific research. Scientists are trying to solve ethical issues. Science has entered in to our daily lives. Proper resource allocation reflects what society at the time deems to be valuable.

Philosophers might emphasize the methodological aspects of science focusing on experimentation, observation and theorizing as elements of the means by which reliable information about the natural world is gleaned through the practice of science. Historians are prone to view science as the accumulation of knowledge, stressing its archival aspect as a significant historical process worthy of special study. Ziman concludes that: **“...science is all these things and more. It is indeed the product of research; it does employ characteristic methods; it is an organized body of knowledge; it is a means of solving problems.”** Scientists have a large body of knowledge that they can use in making decisions. Yet much of this knowledge is not the product of scientific investigation, but instead involves value-laden judgements, personal desires, and even a researcher's personality and style. Debunked is the notion of a rigid Baconian scientific method by which scientists derive truth about the universe by making observations with no preconceptions about what they may discover. Instead the authors claim that: ...research is as varied as the approaches of individual researchers. Some scientists postulate many hypotheses and systematically set about trying to weed out the weaker ones. Others describe their work as asking questions of nature: “What would happen if ...? Why is it that...?” Some researchers gather a great deal of data with only a vague idea about the problem they might be trying to solve. Others develop a specific hypothesis or conjecture that they then try to verify or refute with carefully structured observations. Rather than following a single scientific method, scientists use a body of methods particular to their work.

The tendency of many scientists and teachers of science to portray science and scientists in an idealistic and unrealistic manner is often motivated by belief that this will result in a greater willingness on the part of students and the public to accept scientific, rational thought as a powerful tool for learning about, and understanding, the world and the universe. There is no evidence to support this view. On the contrary, when students are taught that scientists are mere mortals who are subject to the same social pressures and temptations, in their work as well as in their private lives, that influence all human endeavours, they are more likely to identify with scientists. The powerful methods that science offers for seeking knowledge about the universe then become personally accessible rather than a set of exotic tools available only to the members of an elite priesthood. Recent surveys have shown that despite a renewed interest in mysticism, and growing concern about the contribution of technological development to environmental degradation, public regard for science and technology remains very high. This is particularly true in the United States and other industrialized nations, but also in the developing world. While a high regard for science is certainly a desirable public attitude, it can be associated with an uncritical acceptance of any conclusion or opinion that is presented in the name of science. This is contrary to the essence of the scientific approach to knowledge, which seeks to engender a critical attitude and recognizes that all of the results of science are to be viewed as subject to further verification and revision.

### Attitudes to science:

According to Wittgenstein **“scientific terms are interpreted in social context”**. This has greater contribution to the economy growth. Post modernism says that results are not experimentally built but socially constructed. Science and technology are as central as ever. Keep in mind science is not done by robots actually public define science, think about research and policies. Impact on the public/ explore as a subject or career. It is a duty of scientific institutions to maintain public confidence. Three-quarters (76%) think scientific research makes a direct contribution to economic

growth in the UK, and nine-in-ten (91%) agree that young people's interest in science is essential for our future prosperity. Many also value the contribution it has made to their own lives. Half (51%) think the science they learnt at school has been useful in their everyday lives, while three-quarters (76%) think this of the maths they learnt at school. Most people still find out about science most regularly from traditional media. Six-in-ten (59%) say TV is one of their most regular sources of information on science and a quarter (23%) say print newspapers are one of their most regular sources. By contrast, under two-in-ten (15%) say online newspapers or news websites are one of their two most regular sources. The online qualitative research found TV and newspapers to be particularly passive sources, through which participants found out about science even when they were not actively looking for science stories or information. On the other hand, the internet was, among these online participants, a far more common source when they were actively seeking out information on science issues. Within this, there was no pattern in how participants chose their online sources – some had specific websites that they trusted, and some would check multiple sources, but others would simply look at the higher-ranking pages on Google.

## **What is ethics?**

**Ethics**, or **moral philosophy**, is the branch of philosophy that involves systematizing, defending, and recommending concepts of right and wrong conduct. Ethics has to do with what my feelings tell me is right or wrong and also with my religious beliefs. Being ethical is doing what the law requires. Ethics consists of the standards of behaviour our society accepts. Ethics is a requirement for human life. It is our means of deciding a course of action. Without it, our actions would be random and aimless. There would be no way to work towards a goal because there would be no way to pick between a limitless numbers of goals. Even with an ethical standard, we may be unable to pursue our goals with the possibility of success. To the degree which a rational ethical standard is taken, we are able to correctly organize our goals and actions to accomplish our most important values. Any flaw in our ethics will reduce our ability to be successful in our endeavours. A proper foundation of ethics requires a standard of value to which all goals and actions can be compared to. This standard is our own lives, and the happiness which makes them liveable. This is our ultimate standard of value, the goal in which an ethical man must always aim. It is arrived at by an examination of man's nature, and recognizing his peculiar needs. A system of ethics must further consist of not only emergency situations, but the day to day choices we make constantly. It must include our relations to others, and recognize their importance not only to our physical survival, but to our well-being and happiness. It must recognize that our lives are an end in themselves, and that sacrifice is not only not necessary, but destructive.

The three major areas of study within ethics are:

1. Meta ethics, concerning the theoretical meaning and reference of moral propositions, and how their truth values can be determined
2. Normative ethics, concerning the practical means of determining a moral course of action
3. Applied ethics, concerning what a person is obligated or permitted to do in a specific situation or a particular domain of action

## **The development of ethics:**

Terence Irwin describes “a selective historical and critical study in the Socratic tradition, with special attention to Aristotelian naturalism, its formation, elaboration, criticism, and defence”. ‘Socratic’ refers to Irwin’s method: not merely describing “a collective Socratic inquiry” historically but also evaluating it and taking part in it. Unlike Alasdair MacIntyre and J. B. Schneewind, who think that “a moral theory cannot be assessed timelessly, and there are no timelessly appropriate questions that different moral theories try to answer,” Irwin declares that history reveals substantial agreement on the main principles of ethics. The historian’s task is to discover them. Small wonder, then, that Development does so little to illuminate how ethics changed over time. When an author seeks unity among moral philosophers of the past, or at least all the good ones, he can hardly be expected to highlight significantly new issues or approaches, let alone differences in historical context.

Irwin’s focus on “Aristotelian naturalism” and also on Thomas Aquinas as its finest exponent. Neo-Platonists, “pagan” Roman philosophers, Jews, Muslims, Church Fathers other than Augustine, and Aristotle commentators

in medieval faculties of arts views on the development of ethics are also there. This strangely Kantian but now-fashionable reading of pre-modern ethics belongs to a pattern prominent in Development as a whole, though controversial even among specialists in ancient philosophy. According to Irwin, Aristotle teaches that all virtues aim at “the fine” (kalon), and it is characteristic of the virtuous person to choose virtuous actions because they are fine. The Stoics’ ethical theory does not depend on their idea of a divine intelligence that orders everything for the good of the universe, nor does their claim that virtue is identical to happiness represent a major departure from Aristotle’s ethics. The later Christian claim that “the virtuous person does the right actions because they are right” represents no major departure, either, for “that motive is central both to the Aristotelian and to the Stoic account of the virtues”. Might one at least see a major departure in Aquinas’s demotion of naturally acquired moral virtues to “virtues” only in a relative sense, and especially in his argument that all moral virtues simpliciter are gifts of grace, infused by God together with the theological virtue of charity? While Irwin grants that Aquinas “introduces a Christian element” by treating charity as “an appropriate directing principle,” he emphasizes that “the directive role of moral virtue is Aristotelian.”

### **The growth of bioethics:**

Ethical questions in medicine and the life sciences are the subject of not one but two relatively new academic fields: “bioethics” and “health and human rights”. Although moral questions about the ethics of medicine and related areas have been asked for as long as people have asked questions about ethics, it is only within the last few decades that new fields devoted specifically to such questions have arisen. The growth of these fields has stimulated further attention to important moral questions in medicine and biology. Although this is to be welcomed, there is also much to be regretted about the route bioethics has taken and about the very emergence of health and human rights as a distinct academic field. More specifically, bioethics suffers from some serious quality control problems, while health and human rights seems to be in violation of a disciplinary version of Occam’s razor, which proscribes the proliferation of disciplines or fields beyond necessity. In other words, health and human rights, as an academic field, does not seem to do anything that cannot be done either by bioethics, if the rights in question are moral rights or by the law if the rights are legal rather than moral. Moreover, it is characterised by weaknesses that, unlike those of bioethics, cannot be overcome.

“Bioethics” can be understood in a broader or narrower way. Following the broader construal, bioethics includes not only philosophical study of the ethics of medicine, but also such areas as medical law, medical anthropology, medical sociology, health politics, health economics and even some areas of medicine itself. On the narrower construal, bioethics, although it may draw on these other disciplines, is itself only an area of philosophical inquiry. More specifically, bioethics is one branch of practical or applied ethics, which is one branch of ethics, which in turn is one branch of philosophy. Although the first of these views of bioethics is the dominant one, it is the latter view that is preferable. A number of reasons can be advanced in support of this. Firstly, given that law and anthropology, for example, are not part of ethics, there is no reason to think that medical law and medical anthropology should be part of *bioethics*. Secondly, the broader view of bioethics fosters some unfortunate mistakes that many are already prone to make. For example, taking medical law to be part of bioethics encourages the common confusion between law and ethics, terms that are neither synonymous nor coextensive. Viewing such areas as medical anthropology or medical sociology as part of bioethics encourages the mistake of confusing descriptions with prescriptions. Social scientific study of the ethics of medicine is aimed at describing what the case is. For example, anthropologists tell us what a particular culture’s ethical view of some medical practice is. This is not to deny that anthropologists, lawyers, psychologists, or economists engage in complicated ways of reasoning. It is to say that they reason and argue about the way things are—what some culture thinks, or what the law is, for example. By contrast, practical ethics involves advancing and examining arguments about what ought, morally, to be done and not done—about what is right and wrong.

To say that bioethics should be construed in the narrow way is not to deny the importance of the sciences, social sciences, and law to bioethics. These disciplines are clearly indispensable to practical ethics. One cannot reach an informed conclusion about what should be done in some practical case if one does not have all the relevant information about the way things are. Indeed, there are even circumstances where moral disagreement is entirely eliminated once the relevant facts are established. Disciplines other than moral philosophy therefore play a crucial role. However, a problem arises when scientists, social scientists, and lawyers slip from doing what they are trained to do into doing moral philosophy. Although some do a reasonable job with the latter, very many do not. There is a parallel problem for philosophers who work in the area of practical ethics. Because this area requires knowledge of science, social science, and sometimes law, practical philosophers have to familiarise

themselves with scholarly discussions in these disciplines. This is unavoidable and is untroubling as long as the philosopher does not purport to be doing science, social science, or law but only reporting its findings. There are some cases, it must be conceded, where the analytic tools of the philosopher can actually help in assessing the evidence. In these cases the philosopher does more than simply report. Nevertheless, philosophers are ill advised to masquerade as scientists, social scientists, or lawyers.

The problem of “disciplinary slip”, where one slips from working in one's own discipline, in which one is trained, to working in another, in which one is not, is more acute in some cases than in others. For example, there are fewer obstacles to health care workers or scientists slipping into doing moral philosophy than there are obstacles to philosophers slipping into medicine or science. This is partly because of the obviously special knowledge and training required to become a healthcare professional or a scientist. But it is also partly because of the widespread but mistaken assumption that doing philosophy does not really require any training or aptitude. Indeed, it is this attitude that underlies the common confidence to pronounce about moral and other philosophical matters without any sense of the complexity of these matters. I am not suggesting that only philosophers are entitled to make moral judgements, but I am suggesting that the expertise and skills of philosophers are often underrated. There are somewhat lesser obstacles to philosophers drifting into the softer sciences that are to be found under the umbrella of bioethics but even these obstacles are greater than the obstacles in the reverse direction. Social scientists, I suspect, can slip into doing moral philosophy more readily than philosophers can slip into doing social science.

A second reason why there are fewer obstacles to medical professionals and scientists slipping into bioethics, is the fact that bioethics is making greater inroads into academic medical contexts than medicine and medical science are making into academic philosophy. Thus articles on bioethics are now quite commonly published in medical journals, and so-called “bioethicists” are invited to speak to groups of medical practitioners. It is much rarer for doctors and scientists to be publishing in philosophy journals or for doctors to be giving academic talks to philosophers. The upshot of this, again, is that the audience for much bioethics writing and talk are people who, because they are not trained in philosophy, are much less discerning about what constitutes good philosophy. A parallel problem can occur when scientists do publish science in a bioethics journal. For example, Stuart Derbyshire advanced a scientific view—that neither foetuses nor neonates can feel pain—that would be rejected as outlandish by most experts. Yet many non-scientists would not readily see this and might simply be misled by the needless technicality of his argument. Anybody purporting to be a bioethicist and who either knows slightly more than the audience or who can make it seem as though he or she does, can gain a hearing in many a medical audience.

These problems of disciplinary quality are exacerbated by a number of factors. Firstly, because the discipline of bioethics is currently understood in the broader way, it is filled with people who have slipped from their area of medical, scientific, or other non-philosophical expertise into moral philosophy. Given that the discipline is so populated with such people, many of them do not see that many of the rest are not doing moral philosophy very well. Secondly, there has been a proliferation of courses, diplomas, and degrees in bioethics. As these courses are often aimed at those without philosophical training and lack the rigour and often duration of other courses of study, there are more and more people with formal but poor bioethics education. There is a whole enterprise of bioethics education that is creating “experts” if not instantly then certainly very quickly. In some cases, a brief course or a diploma is thought sufficient to transform a novice into a so-called “ethicist”, “bioethicist” or, worse still, a bioethics educator. Thirdly, the bioethics literature is also of very uneven quality. There is some outstanding work being done, but there are also an unusually large number of poor quality bioethics publications. It is striking, for example, that each issue of a widely read bioethics journal consists mainly of brief responses to a few substantial articles in the journal. The responses, which do not seem to have to pass the usual sort of professional peer review, have included quite a number that never would pass such review.

There are no such standards in bioethics.\* Indeed, much of what goes on in bioethics is undisciplined. Some think that the absence of disciplinary standards is acceptable in bioethics because it is a “field” rather than a “discipline”, but this semantic point does not undermine the substantive points I have made about disciplinary slip within the field. Others seek some consolation in the claim that bioethics is a *new* field, which has yet to find its feet and establish standards. This, however, seems overly optimistic. It is not clear how the field's becoming older and more established would prevent the disciplinary slip from occurring. Nor can we expect future bioethicists to be sufficiently expert in all the component disciplines that the problem of disciplinary slip

evaporates. Even if disciplinary training in bioethics broadens it is more likely to produce Jacks and Jills of many trades, rather than experts in any.

Defenders of the broader conception of bioethics may wish to defend it in the following way. They may say that because answering bioethics questions involves answering both philosophical and non-philosophical questions, the field of bioethics must incorporate both. To bolster their point, they might want to claim that what unites these two kinds of questions and marks out the field is a distinctive kind of bioethics reasoning. But this suggestion is implausible on at least two counts. Firstly, it is unlikely that bioethics reasoning from other forms of practical ethics reasoning. Secondly, although answering practical ethics questions does require both philosophical and non-philosophical reasoning, there is no overarching distinct form of reasoning that unites these two. As the scientific, social scientific and legal questions that are integral to bioethics can also be asked and answered quite independently of any ethical interest, they are not distinctively ethical. They are scientific, social scientific and legal questions and must be answered by those best equipped to answer them, employing the tools of the relevant discipline. How the answers to those questions are to be woven into answering an ethical question is part of ethical reasoning and thus is in the domain of moral philosophy, or at least its practical branch.

Although the problem of academic standards in bioethics might not be avoided entirely if the narrower construal of bioethics were to prevail, it is certainly the case that the broader construal contributes significantly to the problem. There is a real danger that the surge of interest in bioethics that we have witnessed will give way, in due course, to a pendulum swing in the opposite direction, once the poverty of bioethics, as it is currently practised, becomes evident. That would be regrettable. Some of those engaged in academic work on moral problems in medicine identify their field as “health and human rights”, which they see as distinct from bioethics. According to the health and human rights view, the moral defects of medical practice and human life more generally, are to be rectified through the promotion of human rights. Those advocates of health and human rights who think that the relevant rights are legal ones, either national or international, face an obvious difficulty. Law and morality are neither the same thing nor are they coextensive. The law can be morally defective, and moral rights can fail to be incorporated into law, or be incorporated only inadequately. The upshot of this is that legal rights, like law in general, are inadequate to the task of resolving *moral* dilemmas or rectifying the *moral* defects of medical practice.

The health and human rights paradigm is defective, however, even if the rights in question are moral rather than legal ones. The poverty of this paradigm becomes apparent when we consider what human rights are and how these relate to ethics and bioethics. One of the distinctive features of rights is that they have correlative duties. To ascribe a right is also to ascribe the correlative duty. There simply could not be a right without its correlative duty. For example, my right not to be killed is correlated with the duty of others not to kill me. I could not have a right not to be killed if others were under no duty not to kill me. A second distinctive feature of rights is that they have unusual moral strength. They are said to have “trumping” power. That is to say, they can defeat other moral considerations. Human rights, presumably, are rights someone has in virtue of being human. In other words, a human right is a kind of natural right—a right that somebody has on account of his (human) nature. Not all rights that humans have are human rights. Some rights are possessed not on account of the bearer's nature but rather because of some other consideration. For example, if you lend me £100, you acquire a right to receive £100 from me. This is not a human right, but rather a right arising from the loan.

We see, then, that human rights are but one kind of right. However, even the expanded class of rights obviously does not exhaust the range of moral concepts that can be employed to understand and evaluate an ethical issue. There are a host of other moral concepts including “duty”, “the good”, “virtue”, and “supererogation”. Although rights have correlative duties, it does not follow that all duties have correlative rights. There may well be duties, such as the duty to give charity that is not correlated with anybody's right. One has a duty to give, without anybody else having a right to receive. A duty to give charity would be one that, though binding, would carry a degree of discretion with regard to how it is discharged. An ethical approach, such as health and human rights, that takes rights to be the only concept necessary for discussion of ethical issues in medicine, ignores those duties that are not correlated with rights. Nor can it consider “the good”. There are different conceptions of the good, but we do not need to decide between these to realise that an ethical evaluation that fails to consider any such conception is impoverished. Rights may be able to trump the good, at least sometimes, but this is not to say that the good has no value. If one only considers rights, one will not be able to assess the value of the good.

Neither can the virtues or good character be discussed comprehensively in the language of rights, unless one has such an impoverished notion of the virtues that respecting rights is the only virtue. Speaking only the language of rights, one cannot comprehensively explain the value of courage, patience, or temperance. A moral lexicon consisting only of rights is similarly unable to explain the concept of supererogation—that is, the concept of going beyond the call of duty. One can say that others have no right to one's acting in a supererogatory manner but that one has a right to act in such a way if one so wishes. This, however, does not begin to capture the moral value of supererogation. For example, rights language cannot distinguish supererogation from a mere liberty right. In both cases one has a right to do something and others have no right that one does it.

Morality is a complex matter. This complexity cannot be managed competently with only the concept of rights—and *a fortiori* with only the concept of *human* rights. A health and human rights approach is unable to consider a non-natural right, such as a right arising from a promise or from membership in a medical insurance scheme. Even if the notion of “human rights” were extended to include not only natural rights possessed by humans but also non-natural rights possessed by humans, the human rights approach would still be unable adequately to approach important issues in medicine. For example, it could not take account of the interests of those animals on which medical experimentation is conducted. Even those who think that such experimentation is morally justifiable must agree that reaching that conclusion via an ethical approach that considers only the *rights of humans*, and nothing else, is highly unreliable. Using only the language of rights to grapple with every moral issue is analogous to treating every sickness with the same medication (or class of medication) or it is like trying to speak by using only nouns. It is crude and ineffective.

Discussion about (moral) rights is part of what ethics or bioethics involves, but these disciplines need not restrict themselves to this one moral concept. Unlike the human rights approach, those who do bioethics need not commit the error of mistaking the part for the whole. Rights are part of ethics, but they are not all there is to ethics. Thus, those doing ethics or bioethics can and do employ whatever moral concepts are relevant to some issue. It is hard to see, therefore, why advocates of the human rights approach think that their approach can either replace bioethics or be superior to it. One suggestion could be that the human rights approach to ethical problems in health and health care is an activist approach. It aims at bringing about positive change. The objection here is that bioethics is too much of an academic exercise and too little a mechanism for social change. (This is the explanation also for the more subtle position that instead of replacing bioethics with health and human rights, bioethics should focus more on human rights issues.)

There are a few ways to respond to this. The first is to note that bioethics can (although it need not) be coupled with activism. The second response is to question whether activism is really a desirable feature in a field of academic work. The primary purpose of academic work is to enlighten. Some may choose to enlist such enlightenment for political or moral purposes in order to bring about positive change, but that enterprise, although linked to the academic one, is distinct from it. A third response takes the second one a step further. Activism *in* (rather than as a *consequence of*) an academic field may actually undermine the academic enterprise. Indeed the health and human rights approach runs this very risk. It is prone to join popular moral discourse in employing rights claims as a substitute for moral argument. In other words, instead of doing the difficult academic work of determining whether some action is right or wrong, there will be the temptation simply to ascribe either a right to perform that action or a right against others acting in this way. An activist agenda is more likely to presuppose which rights should be ascribed (or which rights should prevail) than it is to engage, as dispassionately as possible, the question about whether these rights ascriptions are warranted. Scholarship becomes but a handmaiden to the predetermined activist agenda.

### **Bioethics in 21<sup>st</sup> Century:**

In the field of human procreation, the problems raised by bioethics are multiple and complex. First, there is the request from couples and individuals with regards to the management of procreation, not only the negative requests, be it contraception or abortion, but also the positive requests concerning medically assisted procreation. Then there is the practitioner's response to the request, particularly for assisted procreation. The practitioner is at the heart of conflicting interests between the needs or desires of the patients and the reluctance, legitimate or not, of society, with the implication of a third person, embryo, fetus or newborn. And here again we are confronted with the aims of researchers wishing to obtain information concerning the efficacy, possibilities of application and potential dangers. The legists and magistrates are concerned with the legal status of the embryo and the fetus. However, if the fact of giving a legal status can solve many legal problems, it does

not solve the problem of the eventual use of an embryo, and of its interpretation by philosophers and moralists. Moreover, public opinion should not be forgotten, including the attraction of rapid anathema, without recourse. Finally, there is also the role of the legislator who, here again, is confronted with several controversial conceptions.

Four commonly accepted principles of health care ethics. First is the respect for autonomy. Any notion of moral decision-making assumes that rational agents are involved in making informed and voluntary decisions. In health care decisions, our respect for the autonomy of the patient would, in common parlance, imply that the patient has the capacity to act intentionally, with understanding, and without controlling influences that would mitigate against a free and voluntary act. This principle is the basis for the practice of "informed consent" in the physician/patient transaction regarding health care. The principle of non-maleficence requires of us that we not intentionally create a harm or injury to the patient, either through acts of commission or omission. In common language, we consider it negligent if one imposes a careless or unreasonable risk of harm upon another. Providing a proper standard of care that avoids or minimizes the risk of harm is supported not only by our commonly held moral convictions, but by the laws of society as well. This principle affirms the need for medical competence. It is clear that medical mistakes may occur; however, this principle articulates a fundamental commitment on the part of health care professionals to protect their patients from harm.

The ordinary meaning of this principle is that health care providers have a duty to be of a benefit to the patient, as well as to take positive steps to prevent and to remove harm from the patient. These duties are viewed as rational and self-evident and are widely accepted as the proper goals of medicine. This principle is at the very heart of health care implying that the patient can enter into a relationship with one whom society has licensed as competent to provide medical care, trusting that the physician's chief objective is to help. The goal of providing benefit can be applied both to individual patients, and to the good of society as a whole. For example, the good health of a particular patient is an appropriate goal of medicine, and the prevention of disease through research and the employment of vaccines is the same goal expanded to the population at large. It is sometimes held that non-maleficence is a constant duty, that is, one ought never to harm another individual, whereas beneficence is a limited duty. A physician has a duty to seek the benefit of any or all of her patients, however, a physician may also choose whom to admit into his or her practice, and does not have a strict duty to benefit patients not acknowledged in the panel. This duty becomes complex if two patients appeal for treatment at the same moment. Some criteria of urgency of need might be used, or some principle of first come first served, to decide who should be helped at the moment. Justice in health care is usually defined as a form of fairness, or as Aristotle once said, "Giving to each that which is his due." This implies the fair distribution of goods in society and requires that we look at the role of entitlement. The question of distributive justice also seems to hinge on the fact that some goods and services are in short supply, there is not enough to go around, thus some fair means of allocating scarce resources must be determined. It is generally held that persons who are equals should qualify for equal treatment.

### **Making ethical decisions:**

Making ethical choices requires the ability to make distinctions between competing options. Here are seven steps to help you make better decisions:

1. **Stop and think:** This provides several benefits. It prevents rash decisions, prepares us for more thoughtful discernment, and can allow us to mobilize our discipline.
2. **Clarify goals:** Before you choose, clarify your short-term and long-term aims. Determine which of your many wants and "don't want" affected by the decision are the most important. The big danger is that decisions that fulfill immediate wants and needs can prevent the achievement of our more important life goals.
3. **Determine facts:** Be sure you have adequate information to support an intelligent choice. To determine the facts, first resolve what you know, then what you need to know. Be prepared for additional information and to verify assumptions and other uncertain information. In addition:
  - Consider the reliability and credibility of the people providing the facts.
  - Consider the basis of the supposed facts. If the person giving you the information says he or she personally heard or saw something, evaluate that person in terms of honesty, accuracy and memory.
4. **Develop options:** Once you know what you want to achieve and have made your best judgment as to the relevant facts, make a list of actions you can take to accomplish your goals. If it's an especially important

decision, talk to someone you trust so you can broaden your perspective and think of new choices. If you can think of only one or two choices, you're probably not thinking hard enough.

5. **Consider consequences:** Filter your choices to determine if any of your options will violate any core ethical values, and then eliminate any unethical options. Identify who will be affected by the decision and how the decision is likely to affect them.
6. **Choose:** Make a decision. If the choice is not immediately clear, try:
  - Talking to people whose judgment you respect.
  - Think of a person of strong character that you know or know of and ask yourself what they would do in your situation.
  - If everyone found out about your decision, would you be proud and comfortable?
  - Follow the Golden Rule: treat others the way you want to be treated, and keep your promises.
7. **Monitor and modify:** Ethical decision-makers monitor the effects of their choices. If they are not producing the intended results, or are causing additional unintended and undesirable results, they re-assess the situation and make new decisions.

### **The place of humans in nature:**

Humans in western and developed countries are thought to have developed a sense of being separate from nature for a variety of reasons. The Enlightenment brought with it feelings of domination over nature. Descartes (1637) advanced the philosophy that human minds and bodies were separate. Other forces in play made it a relatively short logical link to the idea that humans were separate from nature and dominant over it. With the increasing focus on a scientific and empirical approach to nature came developments in science and technology. Many of these discoveries further enhanced people's abilities to control or transform nature into the pristine gardens present in the biblical story of Adam and Eve. Merchant (1996) wrote that "The controlling image of Enlightenment is the transformation from desert wilderness to cultivated garden." A number of authors have argued that humans were once psychologically and physically closer to nature than residents of industrialized nations are now. Advances in scientific knowledge drove the twin forces of industrialization and urbanization to further split humans from their environments (Franklin 1999).

In an analysis of the shift from a land-based economy to an urban and industrialized world, Cronon (1995) spoke of the alienation from nature that resulted. As he and others have pointed out, this shift from a living environment in which humans were closer to nature led to an urban context in which meat comes from the grocery store. Ironically, the very conquest of nature, in combination with the alienation from it, promoted the idea of the sacredness of nature, with legislation enacted in many developed countries to protect tracts of pristine land from human influences. As Vining (2003) and others (e.g. Melson 2001; Winter 1996; Winter and Koger 2004) noted, the affection for pets and gardening may also reflect a yearning for a closer relationship with nature and the natural. The value that a person places on the environment may play a role in whether or not she views herself as part of or separate from nature. Lamb (1996) proposed that the term "anthrocentric" be used to describe individuals who place themselves in an ethical state above nature. She compared these individuals with biocentric people who place all life at an equal level. Lamb stated that the value we place on nature will have an effect on how we view ourselves in connection with nature. Nature itself can also be seen as purely a reflection of a person's beliefs and desires (Cronon 1995).

Thus, if an individual desires a sense of connectedness with nature, he or she may have a more connected view of nature with humans than would an individual desiring isolation. Likewise, if an individual believes that being a steward of the land requires a separation between nature and self, he or she is likely to view themselves as separate from nature. An important question is what is meant by nature or to be considered natural? While this may seem like a simple question, researchers, philosophers, and the general public have been addressing it for quite some time. A simple definition for nature does not exist. A search for literature on the subject reveals hundreds of books on the matter, and many more research articles seeking to define nature or to give an historical account of how the difficulties in defining nature came about (see for example Lewis 1967; Soper 1995; Evernden 1992; and Macnaghten and Urry 1998). In one study, participants in a wilderness camp defined nature as the opposite of civilization. They also said that nature was something that is "out there" without human involvement. Nature was also said to be relaxing and undisturbed, and nature was said to be not at home (Haluzá-Delay 2001). Hartig (1993) offered the transactional perspective of nature, stating that aspects of humans and the environment act in defining each other. Thus, defining whether something is natural or is

unnatural requires a person to reflect on a holistic basis. Hartig maintains that dividing the person and environment into discrete elements is not the goal of this perspective. He believes that each entity acts to define the other and is thus interconnected. Cronon (1995) argued that people should stop putting up borders between themselves and nature. He stated that in order to successfully protect the whole environment, not just small parts of it and one must eliminate these human-perceived barriers. Credence for Cronon's statement is garnered in work done by Schultz (2000), who argues that an individual's level of concern for the environment is directly related to the sense of connectedness the individual feels with nature. Schultz examined the type of concern people have for the environment and discovered three different types of concern: egoistic, altruistic, and biospheric, which he has shown empirically to be three distinct types of environmental orientations (Schultz 2001). In a study of perspective taking, he asked participants to imagine how they might feel or think if they were the people in a set of images of humans in various environments. Schultz concluded that participants reduced their level of separation between themselves and nature, which then led to an increase in their biospheric concern for nature. Furthermore, Schultz et al. (2004) stated that the connection an individual feels with nature is implicit or unconscious.

Therefore, the use of techniques like perspective taking might enable an individual to bring their awareness of their connection to nature to a more conscious level. However, it is quite possible that the connection an individual feels with nature cannot be altered, but perhaps making people more aware of their views would lead to conscious thought on the issue. Individuals in developed countries tend to view some natural areas as worth protecting, while ignoring physically similar natural areas. Schroeder (2002) argued for the importance of maintaining special places, which are areas in the natural environment that a person values for aesthetic or emotional reasons (or both). Public participants defined these special places as areas that are natural, serene, act as a refuge and have an element of beauty, among other things. These special places are areas that people can go to experience nature. Schroeder noted that an individual's concerns over public land management are likely to be affected by their feelings toward their special place. Thus, working with feelings toward various natural areas may help to attract the support of people who normally are indifferent to conservation issues. We believe it is important to understand what people construe as natural or unnatural and to examine whether people view themselves as part of or separate from nature. First, while there has been significant attention paid to categorizing humans as anthropocentric or biocentric, we are not aware of another study that has asked people to specifically define themselves as part of or separate from nature or to ask directly for reasons why. Secondly, the connection between a definition of oneself as natural or unnatural may have implications for environmental action. It seems to be possible for people to view themselves as a part of nature, but then define nature as the non-human world. This difficulty in conceptualizing the role of humans in the ecosystem may lead to behaviours, beliefs, or attitudes, which are either environmentally responsible or irresponsible. Thirdly, since feeling connected to nature is thought to be a predictor of environmentally responsible behaviour and overall well-being of the individual, it is important to elucidate why there are differences between individuals in how connected they are with nature.

### **Valuing the environment:**

Natural world except humans but today over-exploitation of nature is increasing. Economists have attempted to value such resources. Intrinsic value is the value that environment and living forms have their own rights e.g., intrinsic value of birds/green and pleasant places have their own values. It mainly involves religion. On the other hand, instrumental value is the supply of human's material needs. It has actual and potential use in supplying resources for human living. This topic is still debatable. Keeping in view the environmental challenges one must value environment for decision making like air/water quality, green house gas, protect biodiversity, maintain ecosystem, marine environment.

### **Ken Henry said:**

**“We have made a start, much more needs to be done, if we are able to say that the wellbeing of future generation is not threatened by poor valuation of environment”**

Making thoughtful decisions about environmental challenges that involve wide-ranging and potentially irreversible consequences is of profound importance for current and future human wellbeing. How much and how fast should greenhouse gas emissions be reduced to minimize global climate change? What standards should be set for air and water quality? What should be done to protect biodiversity and to maintain ecological processes? Addressing such questions involves weighing benefits and costs in multiple dimensions. In spite of

the high stakes, however, the nation—its government and society—often fails to take systematic account of the environmental consequences in its actual decision making and instead follows standard operating procedures or existing legislative mandates, or simply muddles through.

Virtually all important environmental management and policy decisions have a wide range of effects. For example, zoning or development decisions about land use can have a variety of environmental impacts as well as economic and social effects. Similarly, decisions on limits on emissions of air pollutants or greenhouse gases can affect a range of environmental, economic, and social concerns. These results affect multiple groups who often have very different views about desired outcomes. Effects differ across geography and time. Choosing among management or policy options that differ in terms of environmental, economic, and social outcomes with spatial and temporal components may at first glance seem overwhelmingly complex, with dimensions that seem incomparable. Good environmental management and policy decision making, however, necessitates systematic evaluation and consideration of the effects of management and policy on the affected public. Even though the quantitative valuation of these effects will never be perfect, the outcome of attempts to assess value provides important information to help guide decision making.

### **Themes in environmental ethics:**

Global environmental change gives rise to ethical challenges that need to be grasped within a framework of critical and forward-looking thinking. Environmental challenges often tend to be framed as costs to be borne and technologies to be discovered, leaving behind the opportunities and co-benefits associated with serious engagement with their ethical dimensions. Today human population has put and putting lots of load on the environment. There is lots of pressure on the natural resources for humans to live because certain activities of humans can damage the environment. According to Rio Declaration two current themes are used in environmental ethics (1992). One is precautionary principle and the other one is sustainability. Precautionary principle is the old concept which is applied to different areas like deontological and consequentialist ethical thinking. The precautionary principle is a principle of practical decision-making which may be justified on the basis of ethical and socio-political grounds and/or as a form of rational action. In general, the principle states that serious environmental threats and health hazards should be anticipated and that they ought to be forestalled before the realisation of damage even if scientific understanding of the risks is inadequate. While in case of sustainability, activity should be conducted repeatedly without accumulating environmental damage e.g., agriculture has no lasting effect on the environment (local/large level). Sustainability both challenges and gives shape to the discipline of environmental ethics by blurring classical distinctions such as that between anthropocentrism, biocentrism, and ecocentrism, while bringing attention to important theoretical dimensions of the ecological, social, and economic. These three dimensions are in turn informed by matters pertaining to human cognition and perception, highlighting the complex and multidisciplinary nature of the emerging conversations.

### **Current issues in environmental ethics:**

There is a list of current issues but the most common one are human-environment interaction/increase in human population, bioaccumulation and biomagnifications, ozone depletion, acid rain, green house gases. Around the world, scientists are expressing their concerns about the ability of the earth system to sustain a growing population with an ever increasing demand for the Earth's resources. A stark example of such published concern is Rockström et al.'s (2009) analysis of what they call the "safe operating space for humanity", published in *Nature*. Rockström et al. (2009) developed a model of the safe operating space for nine environmental systems, contrasting what they considered to be the safe operating limits against the current position for those variables they consider measurable. In their analysis, the boundaries in three systems – climate change, rate of biodiversity loss, and human interference with the nitrogen cycle – have already been exceeded. Importantly, they also argue that two others – chemical pollution and atmospheric aerosol loading – cannot yet be quantified. Such studies reflect engagement with the Forecasting-Observations-Thresholds aspects of the Grand Challenges model, and in doing so, draw attention to the need for social engagement through the Responses-Innovation component. In response to this latter need, Bradshaw et al. (2010), for example, in describing the relative environmental impact of human activity across the globe, provide evidence-based modelling that contributes directly to Response-Innovations end of the Grand Challenges model, with clear implications on the setting of priorities. Their modelling used available indicator data – measures of natural forest loss, habitat conversion, marine captures, fertilizer use, water pollution, carbon emissions and species threat – and concluded that suitable data is available for the majority of the 228 countries considered. Their study demonstrates that environmental performance is complex, drivers of environmental impact are variable, and countries perform

poorly for different reasons; increasing wealth was the most important driver of environmental impact. Their study also draws attention to the science-society linkages in this matter, and supports calls to better integrate disciplinary and/or scientific paradigms for more holistic approach to understanding and social action. Reid et al. (2010) argue that “progress in understanding and addressing both global environmental change and sustainable development requires better integration of social science research”.

### **Terrestrial and aquatic pollution: Environmental ethics**

Pollution problems in aquatic sediments and on land can be quite varied—from the widespread contamination of a coastal bay receiving untreated urban or industrial discharge to the local leakage from underground petroleum tanks or pipelines. Such problems are related to the range of sediment and soil in which they occur. Sediments and soil particles can be carriers, receptors, and sources for contaminants. The effectiveness of these roles is largely related to their adsorptive capacity and is governed mainly by particle size, mineralogy, and organic matter as well as site-specific geochemical conditions. Sustainable use of land and marine areas requires a source-to-sink system perspective in order to prescribe remedial actions. Measures can focus on preventing release from the source, spreading along selective pathways, stabilization, and isolation to protect the receptor. Therefore, many traditional scientific goals, such as sediment source identification, the interpretation of sediment transport modes and directions, and post-depositional changes, are applicable and complementary tools to increase predictability between sampled sites.

The carrier function of aquatic sediments is emphasized when contaminants are transported to the site of accumulation. Ground pollution in terrestrial settings, on the other hand, is often due to more local sources. Nevertheless, retention and ecological exposure is dependent on the particle-solute interactions. The stratigraphic architecture of ground environments can also decisively influence the spread of contaminants, contrasting with the largely two-dimensional redistribution of eroded aquatic sediments. Diffuse pollution sources, including agriculture, urban, transportation, and industrial sources, contribute significantly to overall environmental stress. Quantitative modeling of contaminant fluxes is increasingly possible with database availability, but relative risk ranking is still a necessary simplification in many decision-support evaluations due to the complexity of sediment and ground environments. In Pakistan environment protection laws are very weak. Terrestrial and aquatic pollution are caused by the use of certain chemicals, unregulated disposal on land as well as by the industrial byproducts and by poisoning metals. Rachel Carson was the first one to introduce the chemical- pollution. Today agri-chemicals have accumulated in our food chain. Chemical reaction in the atmosphere results in the formation of aerosols. Aerosol sprays are used in refrigerator as a coolant that also destroy ozone layer. Every year number of accidents occurs like major oil spillages, spread of radioactive isotopes or the accidents' that occur due to the generation of electricity from nuclear energy.

### **Global climate change: Environmental ethics**

Climate change has been described as a "perfect moral storm" because it brings together three major challenges to ethical action in a mutually reinforcing way. The first challenge stems from the fact that climate change is a truly global phenomenon. Once emitted, greenhouse gas emissions can have climate effects anywhere on the planet, regardless of their source. This is often said to result in a prisoner's dilemma or tragedy of the commons structure played out between nation states: although collectively all countries would prefer to limit global emissions so as to reduce the risk of severe or catastrophic impacts, when acting individually, each still prefers to continue emitting unimpeded. At the same time, there are skewed vulnerabilities: at least in the short- to medium-term, many of the most vulnerable countries and people are those who have emitted the least historically and whose emissions levels continue to be relatively low. This appears to be seriously unfair and casts a notable shadow over both practical and theoretical efforts to secure global cooperation. The second challenge is that current emissions have profoundly intergenerational effects. Emissions of the most prominent greenhouse gas, carbon dioxide, typically persist in the atmosphere for a long time, contributing to negative climate impacts for centuries, or even millennia. This too seems unfair, especially if future negative impacts are severe and cumulative. Factors that increase atmospheric CO<sub>2</sub> are industrial revolution, burning of fossil fuels or by the burning of wood. CO<sub>2</sub> is a greenhouse gas it traps infrared rays from the sun. Earth climate zone is

shifting, polar ice start melting, sea level increases and metabolic rate of methane producing bacteria increases, certain species may extinct. This is collectively known as global warming.

In addition, the temporal diffusion of climate change gives rise to an ethical collective action problem that is even more challenging than the traditional tragedy of the commons both in its shape and because normal kinds of cooperation do not seem to be possible across generations. The third challenge to ethical action is that our theoretical tools are underdeveloped in many of the relevant areas, such as international justice, intergenerational ethics, scientific uncertainty, and the appropriate relationship between humans and the rest of nature. For example, climate change raises questions about the value of nonhuman nature, such as whether we have obligations to protect nonhuman animals, unique places, or nature as a whole, and what form such obligations take if we do. In addition, the presence of scientific uncertainty and the potential for catastrophic outcomes put internal pressure on the standard economic approach to environmental problems and play a role in arguments for a precautionary approach in environmental law and policy that some see as an alternative. The global and intergenerational dimensions of the perfect moral storm provide serious temptations for those in the current generation who contribute heavily to climate change to pass most of the burden of their activities on to people in other parts of the world and the future in unfair ways. In particular, the complexity of the ethical and scientific terrain may make us susceptible to arguments for inaction that shroud themselves in moral language but which are actually weak and self-deceptive. Unfortunately, there is some evidence for this in the ongoing political inertia in developing a robust global regime. This suggests the need for work in moral and political philosophy that exposes inadequate rationales and articulates compelling reasons as to how and why we should address climate change. Such work can help preserve and extend the limited progress currently being made and reinforce arguments against those who have failed to deliver on their promises to reduce emissions and contribute to adaptation funds.

#### **Environmental degradation and loss of biodiversity:**

Biodiversity as the variability of living creatures genetically, individually and ecosystem wide. With losses of 50-150 species daily, a level 10,000 times greater than the natural rate of species extinction from the fossil record, biodiversity loss is clearly a pressing global threat. Not only is the number of species shrinking, but genetic and ecosystem diversity are also declining, the other two components of biodiversity in general. Humans have much to lose if biodiversity loss continues at its current rate. Food production, which is dependent on just 20 plant species, will be further at risk as crop yields become difficult to maintain due to soil erosion, loss of dependable water supplies, and a decline of pollinators. The loss of biodiversity could also lead to a loss of medicines and the emergence and spread of infectious diseases. It is possible that the study of Earth's biodiversity may be the easiest method of predicting future dangers to human health from global environmental degradation.

Current rates of biodiversity loss have been estimated to be as high as 1,000 to 10,000 times faster than rates indicated in fossil records. The main drivers of biodiversity loss are deforestation, desertification, overexploitation, invasive species, pollution, and climate change. Overuse of natural resources can lead to ecosystem degradation, and ultimately to extinction of flora and fauna. This problem is particularly noted in fisheries, where 50% of commercial marine fisheries are fully exploited, and another 25% are over exploited. Climate change affects temperature, precipitation, and weather patterns, all of which can affect reproduction and migration timing, species distribution, population size, the length of the growing season, and the frequency of pest and disease outbreaks. As habitats change, more extinction will occur as species struggle to adapt. Human activity has transformed forests in to lands. Pollution affects the ecosystem-loss of biodiversity as well as tropical rain forest-climax ecosystem. Clearance of tropical forest is due to the use of wood, need of a land. We are losing 7 million hectares per year and thus soil is also degrading without trees. Thus there is need for an international consensus to combat further loss. An important feature of biodiversity loss that must be taken into consideration when addressing this problem is the differentiated responsibility that states have; species and ecosystem diversity are concentrated in less developed states located in the tropics, but the impetus for conservation comes most adamantly from developed nations. The developed states have both the interest and the wealth to protect diversity, thus there is the need for international cooperation to bring the two sets of actors together.

#### **The ethics of animal research:**

An estimated 100 million nonhuman vertebrates worldwide--including primates, dogs, cats, rabbits, hamsters, birds, rats, and mice--are bred, captured, or otherwise acquired every year for research purposes. Much of this research is seriously detrimental to the welfare of these animals, causing pain, distress, injury, or death. Ethical controversies that have arisen over animal research, examining closely the complex scientific, philosophical, moral, and legal issues involved. Animal research has had a vital role in many scientific and medical advances of the past century and continues to aid our understanding of various diseases. Throughout the world, people enjoy a better quality of life because of these advances, and the subsequent development of new medicines and treatments all made possible by animal research. The use of animals in research can be ethically and morally justified. The benefits of animal research have been enormous and it would have severe consequences for public health and medical research if it were abandoned. However, the use of animals in scientific and medical research has been a subject of heated debate for many years in the UK. Opponents to any kind of animal research including both animal-rights extremists and anti-vivisectionist groups believe that animal experimentation is cruel and unnecessary, regardless of its purpose or benefit. There is no middle ground for these groups; they want the immediate and total abolition of all animal research. If they succeed, it would have enormous and severe consequences for scientific research.

No responsible scientist wants to use animals or cause them unnecessary suffering if it can be avoided, and therefore scientists accept controls on the use of animals in research. More generally, the bioscience community accepts that animals should be used for research only within an ethical framework. The UK has gone further than any other country to write such an ethical framework into law by implementing the Animals (Scientific Procedures) Act 1986. The Act requires that proposals for research involving the use of animals must be fully assessed in terms of any harm to the animals. This involves detailed examination of the particular procedures and experiments, and the numbers and types of animal used. These are then weighed against the potential benefits of the project. This cost-benefit analysis is almost unique to UK animal research legislation; only German law has a similar requirement. In addition, the UK government introduced in 1998 further 'local' controls that is, an Ethical Review Process at research institutions which promote good animal welfare and humane science by ensuring that the use of animals at the designated establishment is justified. The aims of this additional review process are: to provide independent ethical advice, particularly with respect to applications for project licences, and standards of animal care and welfare; to provide support to licensees regarding animal welfare and ethical issues; and to promote ethical analysis to increase awareness of animal welfare issues and to develop initiatives for the widest possible application of the replacement, reduction and refinement of the use of animals in research.

### **Animals in sports, companionship, leisure and fashion:**

Animals in sport, companionship, leisure and fashion are all very important aspects of human association with animals. However, none of these is free of ethical implication. Much of the debate centres on the extent of the exploitation of animals. Some people argue the specially bred animals enjoy what people get them to do, but others might say that the animals have no choice. The horse, throughout history, has held a particularly important place in people's lives, and since the industrial revolution, sport has taken the place of work for the horse. The Grand National, held every spring at Aintree, near Liverpool, is a famously tough horse race: a steeplechase, over four miles long with over 30 large fences to jump. Each year it attracts protesters claiming that it is cruel. Racehorses and other competition horses such as show jumpers and eventers are highly bred and rigorously trained to peak fitness. They can very easily suffer injuries in their sports, and often these injuries are difficult or impossible to treat. Sometimes it is economical to try to save a horse for breeding, but generally if the injury is severe, owners will cut their losses and have the animal destroyed (i.e. shot). Animal protection groups see this as a form of cruelty that should be stopped. They often organise protests at race and other equestrian meetings.

Pets, such as dogs, cats and caged birds, come into a similar moral category to the horse, although perhaps the physical strains that people put upon them many not always be so great. Ethical questions have been raised about certain breeding programmes to produce breed characteristics for people's aesthetic satisfaction. For example, the English bulldog has become so refined by selective breeding that it has difficulty in breathing and giving birth naturally. For some people, companion animals such as dogs and cats, have the status of children or friends. As such, if they are kept in the home, owners have the moral obligation to look after them. But sometimes people may go too far in this direction and the animal may actually be harmed, for example when it is excessively pampered. Some people believe that pampering pets is a form of cruelty. In some cases, where

their health is affected, such as happens when an animal is overfed, this may well be true. But subjecting them to for instance beauty treatments is more difficult because many pets may enjoy this sort of attention. However there is no doubt that this constitutes a subversion of their natural behaviour.

Throughout history, fur has been seen as a luxury item of clothing, conferring high status on its wearer. Opponents of the fur trade have engaged in direct action for many years, and have had a high level of publicity. This has meant that fur has become less fashionable since people's awareness of animal welfare and conservation issues has been raised. Nevertheless, although the big cats such as leopard and jaguar are protected, there is still a demand for spotted cat skins for the fashion trade. In the USA for example thousands of wild lynx and bobcat are trapped for their fur each year. Fur farms are now largely outlawed in the UK. Originally imported from North America in the 1920s, the mink was bred for fur. Some mink escaped and others were released by animal rights activists and they soon spread rapidly throughout most areas of the UK. The mink is aggressive and powerful for its size. Adult males average 1.2 kg and about 600mm from the nose to the tip of the tail. Females are only half this weight and about 500mm in length. Mink are mainly nocturnal, usually live near water and prefer areas of thick bank-side vegetation. They can run, climb trees, burrow underground and swim and usually prey on the vulnerable; fish at spawning time, birds at nesting time and fledglings, as well as poultry. Mink are primarily responsible for the decline of our native water vole. An adult breeding female will make up to 1,000 kills every year.

### **Animals for food and draughting:**

Keeping the balance of interests between animals, the environment, the farmer and the retail chain is among the most complex of current political challenges. The well-being of consumers, farmers and animals is dependent upon a balance of autonomy and justice. This balancing act is fraught with ethical dilemmas. For farmers, their well-being depends upon whether they have a satisfactory income and whether their farms thrive. This will be achieved by a balance of how free they are to manage their land, crops and animals (autonomy) and how fair they can be in selling on their produce (justice). For the animals, their well-being will depend upon the care given them. This will determine the extent to which they can engage in their natural behaviour and how they are respected for their intrinsic value. It is the interests of the consumers that cause the ethical problems. For example, bacon is cheaper for consumers (in the interests of their well-being and autonomy) if the breeding sow is kept tethered in a stall to prevent her from rolling onto the piglets and crushing them. However this compromises the well-being and autonomy of the sow and the fairness for her.

Draft animals are the beast of burden. They are trained to perform task such as perform light harness work and become a part of rural development-agriculture. Draught animal power is a critical input to increased productivity of land and labour and therefore to sustainable agricultural production in low input systems in West Africa humid and subhumid zones. In these mixed farming systems, farmers make use of trypanotolerant N'Dama cattle to supply draught force for ploughing and weeding heavy soils and for transport. There is recently a growing southward movement of horses and donkeys into these areas and this is going to lead to major changes in the subhumid zones mixed crop-livestock production systems systems. However, optimum exploitation of trypanotolerant cattle and equines for draught purposes is constrained by health, feeding and management factors.

### **A code of ethics for biologist:**

- investigators will promote and follow practices that enhance the public interest or well-being;
- investigators will use funds appropriately in the pursuit of their research;
- investigators will follow government and institutional requirements regulating research such as those ensuring the welfare of human subjects, the comfort and humane treatment of animal subjects and the protection of the environment;
- investigators will report research findings resulting from public funding in a full, open, and timely fashion to the scientific community; and
- investigators will share unique propagative materials developed through publicly-funded research with other scientists in a reasonable fashion.
- investigators will have actually carried out experiments as reported;

- investigators will represent their best understanding of their work in their descriptions and analyses of it;
- investigators will accurately describe methods used in experiments;
- investigators will not report the work of others as if it were their own;
- investigators in their publications will adequately summarize previous relevant work;
- investigators acting as reviewers will treat submitted manuscripts and grant applications confidentially and avoid inappropriate use; and
- investigators will disclose financial and other interests that might present a conflict-of-interest in their various activities such as reporting research results, serving as reviewers, and mentoring students.
- investigators serving as mentors will provide training and experience to advance the trainees' scientific skills and knowledge of ethical research practices;
- investigators will provide appropriate help in advancing the careers of the trainees;
- investigators will recognize research contributions of the trainees appropriately;
- investigators will encourage and support the publication of results of trainees' research in a timely fashion without undisclosed limitations; and
- investigators will create and maintain a working environment that encourages cultural diversity.

### **Fundamental elements of the patient-physician relationship:**

From ancient times, physicians have recognized that the health and well-being of patients depends upon a collaborative effort between physician and patient. Patients share with physicians the responsibility for their own health care. The patient-physician relationship is of greatest benefit to patients when they bring medical problems to the attention of their physicians in a timely fashion, provide information about their medical condition to the best of their ability, and work with their physicians in a mutually respectful alliance. Physicians can best contribute to this alliance by serving as their patients' advocate and by fostering these rights:

(1) The patient has the right to receive information from physicians and to discuss the benefits, risks, and costs of appropriate treatment alternatives. Patients should receive guidance from their physicians as to the optimal course of action. Patients are also entitled to obtain copies or summaries of their medical records, to have their questions answered, to be advised of potential conflicts of interest that their physicians might have, and to receive independent professional opinions.

(2) The patient has the right to make decisions regarding the health care that is recommended by his or her physician. Accordingly, patients may accept or refuse any recommended medical treatment.

(3) The patient has the right to courtesy, respect, dignity, responsiveness, and timely attention to his or her needs.

(4) The patient has the right to confidentiality. The physician should not reveal confidential communications or information without the consent of the patient, unless provided for by law or by the need to protect the welfare of the individual or the public interest.

(5) The patient has the right to continuity of health care. The physician has an obligation to cooperate in the coordination of medically indicated care with other health care providers treating the patient. The physician may not discontinue treatment of a patient as long as further treatment is medically indicated, without giving the patient reasonable assistance and sufficient opportunity to make alternative arrangements for care.

(6) The patient has a basic right to have available adequate health care. Physicians, along with the rest of society, should continue to work toward this goal. Fulfillment of this right is dependent on society providing resources so that no patient is deprived of necessary care because of an inability to pay for the care. Physicians should continue their traditional assumption of a part of the responsibility for the medical care of those who cannot afford essential health care. Physicians should advocate for patients in dealing with third parties when appropriate.

### **Codes for nurses:**

The nurse, in all professional relationships, practices with compassion and respect for the inherent dignity, worth, and uniqueness of every individual, unrestricted by considerations of social or economic status, personal attributes, or the nature of health problems.

- The nurse's primary commitment is to the patient, whether an individual, family, group, or community.
- The nurse promotes, advocates for, and strives to protect the health, safety, and rights of the patient.
- The nurse is responsible and accountable for individual nursing practice and determines the appropriate delegation of tasks consistent with the nurse's obligation to provide optimum patient care.
- The nurse owes the same duties to self as to others, including the responsibility to preserve integrity and safety, to maintain competence, and to continue personal and professional growth.
- The nurse participates in establishing, maintaining, and improving health care environments and conditions of employment conducive to the provision of quality health care and consistent with the values of the profession through individual and collective action.
- The nurse participates in the advancement of the profession through contributions to practice, education, administration, and knowledge development.
- The nurse collaborates with other health professionals and the public in promoting community, national and international efforts to meet health needs.
- The profession of nursing values, for maintaining the integrity of the profession and its practice, and for shaping social policy.

### **Patient's right and responsibilities:**

#### It is your responsibility to:

- Give correct and complete information about your health status and health history.
- Ask questions if you do not understand information or instructions.
- Inform your caregivers if you do not intend to or cannot follow the treatment plan.
- Accept health consequences that may occur if you decide to refuse treatment or instructions.
- Cooperate with your caregivers.
- Respect the rights and property of other patients.
- Tell your caregivers of any medications you brought from home.
- Report any changes in your health status to your caregivers.

#### You have the right to:

##### Respect and Privacy

- Respect in a caring and safe environment
- Personal privacy and confidentiality of your health information

##### Quality Care

- Proper evaluation and treatment
- Proper pain assessment and pain management
- Be free from restraints, except when needed to protect you or others from harm.
- Be free from abuse.
- Have access to protective services.
- Spiritual services upon request
- Have your concerns heard and resolved when possible.

##### Information & Communication

- Know the names and roles of those caring for you.
- Communicate with your caregivers in a language or method you can understand.
- Have your personal physician and a person of your choice notified when you are admitted to the hospital.
- Communicate with people outside the hospital by way of visitors, phone and mail, except when doing so would interfere with your care. Any restrictions will be explained to you.
- Be informed about your health status, recommended treatments, options, risks and benefits.
- Information about the costs of your care and payment methods.

- Review and receive a copy of your medical record, subject to state law and hospital policy.

#### Make Decisions

- Be involved with your care through discussions with your caregivers.
- Be informed of benefits and risks of your treatment options and agree to or refuse a course of action.
- Designate a support person (or persons) of your choosing to be involved in your care when appropriate. You may restrict access of your support person or visitors at any time. University of Utah Hospitals and Clinics will not restrict your support person(s) or visitor based upon their race, color, culture, language, ethnicity, religion, sex, sexual orientation, gender identity or expression, socioeconomic status, age, national origin, physical or mental disability, and/or veteran status.
- Direct your care through an Advance Directive. Advance Directives are legal forms which state your choices about the care you want to receive in serious health situations. Advance Directives are also used to name someone to make decisions for you if you cannot speak for yourself. At your request, we will help you create an Advance Directive.
- Request a discharge plan evaluation. A designated support person (or persons) acting on your behalf can also request a discharge plan evaluation.
- Choose whether or not to take part in research studies and to have studies explained to you before you decide. Other care will continue regardless of your decision to take part in research studies.
- Seek an alternate doctor or ask for a second opinion.

#### **Truth telling and the management of bad news:**

Number of studies has demonstrated that patients do want their physicians to tell them the truth about diagnosis, prognosis, and therapy. For instance, 90% of patients surveyed said they would want to be told of a diagnosis of cancer or Alzheimer's disease. Similarly, a number of studies of physician attitudes reveal support for truthful disclosure. For example, whereas in 1961 only 10% of physicians surveyed believed it was correct to tell a patient of a fatal cancer diagnosis, by 1979 97% felt that such disclosure was correct. In addition to fostering trust and demonstrating respect, giving patients truthful information helps them to become informed participants in important health care decision. Thus, patients should be told all relevant aspects of their illness, including the nature of the illness itself, expected outcomes with a reasonable range of treatment alternatives, risks and benefits of treatment, and other information deemed relevant to that patient's personal values and needs. Treatment alternatives that are not medically indicated or appropriate need not be revealed. Facts that are not important to the patient's ability to be an informed participant in decision making, such as results of specific lab tests, need not be told to the patient. Also, complete and truthful disclosure need not be brutal; appropriate sensitivity to the patient's ability to digest complicated or bad news is important.

There are many physicians who worry about the harmful effects of disclosing too much information to patients. Assuming that such disclosure is done with appropriate sensitivity and tact, there is little empirical evidence to support such a fear. If the physician has some compelling reason to think that disclosure would create a real and predictable harmful effect on the patient, it may be justified to withhold truthful information. Often families will ask the physician to withhold a terminal or serious diagnosis or prognosis from the patient. Usually, the family's motive is laudable; they want to spare their loved one the potentially painful experience of hearing difficult or painful facts. These fears are usually unfounded, and a thoughtful discussion with family members, for instance reassuring them that disclosure will be done sensitively, will help allay these concerns. In unusual situations, family members may reveal something about the patient that causes the physician to worry that truthful disclosure may create real and predictable harm, in which case withholding may be appropriate. These occasions, however, are rare. There are two main situations in which it is justified to withhold the truth from a patient. As noted above, if the physicians has compelling evidence that disclosure will cause real and predictable harm, truthful disclosure may be withheld. Examples might include disclosure that would make a depressed patient actively suicidal. This judgment, often referred to as the "therapeutic privilege," is important but also subject to abuse. Hence it is important to invoke this only in those instances when the harm seems very likely, not merely hypothetical.

The second circumstance is if the patient him- or herself states an informed preference not to be told the truth. Some patients might ask that the physician instead consult family members, for instance. In these cases, it is critical that the patient give thought to the implications of abdicating their role in decision making. If they chose to make an informed decision not to be informed, however, this preference should be respected. Patient with certain religious beliefs or ethnic or cultural backgrounds may have different views on the appropriateness of truthful disclosure.

A placebo is any substance given to a patient with the knowledge that it has no specific clinical effect, yet with the suggestion to the patient that it will provide some benefit. The placebo effect is powerful, in many cases providing measurable improvement in symptoms in 20-30% of patients. In general, the deceptive use of placebos is not ethically justifiable. Specific exceptions should be rare and only considered if the following conditions are present:

- the condition is known to have a high placebo response rate
- the alternatives are ineffective and/or risky
- the patient has a strong need for some prescription

### **Informed consent:**

Informed consent is the process by which the treating health care provider discloses appropriate information to a competent patient so that the patient may make a voluntary choice to accept or refuse treatment. It originates from the legal and ethical right the patient has to direct what happens to her body and from the ethical duty of the physician to involve the patient in her health care.

The most important goal of informed consent is that the patient has an opportunity to be an informed participant in her health care decisions. It is generally accepted that informed consent includes a discussion of the following elements:

- The nature of the decision/procedure
- Reasonable alternatives to the proposed intervention
- The relevant risks, benefits, and uncertainties related to each alternative
- Assessment of patient understanding
- The acceptance of the intervention by the patient

In order for the patient's consent to be valid, she must be considered competent to make the decision at hand and her consent must be voluntary. It is easy for coercive situations to arise in medicine. Patients often feel powerless and vulnerable. To encourage voluntariness, the physician can make clear to the patient that she is participating in a decision-making process, not merely signing a form. With this understanding, the informed consent process should be seen as an invitation for the patient to participate in health care decisions. The physician is also generally obligated to provide a recommendation and share his reasoning process with the patient. Comprehension on the part of the patient is equally as important as the information provided. Consequently, the discussion should be carried on in layperson's terms and the patient's understanding should be assessed along the way.

Basic or simple consent entails letting the patient know what you would like to do; giving basic information about the procedure; and ensuring that the patient assents or consents to the intervention. Assent refers to a patient's willing acceptance of a treatment, intervention, or clinical care. Basic consent is appropriate, for example, when drawing blood in a patient who has given blood before. Sometimes consent to the procedure is implied (e.g. the patient came in to have blood drawn), but an explanation of the elements of the procedure remain necessary. Decisions that merit this sort of basic informed consent process require a low-level of patient involvement because there is a high-level of community consensus that the treatment being offered is the only or best option and/or there is low risk involved in the treatment. If a patient does not consent under the paradigm of basic consent, then a fuller informed consent discussion is warranted. How do you know when you have provided enough information about a proposed intervention? Most of the literature and law in this area suggest one of three approaches:

- **Reasonable physician standard:** *what would a typical physician say about this intervention?* This standard allows the physician to determine what information is appropriate to disclose. However, this standard is often inadequate, since most research shows that the typical physician tells the patient very little. This standard is also generally considered inconsistent with the goals of informed consent, as the focus is on the physician rather than on what the patient needs to know.
- **Reasonable patient standard:** *what would the average patient need to know in order to be an informed participant in the decision?* This standard focuses on considering what a typical patient would need to know in order to understand the decision at hand.
- **Subjective standard:** *what would this particular patient need to know and understand in order to make an informed decision?* This standard is the most challenging to incorporate into practice, since it requires tailoring information to each patient.

Most states have legislation or legal cases that determine the required standard for informed consent. In the state of Washington, we use the "reasonable patient standard." The best approach to the question of how much information is enough is one that meets both your professional obligation to provide the best care and respects the patient as a person, with the right to a voice in health care decisions. All health care interventions require some kind of consent by the patient, following a discussion of the procedure with a health care provider. Patients fill out a general consent form when they are admitted or receive treatment from a health care institution. Most health care institutions, including UWMC, Harborview, and VAMC also have policies that state which health interventions require a signed consent form. For example, surgery, anesthesia, and other invasive procedures are usually in this category. These signed forms are the culmination of a dialogue required to foster the patient's informed participation in the clinical decision.

For a wide range of decisions, explicit written consent is neither required nor needed, but some meaningful discussion is always needed. For instance, a man contemplating having a prostate-specific antigen screen for prostate cancer should know the relevant arguments for and against this screening test, discussed in lay terms. Exceptions to full informed consent are:

- If the patient does not have decision-making capacity, such as a person with dementia, in which case a proxy, or surrogate decision-maker, must be found.
- A lack of decision-making capacity with inadequate time to find an appropriate proxy without harming the patient, such as a life-threatening emergency where the patient is not conscious
- When the patient has waived consent.
- When a competent patient designates a trusted loved-one to make treatment decisions for him or her. In some cultures, family members make treatment decisions on behalf of their loved-ones. Provided the patient consents to this arrangement and is assured that any questions about his/her medical care will be answered, the physician may seek consent from a family member in lieu of the patient.

In most cases, it is clear whether or not patients have capacity to make their own decisions. Occasionally, it is not so clear. Patients are under an unusual amount of stress during illness and can experience anxiety, fear, and depression. The stress associated with illness should not necessarily preclude one from participating in one's own care. However, precautions should be taken to ensure the patient does have the capacity to make good decisions. There are several different standards of decision-making capacity. Generally you should assess the patient's ability to:

- Understand his or her situation,
- Understand the risks associated with the decision at hand, and
- Communicate a decision based on that understanding.

When this is unclear, a psychiatric consultation can be helpful. Of course, just because a patient refuses a treatment does not in itself mean the patient is incompetent. Competent patients have the right to refuse treatment, even those treatments that may be life-saving. Treatment refusal may, however, be an indication that it is necessary to pause to discuss further the patient's beliefs and understanding about the decision, as well as your own. A patient's decision-making capacity is variable as their medications or underlying disease processes ebb and flow. You should do what you can to catch a patient in a lucid state - even lightening up on the medications if necessary and safe - in order to include her in the decision making process. Delirious patients have waxing and waning abilities to understand information. However, if a careful assessment is done and

documented at each contact, and during lucid periods the patient consistently and persistently makes the same decision over time, this may constitute adequate decisional capacity for the question at hand. If the patient is determined to be incapacitated or incompetent to make health care decisions, a surrogate decision maker must speak for her. There is a specific hierarchy of appropriate decision makers defined by state law. If no appropriate surrogate decision maker is available, the physicians are expected to act in the best interest of the patient until a surrogate is found or appointed. In rare circumstances, when no surrogate can be identified, a guardian ad litem may have to be appointed by the court. Confer with social work and risk management if you have trouble finding a legal surrogate for the patient.

Children do not have the decision-making capacity to provide informed consent. Since consent, by definition, is given for an intervention for oneself, parents cannot provide informed consent on behalf of their children. Instead they can provide informed permission for treatment. For older children and adolescents, assent should always be sought in addition to the authorization of legal surrogates. Adolescents and mature minors are legally and ethically authorized to provide informed consent if they are emancipated, and in many states, including Washington, they may provide consent for matters regarding sexual and reproductive health, mental health, and substance abuse. See your state's legislation regarding mature minors and consent laws. The primary responsibility of the physician is the well-being of the child. Therefore, if the parental decision places the child at risk of harm then further action may be indicated. When there are differences in opinion between the parents and physicians that cannot be resolved ethics consultation may be pursued, and legal avenues may be pursued when all other means have failed. Children should be included in decision-making at a developmentally appropriate level and assent should be sought when possible. The patient's consent should only be "presumed," rather than obtained, in emergency situations when the patient is unconscious or incompetent and no surrogate decision maker is available, and the emergency interventions will prevent death or disability. In general, the patient's presence in the hospital ward, ICU or clinic does not represent implied consent to all treatment and procedures. The patient's wishes and values may be quite different from the values of the physician. While the principle of respect for person obligates you to do your best to include the patient in the health care decisions that affect her life and body, the principle of beneficence may require you to act on the patient's behalf when her life is at stake.

#### **Patient self-determination and advance directives:**

The 1990 Patient Self-Determination Act (PSDA) encourages everyone to decide now about the types and extent of medical care they want to accept or refuse if they become unable to make those decisions due to illness. The PSDA requires all health care agencies to recognize the living will and durable power of attorney for health care. The Act applies to hospitals, long-term care facilities, and home health agencies that get Medicare and Medicaid reimbursement. Under the PSDA, health care agencies must ask you whether you have an advance directive. They also must give you information about your rights under state law.

Everyone getting medical care in hospitals or extended care facilities (nursing homes), enrolling in HMOs, and entering into hospice or home care agreements must be given certain information in writing. This must include information on your state's laws about your rights to make decisions about medical care, such as your right to accept or refuse medical or surgical treatment. You are also entitled to receive information about your right to create an advance directive. They may even offer simple advance directive forms for you to use. But it's not a good idea to wait until you are in the hospital to fill out a form. Chances are you won't be feeling well, and you might not be able to complete the form when you are admitted.

#### **The management and confidential information:**

A duty of confidence arises when one person discloses information to another in circumstances where it is reasonable to expect that the information will be held in confidence. It is a legal obligation that is derived from case law. It is a requirement established within professional codes of conduct. It must be included within NHS employment contracts as a specific requirement linked to disciplinary procedures. Patients entrust us with, or allow us to gather, sensitive information relating to their health and other matters as part of their seeking treatment. They do so in confidence and they have the legitimate expectation that staff will respect their privacy and act appropriately. In some circumstances patients may lack the competence to extend this trust, or may be unconscious, but this does not diminish the duty of confidence. It is essential, if the legal requirements are to be met and the trust of patients is to be retained, that the NHS provides, and is seen to provide, a confidential service. What this entails is described in more detail in subsequent sections of this document, but a key guiding principle is that a patient's health records are made by the health service to support that patient's healthcare. One

consequence of this is that information that can identify individual patients, must not be used or disclosed for purposes other than healthcare without the individual's explicit consent, some other legal basis, or where there is a robust public interest or legal justification to do so. In contrast, anonymised information is not confidential and may be used with relatively few constraints. It is a local technical entity in charge of organizing the regulations on the processing, use, custody, preservation and confirmation of clinical records, in accordance with the national and institutional regulations. It is composed of representatives from each of the following services: Medical Directorate, Nursing Directorate, Legal Advice, Medical Records, Admission and Hospital Quality Unit. Each of the patients who receive attention at our hospital has a medical record, in order to secure the integration and continuity of the attention. Being such record a legal medical document, we seek at all times to oversee and exercise control over the quality of the clinical information, and the protection of the confidentiality we provide to the users. The content of the information of the medical record is confidential, in accordance with the regulations in force in the country, and we see to compliance with such confidential status by means of the enforcement of hospital protocols, regulations and policies.

It is extremely important that patients are made aware of information disclosures that must take place in order to provide them with high quality care. In particular, clinical governance and clinical audits, which are wholly proper components of healthcare provision, might not be obvious to patients and should be drawn to their attention. Similarly, whilst patients may understand that information needs to be shared between members of care teams and between different organisations involved in healthcare provision, this may not be the case and the efforts made to inform them should reflect the breadth of the required disclosure. Many current uses of confidential patient information do not contribute to or support the healthcare that a patient receives. Very often, these other uses are extremely important and provide benefits to society e.g. medical research, protecting the health of the public, health service management and financial audit. However, they are not directly associated with the healthcare that patients receive and we cannot assume that patients who seek healthcare are content for their information to be used in these ways.

Patients generally have the right to object to the use and disclosure of confidential information that identifies them, and need to be made aware of this right. Sometimes, if patients choose to prohibit information being disclosed to other health professionals involved in providing care, it might mean that the care that can be provided is limited and, in extremely rare circumstances, that it is not possible to offer certain treatment options. Patients must be informed if their decisions about disclosure have implications for the provision of care or treatment. Clinicians cannot usually treat patients safely, nor provide continuity of care, without having relevant information about a patient's condition and medical history. Patients have been informed of the use and disclosure of their information associated with their healthcare, about the choices that they have and the implications of choosing to limit how information may be used or shared; then explicit consent is not usually required for information disclosures needed to provide that healthcare. Even so, opportunities to check that patients understand what may happen and are content should be taken. Where the purpose is not directly concerned with the healthcare of a patient however, it would be wrong to assume consent. Additional efforts to gain consent are required or alternative approaches that do not rely on identifiable information will need to be developed. There are situations where consent cannot be obtained for the use or disclosure of patient identifiable information, yet the public good of this use outweighs issues of privacy.

### **The problem of moral justification:**

Ethical debates involve moral facts in several ways. One dispute concerns the accounts of truth and falsity for moral judgments. Radical emotivism may be used as a point of departure. On this view, value judgments express and evoke various moral sentiments. Since no such judgment expresses a proposition capable of being true or false, none has any factual or cognitive meaning. The attribution of truth or falsity to value judgments makes no sense? This radical view is unconvincing. For one, it stands in too sharp a contrast with the standard linguistic practice of attributing truth and falsity to value claims. This practice cannot be simply dismissed as odd or unintelligible. The real challenge for a non-realist is to conform to this practice and yet be able to explain why, although there are no moral facts, the predicates 'true' and 'false' are still applicable to value judgments. Moderate emotivism, developed by Charles Stevenson, is an attempt to meet this challenge. Stevenson acknowledges that emotive meaning is central for value judgments. On his account, to say, e.g., that something is good is to express a feeling of moral approval for something and to evoke a similar feeling on the part of hearers. Such judgments also have, however, some factual or cognitive meaning. On his first pattern of analysis, the judgment 'X is good' expresses the proposition that its utterer feels moral approval for X. On the second

pattern of analysis, the cognitive meaning of this judgment is that X has certain factual qualities. According to Stevenson, to predicate the truth of moral judgments is to say that the propositions constituting the cognitive meaning of these judgments are true. Stevenson supplements this account with another, complementary view. On this view, the predication of truth of a moral judgment has little to do with the propositions expressed by this judgment. This predication indicates rather an agreement with the judgment's emotive meaning; i.e., an agreement with the attitude or feeling expressed by this judgment. A similar view is developed further in *Facts and Values*. Stevenson submits there that the predicates 'true' and 'false' are governed by the following purely syntactical rule: sentences of the form 'It is true/false that p' are linguistically permissible if and only if 'p' is replaced by a sentence in the declarative mood. It must be replaced by some well-formed declarative sentence, it does not matter whether this sentence has a cognitive or non-cognitive meaning. It may express 'a belief or an attitude or both or neither'. 'It is true that p' has the same meaning as 'p', and 'It is false that p' has the same meaning as the negation of 'p'.

Moral judgments express, primarily, pro and con attitudes (and, only secondarily, beliefs). Hence, when 'p' is substituted by a moral Sentence, then the judgment 'It is true/false that p' expresses a pro or con attitude, rather than a belief. As Stevenson observes: When Mr. A says "Jones ought not to have done it," and Mr. B replies, "that is true"... he too has said, in abbreviated form, the equivalent of "Jones ought not to have done it." His "that is true"... expresses an attitude that is in agreement with A's. The extent of their agreement in belief will usually not be evident until they go on to give reasons for their judgments. Most irrealist accounts of truth and falsity for moral judgments have their seeds in this view. For example, having adopted a disquotational account of truth, J.J.C. Smart maintains that 'ought' sentences can be true... 'Smith ought to be kind to his grandmother' is true if and only if Smith ought to be kind to his grandmother, no less than 'snow is white' is true if and only if snow is white. Smart denies, however, that ethical sentences express factual beliefs and that attributing truth to such judgments implies that they are 'factual'. He maintains also that 'so-called differences of "ethical belief"' are better described as differences of ultimate attitude or desire'. Simon Blackburn's projectivism is in the same vein. Blackburn maintains that his quasi-realist can mimic the realist in an impressive number of ways. He can legitimately say that moral judgments are true, that there are real values, that some values are mind independent, that the cognition of values is possible, that we can have moral knowledge, etc. If quasi-realism can achieve so much, what is the difference between this view and realism? According to Blackburn, moral judgments reflect the projections of our sentiments onto the world. Consequently: The difference in the theory of the correspondence conditionals. There is no causal story, parallel to that which must be given to justify ourselves as good signallers of cats, to justify us as good signallers of virtues, R.M. Hare is a notable exception. Hare links the attribution of truth and falsity to evaluative judgments with the descriptive elements involved in their meaning.

Blackburn maintains, nevertheless, that because values are 'the children, and not the parents, of our sentiments', there is no need for any analogous theory of the correspondence conditionals: 'its absence is no obstacle to the regulative use of truth in moral contexts'. According to most non-realists, to say that a moral judgment is true is to express an agreement with the attitude, sentiment, or feeling expressed by this judgment. The predication of truth is not supposed to imply that there are any objective moral facts 'out there'. Critics of non-realism find such views too impoverished. Consequently, they typically assume that some moral judgments are objectively true in the sense that they correspond to objective moral facts. Before we move on, we need to address one closely related controversy. This controversy does not concern the predication of truth of moral judgments but rather certain logical constraints involved in moral reasoning. In particular, moral arguments are supposed to be valid and moral views consistent. Some philosophers have argued that non-realists have no grounds for upholding these standards. As Lars Bergstrom summarized the point: it would be pointless or irrational to engage in such a practice of eliminating inconsistencies among one's moral views unless one believes that moral realism is true... For example, Blackburn gives a convincing proposal. Its gist is that inconsistent moral systems would require us to act inconsistently, and that it is irrational to take a pro attitude with respect to any system which is known to impose on us requirements impossible to fulfil. Thus, if the non-realist can account for the constraints of consistency and validity, these constraints do not support ethical realism and moral facts. Non-realists are also criticized on the ground that they allow too limited a role to epistemic considerations. Epistemic rationality will, of course, play some role in their systems. For example, before moral questions can be answered they must be understood; learning to understand moral discourse is a matter of epistemic rationality. In addition, it may be irrational to adopt a system which is known to be internally inconsistent; discovering such inconsistencies is

also an epistemic matter. Finally, if a person does not understand the consequences of acting in accordance with a given principle, then choosing so to act may be irrational. It seems irrational, in a sense akin to a prudential sense of rationality, to adopt a system such that acting in accordance with it would systematically frustrate our basic interests and needs. Moral requirements should be in equilibrium with our natural tendencies. Again, learning the consequences of acting on a given moral principle is a matter of epistemic rationality: Suppose, however, that a person has avoided all the obvious sources of irrationality mentioned above; he understands the meaning of moral terms, his moral system is internally coherent, he does not ignore any relevant (non-moral) facts, and his moral views are in harmony with basic human needs. Could we still say that his decision about fundamental principles is irrational? Non-realists must deny that we could. For choosing the most fundamental moral principles is for them a matter of decision rather than discovery. In effect, such decisions are rational just in case they are informed by knowledge of logic and non-moral facts. No additional epistemic constraints limit us. The moral choice is never made by first finding out what ought to be done (or what has value) and then choosing accordingly. Again, the existence of moral facts seems to provide another possibility. If there are such facts, then we could point to them, saying: this is why your action is morally wrong; this is why this person is morally evil, etc. Thus, moral realists seem to believe that because we have sufficient epistemic access to moral facts, our moral judgments are epistemically justified.

The existence of moral facts is supposed to yield not only the justification of moral claims, but also moral knowledge and, as an effect, rational convergence of conflicting moral views. Non-realists have been criticized for their inability to resolve disagreements that involve the most fundamental moral convictions. According to Sturgeon, for example, non-cognitivists are unable to settle any moral issue objectively. The justification they can provide 'never amounts to the kind of objective warrant one might have on a subject concerning which knowledge is possible'. To test the merits of conflicting metaethical views, imagine a disagreement that cannot be easily removed by the means equally available to both realists and non-realists. Let this disagreement involve a fanatical, albeit consistent, Nazi who agrees with us on all relevant non-moral facts, and yet maintains that all Jews ought to be exterminated. Ex hypothesis, the imaginary Nazi does not want to exterminate Jews simply because he is ill-informed, or because he does not yet fully apprehend all the relevant facts (e.g., how much suffering it would cause, what kind of people Jews are), etc. A disagreement with a confused person would not constitute any problem for non-realists, for it could be removed without engaging in any moral debate. It is harder to see, however, how prescriptivists like Hare, or emotivists like Stevenson or Blackburn, could show that there is anything wrong about the consistent and well-informed view we have just imagined. And, again, it may seem that realists have in this respect an advantage. Philippa Foot, for example, thinks that conceptual connections between certain statements of fact and moral claims suffice to show that the Nazi's moral beliefs are necessarily and evidently false. The human tragedies caused by the extermination of Jews show conclusively that such extermination ought not to be attempted. According to Foot, the judgment that the Nazis' treatment of the Jews is morally indefensible follows from non-moral facts taken together with the concept of morality. Few philosophers agree with Foot that there are the logical and conceptual connections she postulates. Yet most realists seem to think that moral facts are sufficiently epistemically accessible to normal, reflective, intelligent people that such individuals can at least make progress toward finding out, i.e., coming to know, the answers to ethical questions and disputes; such knowledge should lead to a rational convergence of conflicting moral opinions. At the very least, moral facts should help us to refute a fanatical, albeit consistent, Nazi. The principles are generated when ethical problems are treated as primarily metaphysical or epistemic issues. But ethical disputes also involve attitudinal differences. To see whether this factor imposes any additional constraint on moral theories, let us assume that moral judgments are essentially action-guiding? We might now postulate that an adequate ethical theory should provide us with the means to show that moral judgments which are essentially action-guiding are objective in the following sense: in cases of fundamental moral disagreements, there are sufficient and necessary reasons for adopting only one from a set of conflicting judgments, and for rejecting others; in this sense, only some attitudes are morally correct, while all conflicting attitudes are morally incorrect.

### **Maternal-fetal relationship and rights:**

The maternal-fetal relationship is the subject of intense public policy debates. Lisa Harris and Lynn Paltrow report on courts' opinions regarding the prosecution of pregnant women for potential fetal harm. Nathan Stormer explores how contemporary biomedical images of the fetus are changing public perception of the pregnant body and fetus. Amy Salisbury and colleagues describe how researchers are attempting to measure maternal-fetal

attachment and its possible implications for fetal and maternal health during pregnancy. Although fundamental and seemingly unalterable, the definition of the maternal-fetal relationship is undergoing a rapid evolution of context, in part due to advances in imaging, prenatal diagnostics, genetic screening, and fetal surgery. While the formal principles of autonomy and beneficence provide an initial point from which to analyze the sometimes conflicting needs of the pregnant woman and her fetus, the maternal-fetal relationship is becoming too complex to rely on simple algorithms. As medical technology and innovation advance, and as cultural and political dialogues continue to influence the patient-physician encounter, physicians' knowledge of and participation in ethical dialogue on the maternal-fetal relationship will continue to be an increasingly important part of obstetric care.

Consider the following scenario: A thirty-nine year old attorney, about eight months into her first pregnancy, after reading everything that she can find about pregnancy, labor and delivery, requests that she have a cesarian section two weeks prior to her due date. She states that the discomfort of pregnancy and the risks of labor and delivery, in her opinion, are outweighed by the benefits and low risk of morbidity of cesarian section, for both her and the fetus. She argues that if a patient with a previous cesarian section is given the option of trial of labor versus an operative delivery, then she should have the same option, being a fully informed and competent adult. She asks, "if a competent adult has the legal right to refuse life saving care, why can't I request a cesarian section?". A purely legal analysis of this scenario may lead to the same conclusion as reached by the above patient. In contrast, a medical-legal risk-benefit analysis may indicate that the patient with a previous cesarian section has incurred specific risks and personal experiences which can be distinguished from this patient. Thus, the offer of a repeat cesarian section is part of the standard of care that an obstetrician has a duty to provide to a patient who has undergone a prior cesarian section. The risk-benefit analysis offered by the woman in this scenario does not really apply to her situation. Simply put, an elective cesarian section, as requested by the patient, is an unindicated procedure which the doctor has no duty to perform. However, an analysis from the perspective of the physician-patient relationship may lead to an entirely different resolution. A frank discussion between the doctor and patient may reveal that she was quite frightened of the pain of labor and the possibility of having the baby damaged as a result of labor. This type of open-ended dialogue may uncover that the patient's experience as a personal injury attorney was at the root of her fear. The therapeutic alliance engendered in the physician patient relationship would allow for a more compassionate discussion of her fears and may eventually lead to a normal labor and delivery. There are two points to be garnered from this scenario. First, where there is no duty for a physician to provide an unindicated procedure, there does not appear to be any inherent right of the patient to demand such care. Hence, Holmes' axiom that duties precede rights holds true. Second, the unique nature of the physician-patient relationship allows for a resolution of problems that would not flow from a purely legal or a medical legal analysis. This section will illustrate these points as they occur in the area of reproductive health care.

### **Refusal of treatment:**

It may be tempting for physicians to override the patient's refusal of treatment due to the competing ethical principle of beneficence, or the physician's duty to protect the patient's life. However, physicians must ultimately accept the patient's decision because patients have the right to decline treatment due to their autonomy, or freedom to decide. It would be unacceptable and even inhumane if patients were physically and forcefully treated against their will. A patient who refuses treatment must first be well-informed to make the decision, possess proper decision-making capacity to understand the consequences of refusal, and make the decision without manipulation or coercion by outsiders. Patients can refuse all types, even ones that are lifesaving with minimal side-effects. For example, Jehovah's Witnesses possess the right to refuse blood transfusions even though there is minimal risk involved. Other treatments include, but are not limited to surgery, mechanical ventilation, renal dialysis, antibiotics, cardiopulmonary resuscitation, and tube feedings. Patients do not have to possess a terminal illness to refuse treatment—they can be otherwise perfectly healthy. Exceptions may arise if the physician must protect a vulnerable third party. In this case, the duty to protect a third party from harm overrides the duty to accept the patient's refusal of treatment. For example, a patient with an infectious disease, such as tuberculosis, may refuse treatment; as a result, the physician must either treat or quarantine the patient until others are no longer at risk. Another example arises in the situation of a pregnant woman, in which case there may be competing interests between the mother and the fetus. A pregnant woman with syphilis may be forced to undergo Caesarean section in some cases in order to prevent transmission of the disease to the fetus. However, courts have recently begun to overturn these rulings due to the duty to respect the female's autonomy and bodily integrity. Also, parents of a Jehovah's Witness minor cannot refuse blood transfusions for their child; in this case, the course assumes responsibility for the child's safety and

overrides the parents' refusal to treat. Overall, it is helpful to keep in mind that physicians can try to convince patients against refusing treatment, but the decision ultimately lies in the hands of the patient.

### **Introduction to ethical analysis of genetic modification:**

Genetic engineering, or genetic modification, uses a variety of tools and techniques from biotechnology and bioengineering to modify an organism's genetic makeup. Transgenics refers to those specific genetic engineering processes that remove genetic material from one species of plant or animal and add it to a different species. Due to the high similarity in genetic sequences for proteins among species, transgenic organisms are able to effectively assimilate and express these trans-genes. The process of creating a transgene begins by isolating the gene of interest from a donor organism or selecting for purchase any of the thousands of known genes from massive online genomic databases. Once the gene is obtained, it is usually altered so it can function more effectively or be expressed more readily in the host organism. That gene is then combined with other genetic elements and introduced into a second organism (the host), at which point it's known as a transgene. A transgenic organism is further defined as one that contains a transgene introduced by technological methods rather than through selective breeding. Hybrids are transgenic organisms created when reproductive cells from two species combine to form a single embryo (e.g., a mule is the offspring of a horse and a donkey); on the other hand, chimeras are created by artificially combining genetic material from two organisms into a single species. Transgenic biotechnology presents an exciting range of possibilities, from feeding the hungry to preventing and treating diseases; however, these promises are not without potential peril. Some of the issues that need to be considered are the following:

#### *Social Concerns*

- If the blending of animal and human DNA results, intentionally or not, in chimeric entities possessing degrees of intelligence or sentience never before seen in nonhuman animals, should these entities be given rights and special protections?
- What, if any, social and legal controls or reviews should be placed on such research?
- What unintended personal, social, and cultural consequences could result?
- Who will have access to these technologies and how will scarce resources such as medical advances and novel treatments be allocated?

#### *Extrinsic Concerns*

- What, if any, health risks are associated with transgenics and genetically modified foods?<sup>13</sup>
- Are there long-term effects on the environment when transgenic or genetically modified organisms are released in the field?
- Should research be limited and, if so, how should the limits be decided? How should the limits be enforced nationally and internationally?

#### *Intrinsic Concerns*

- Are there fundamental issues with creating new species?
- Are species boundaries hard or should they be viewed as a continuum? What, if any, consequences are there of blurring species boundaries?
- Are chimeras and transgenics more likely to suffer than traditional organisms?

- Will transgenic interventions in humans create physical or behavioral traits that may or may not be readily distinguished from what is usually perceived to be human?
- What, if any, research in genetic engineering should be considered morally impermissible and banned (e.g., research undertaken for purely offensive military purposes)?
- Will these interventions redefine

Some individuals argue that crossing species boundaries is unnatural, immoral, and in violation of God laws, which presumes that species boundaries are fixed and readily delineated. However, several books and journal articles demonstrate that the concept of fixed species boundaries continues to be a hotly debated topic. Some bioethicists point out that a variety of species concepts exist: biological, morphological, ecological, typological, evolutionary, and phylogenetic to name a few. All of these definitions of what a species is reflect both changing theories and the varying purposes for which individuals conceptualize and utilize different species. If species boundaries are simply a matter of a naming convention, and there are no truly fixed boundaries to cross, then many philosophical objections to transgenics are rendered less problematic. While the morality of crossing species boundaries reflects differing worldviews and is subject to disagreement there are, however, several known risks associated with the transplantation of cells or organs from animals to humans. For example, there is a small but significant risk of the transmission of usually fatal zoonotic diseases, such as bovine spongiform encephalopathy, porcine endogenous retroviruses (PERVs) and Nipah encephalitis. The introduction of these diseases to the human population could have devastating consequences. As a result, the U.S. Food and Drug Administration (FDA) has banned xenotransplantation trials using nonhuman primates until the procedures have been adequately demonstrated to be safe and until ethical issues have been sufficiently publicly discussed. However, with the advent of stem cell tissue engineering and 3-D printing, xenotransplantation may quickly become outmoded, opening the doors to more complex social, ethical, and legal issues and discourses.

In addition to the issue of species boundaries, there are other issues that need to be considered and discussed prior to large-scale acceptance and usage of transgenics and other genetic engineering research, including the risks and benefits of the experimental use of animals; the risk of creating new diseases for which there is no treatment by combining animal DNA or human DNA with plant DNA; the potential long-term risks to the environment; the potential for increased suffering of transgenic organisms. Various bioethicists, environmentalists, and animal rights activists have argued that it is wrong to create animals that would suffer as a result of genetic alteration (for example, a pig with no legs) and that such experimentation should be banned. Several bioethicists have called for a ban on species-altering technologies that would be enforced by an international tribunal. Part of the rationale for this ban is the concern that such technologies could be used to create a slave race that is a race of subhumans that could be exploited. In April 1998, scientists Jeremy Rifkin and Stuart Newman, who are both opposed to genetically modified organisms (GMOs), applied for a patent for a part human and part chimpanzee to intentionally fuel debate on the issues and draw attention to potential abuses. The United States Patent and Trademark Office (USPTO) denied the patent on the grounds that it violated the Thirteenth Amendment of the Constitution of the United States, which explicitly prohibits slavery. Although the USPTO has permitted the extensive patenting of bioengineered life forms, the question that was raised by Newman and Rifkin application is one that will not easily be resolved: What constitutes a person? A genetic definition is not very helpful, given the variability of gene sequences between individuals. A species definition can be controversial, as mentioned earlier. If we look to specific characteristics for a definition, we are faced with the fact that humans share many characteristics with primates and other animals so where do we draw the line? If we create a being that has the ability to speak and perhaps even reason, but looks like a dog or a chimp, should that creation be given all the rights and protection traditionally bestowed upon a person? Some bioethicists argue that the definition of human being should be more expansive and protective, rather than more restrictive. Others argue that more expansive definitions could minimize humanity status and create a financial disincentive to patenting creations that could be of potential use. The question of whether the definition should be more expansive or restrictive will need to be considered as courts, legislatures, and institutions address laws regarding genetic discrimination.

In a similar vein, the medical director of the International Olympic Committee (IOC) has expressed concern that athletes have started employing genetic engineering to get an edge over their competition.<sup>29</sup> If individuals are willing to genetically manipulate their children to make them better athletes, then it is likely individuals will be willing to manipulate their children to better looking, more musically inclined, or whatever else might give them an advantage. Opponents of genetic manipulation argue that, by allowing this, we run the risk of creating a race

of superhumans, changing what it means to be normal and increasing the ever-widening gap between the haves and the have-nots. Proponents of genetic manipulation argue that currently parents can and do give their children advantages by sending them to better schools or giving them growth hormones, and that banning genetic manipulation is a denial of individual liberties. These arguments also reflect the opposing philosophies regarding how scarce resources should be allocated.

### **Genetic modifications and risk factors:**

The most important areas of risks which need to be considered in the use of transgenics are:

1. human health
2. biodiversity
3. animal welfare
4. poor communities

In each of these categories there exists a multiplicity of pathways by which effects could, in principle, be brought about. Rational and responsible assessment of risk requires that the following properties are all considered:

1. source of the DNA of the target gene;
2. source of the non target DNA segments of the construct used;
3. site(s) of incorporation of the transgene within the recipient genome;
4. product of the transgene;
5. interaction of the transgenic product with other molecules in host and consumer;
6. possible molecular changes in transgene product during processing;
7. pleiotropic effects of transgene;
8. tissue specificity of transgenic expression; and
9. numbers of transgenic organisms capable of interacting with natural systems).

The risks to health will depend upon all of the factors listed above. In practical terms the most important of these are likely to be the source of the DNA and the nature of the product. The great majority (98 percent) of dietary DNA is degraded by digestive enzymes relatively quickly but use of viruses (disarmed or otherwise) as vectors, must increase the risk factor significantly as these are organisms which are adapted to integrating into host genomes and some represent risk factors for cancer induction. The work of Zhixong Li *et al.* (2002) who induced leukaemia by using retroviral vectors in making transgenics for a commonly used marker gene in mice and a recent report of leukaemia induction in a child undergoing gene therapy for x-SCID using a retrovirus (Hawkes, 2002) show that this is not a trivial risk. Arguments about risks and benefits attached to this form of gene therapy are current. At the other extreme the use of autotransgenics must be seen as posing a risk which is orders of magnitude lower than that for allotransgenics and probably negligible. The major risk from the production of the transgene will lie in the use of novel proteins or other molecules produced by the transgenic organisms. Either in the native form or, following modifications in the human body, such molecules could be inimical to human health (e.g. through allergies). It would seem sensible to avoid the use of such substances except where strictly necessary and under rigorous control.

Other potential risks may lie in incorporation of transgenic DNA into the genomes of resident gut microflora (though this is likely to be very improbable) or a change in the pathogen spectrum of the transgenic fish leading to it hosting a new pathogen which happens to be also a human pathogen. Maclean and Laight (2000) assessed risks to consumers as "very low". The extent of aquatic diversity is both extremely large and relatively poorly understood. This means that the task of estimating the risks to aquatic biodiversity at all of its levels from the use of GMOs or indeed, any genetically distinctive strain used in aquaculture is monumentally large. Aquaculture has a further problem in that the (almost always unintended) escapes of genetically distinct farmed fish are unpredictable and often large in numbers. Stenquist (1996) in discussing transgenics in open ocean aquaculture, quotes some relevant figures. Thus, 15 percent escapes for Atlantic salmon, escapes of 150 000 salmon and 50 000 trout in Chile and catch statistics for Atlantic salmon off Norway in which 15-20 percent of the fish caught were of farmed origin. In Scotland an escape of 100 000 Atlantic salmon was reported recently. It is clear that escapes of these magnitudes pose considerable problems and it is not surprising that in some parts of Norway fish of farmed origin represent a majority of the animals fished.

The major focus of attention in the literature lies, understandably, upon the effects of escapes upon natural populations of the same species, but we must always bear in mind possible impacts across an assemblage or ecosystem as a whole. The first general point to make is that there is, in principle, no difference between the biodiversity risks from escapes of GMOs and from fish genetically improved in some other way, e.g. by selective breeding or (in some respects) from exotic species. The second general principle is that such genetically improved forms including GMOs, are developed for a specific set of environmental circumstances in which they enjoy an advantage conferred by human decisions. In nature, however, such genetically distinct forms may legitimately be regarded as mutant forms of the wild type. A considerable body of genetical knowledge tells us that the probability of survival of mutant forms is extremely low because they are disadvantaged in viability and/or fertility under natural conditions. Thus, for example, in the genetically distinct farmed Atlantic salmon in Norway the males are very much less successful than wild males in securing mates. However, it must be conceded that in species like salmon where the farmed populations outnumber the wild populations by orders of magnitude, the effects of escapes of any genetically distinct genotype upon natural populations may be both deleterious and of significant size simply as a result of “swamping”.

An interesting model of the effects on a medaka (*Oryzias latipes*) population of transgenic release has been produced by Muir and Howard (2001) using estimates of juvenile and adult viability, age at sexual maturity, female fecundity, male fertility and mating advantage. They were able to demonstrate that the transgene would spread in natural populations, despite low juvenile viability, if transgenes have sufficient high positive effects on other fitness components. It has been argued that this might lead to extinction but the selective pressure for recombinant genomes with higher viability would be expected to be immense. Maclean and Laight (2000) simulated the changes in frequency of a transgene expected with different scenarios embracing a range of selective values including heterozyote advantage. They note that “repeated small introductions [of the transgene] can have an effect on ... frequency ... since the frequency of advantageous alleles rises much more rapidly than if a single large introduction is considered”. A major problem in assessing risk to natural populations is that of scale. Even if farmed fish are at a selective disadvantage in natural conditions, the ratio of wild:farmed numbers may in some areas, be relatively small. In these situations significant modification of the “native” population and its role in the ecosystem is inevitable.

Whilst not providing a completely satisfactory answer, there is little doubt that making farmed fish sterile would go a long way towards reducing the pressure upon such threatened ecosystems. A number of research efforts to develop systems for sterile fish production are being made. The techniques include triploidisation, antisense transgenics, ribozymes and gene targeting. Provided that the best containment measures (physical and biological) are adopted, in our opinion, in general risks to biodiversity by GMOs *per se* are probably extremely small, but in specific cases, the risks and consequences may be large. As a general rule and adopting a precautionary approach (OECD, 1995), it is, however, clear that each individual case needs careful study and appraisal and the best possible containment measures before approval for uptake into commercial production is given. The direct or indirect effects of transgenesis upon the welfare of fish GMOs in aquaculture are very poorly understood. In part, no doubt, this is because notions of cruel or unnatural treatment in mammalian species translate, for a variety of reasons, imperfectly to fish. Nevertheless, as life forms with highly developed nervous systems and with a range of behavioural phenotypes which flow from this, fish qualify for welfare consideration.

There are a few studies which bear on this. Thus, for example, Devlin *et al.* (1995b) reported changes in colouration, cranial deformities and opercular overgrowth and lower jaw deformation in coho salmon transgenic for AFP and GH. After one year of development anatomical changes due to growth of cartilage in the cranial and opercular regions were more severe and reduced viability was evident. The larger body of data on species farmed terrestrially shows dysfunctional development leading to acromegaly, lameness and infertility in some GH transgenics in pigs and sheep. However, in pigs dietary modification influencing nutritional levels of zinc proved successful in avoiding such abnormalities. Poor countries are used because all poor countries contain rich people and rich communities. The possible economic disadvantages of use of transgenics centre on two issues: If transgenic fish become widely grown because they are much more efficient, and if special broodstock are required to produce fry for on-growing to adults, which, cannot be used as broodstock, a dependency is created. This dependency may be benign or oppressive, depending on the arrangements made for seed supply. This is a very difficult issue indeed. Since genes may now be patented and therefore, enjoy commercial value, the opportunities for dispute about equitable treatment of stakeholders in cases where ownership of genes and strains is contested, are legion. A recently published report (Commission on Intellectual Property Rights, 2002) states that developing countries are frequently disadvantaged in the use of, and access to, IPR because of increasingly protective attitudes taken by owners of IPR. However, the report also indicates that developing countries are very heterogeneous in respect of their ability to use and develop IPR.

### **Possible misuse of genetic engineering:**

1. Genetic engineering is meant to make food crops more resistant to disease, but the mere act of modification of the naturally selected food crops may actually disturb the delicate balance of biodiversity which exists in nature
2. The production of GMOs has negative impacts on the natural ecosystem which are not apparent now but will be apparent in the future. For example, genetic changes in a particular plant or animal might render it harmful to another organism higher up in the food chain and ultimately this effect may build up to destroy the entire food chain in which that plant plays a role.
3. GMOs have been known to retain some of the genetically modified DNA in the final product made for human consumption. Such remnants of genetic material are harmful to human health and can cause production of previously unknown allergens.
4. Genetically modified plants and animals have the potential to replace traditional farming or say poultry and meat-producing practices. This will result in destruction of economies based on these products.

### **Nanotechnology:**

Nanotechnology, also called *molecular manufacturing*, is "a branch of engineering that deals with the design and manufacture of extremely small electronic circuits and mechanical devices built at the molecular level of matter."The goal of nanotechnology is to be able to manipulate materials at the atomic level to build the smallest possible electromechanical devices, given the physical limitations of matter. Much of the mechanical systems we know how to build will be transferred to the molecular level as some atomic analogy. nanocomputers are no bigger than bacteria and nanomachines, also known as nanites, which could be used as a molecular assemblers and disassemblers to build, repair, or tear down any physical or biological objects. In essence, the purpose of developing nanotechnology is to have tools to work on the molecular level analogous to the tools we have at the macroworld level. Like the robots we use to build cars and the construction equipment we use to build skyscrapers, nanomachines will enable us to create a plethora of goods and increase our engineering abilities to the limits of the physical world. It would not take much of a leap, then, to imagine disassemblers dismantling garbage to be recycled at the molecular level, and then given to assemblers for them to build atomically perfect engines. Stretching this vision a bit, you can imagine a Star Trek type replicator which could reassemble matter in the form of a juicy steak, given the correct blueprints and organization of these nanomachines. Just given the basic premises of nanotechnology, you can imagine the vast potential of this technology. Some of its more prominent benefits would be:

- Manufacturing
  - Precision Manufacturing
  - Material Reuse
  - Miniaturization
- Medicine
  - Pharmaceutical Creation
  - Disease Treatment
  - Nanomachine-assisted Surgery
- Environment
  - Toxin Cleanup
  - Recycling
  - Resource Consumption Reduction

Along with all the obvious manufacturing benefits, there are also many potential medical and environmental benefits. With nanomachines, we could better design and synthesize pharmaceuticals; we could directly treat diseased cells like cancer; we could better monitor the life signs of a patient; or we could use nanomachines to make microscopic repairs in hard-to-operate-on areas of the body. With regard to the environment, we could use nanomachines to clean up toxins or oil spills, recycle all garbage, and eliminate landfills, thus reducing our natural resource consumption. The flip side to these benefits is the possibility of assemblers and disassemblers being used to create weapons, be used as weapons themselves, or for them to run wild and wreak havoc. Other, less invasive, but equally perilous uses of nanotechnology would be in electronic surveillance.

- Weapons: Miniature Weapons and Explosives, disassemblers for Military Use

- Rampant Nanomachines
  - The Gray Goo Scenario
  - Self Replicating Nanomachines
- Surveillance
  - Monitoring
  - Tracking

Weapons are an obvious negative use of nanotechnology. Simply extending today's weapon capabilities by miniaturizing guns, explosives, and electronic components of missiles would be deadly enough. However, with nanotechnology, armies could also develop disassemblers to attack physical structures or even biological organism at the molecular level. A similar hazard would be if general purpose disassemblers got loose in the environment and started disassembling every molecule they encountered. This is known as "The Gray Goo Scenario." Furthermore, if nanomachines were created to be self replicating and there were a problem with their limiting mechanism, they would multiply endlessly like viruses. Even without considering the extreme disaster scenarios of nanotechnology, we can find plenty of potentially harmful uses for it. It could be used to erode our freedom and privacy; people could use molecular sized microphones, cameras, and homing beacons to monitor and track others. With such awesome potential dangers inherent in nanotechnology, we must seriously examine its potential consequences. Granted, nanotechnology may never become as powerful and prolific as envisioned by its evangelists, but as with any potential, near-horizon technology, we should go through the exercise of formulating solutions to potential ethical issues before the technology is irreversibly adopted by society. We must examine the ethics of developing nanotechnology and create policies that will aid in its development so as to eliminate or at least minimize its damaging effects on society.

### **Cybernetics:**

Cybernetics has the ability to explore regulatory system, their structures and functions. It is derived from a Greek word that means "governance". Cybernetics is the study of interactions between man, machine and animals. Today because of this technique we can create "Superhumans". This transforms the way we practice medicine, transmit thoughts and communicate with one another. Softwares are built by cybernetics to read signals from the nervous system to record and condition the data for retransmission. There are number of application of cybernetics:

- replacing limbs instead of wooden limbs
- heart pacemakers
- artificial retinas
- silicon chip function like nerves-replace lost neuronal function
- university ID card-chip

Number of ethical issues has been raised like how machines are in charge of key human functions. By this technique only wealthy ones can communicate through cybernetics. Then whether implants are safe to use because senses and impulses can be transmitted in a harmful way? Can the senses be patented and who regulates?

### **Applications of genetic modification and their ethical issues:**

The field of transgenics allows scientists to develop organisms that express a novel trait not normally found in a species; for example potatoes that are protein rich, or rice that has elevated levels of vitamin A. It may be also used to save endangered species such as the American Chestnut tree, which is currently being repopulated by Chinese-American chestnut hybrids specifically engineered with a genetic resistance to the chestnut blight the deadly fungus that nearly decimated native populations in the early 1900s. Scientists are also using transgenics to develop novel vaccines, including edible vaccines. Transgenic combinations may also include plant-animal-human transgenes, such as when the DNA of human tumor fragments is inserted into tobacco plants in order to develop a vaccine against non-Hodgkin lymphoma. Researchers have similarly developed a flu vaccine using human DNA and tobacco plants. Other transgenic plants have been used to create edible vaccines. By incorporating a human protein into bananas, potatoes, and tomatoes, researchers have been able to successfully create edible vaccines for hepatitis B, cholera, and rotavirus, the latter of which can cause fatal bouts of

diarrhea. Another recent transgenic plant project, known as the “glowing plant project,” incorporated a gene from a firefly into a houseplant, creating plants that display a soft illumination in the darkness. One of the proposed goals is to create trees that could illuminate streets and pathways, thereby saving energy and reducing our dependence upon limited energy resources; however, the public release of such plants has sparked a heated debate centered on potential environmental impacts of introducing highly genetically engineered plants into natural ecosystems.

BioSteel® is a high strength, resilient silk product created by inserting the genes from a silk-spinning spider into the genome of a goat egg prior to fertilization. When the transgenic female goats mature, they produce milk containing the protein from which spider silk is made. The fiber artificially created from this silk protein has several potentially valuable uses, such as making lightweight, strong, yet supple bulletproof vests. Other industrial and medical applications include stronger automotive and aerospace components, stronger and more biodegradable sutures, and bioshields, which can protect military personnel and first responders from chemical threats such as sarin gas. Genetic engineering and transgenic combinations represent a significant aspect of current biotechnology research. Other examples include Xenotransplantation, or the transplantation of living tissues or organs from one species to another, is often seen as a potential way to alleviate the shortage of human hearts and kidneys. Pigs have a similar physiology and organ size, making porcine (pig) organs ideal candidates for transplantation into human recipients. Researchers are also exploring the use of cell transplantation therapy for patients with spinal cord injury or Parkinson’s disease. Genetic manipulation of stem cells now includes the growth of tissues on scaffolding, or a 3-D printer, which then can be used as a temporary skin substitute for healing wounds or burns. Tissue engineering is becoming a viable alternative in procedures that involve replacement of cartilage, heart valves, cerebrospinal shunts, and other organs. Commercial companies are deriving therapeutic proteins, such as monoclonal antibodies, from the milk of transgenic cows, goats, rabbits, and mice, and using them to administer drugs in treatment protocols for rheumatoid arthritis, cancer, and other autoimmune disorders. Clearly, genetic engineering and transgenics represent fields with myriad potential practical applications that are of value to patients and physicians, as well as potentially lucrative research and innovation streams for commercial and industrial consideration.

Ethical issues, including concerns for animal welfare, can arise at all stages in the generation and life span of an individual genetically engineered animal. The following sections detail some of the issues that have arisen during the peer-driven guidelines development process and associated impact analysis consultations carried out by the CCAC. The CCAC works to an accepted ethic of animal use in science, which includes the principles of the Three Rs (Reduction of animal numbers, Refinement of practices and husbandry to minimize pain and distress, and Replacement of animals with non-animal alternatives wherever possible). Together the Three Rs aim to minimize any pain and distress experienced by the animals used, and as such, they are considered the principles of humane experimental technique. However, despite the steps taken to minimize pain and distress, there is evidence of public concerns that go beyond the Three Rs and animal welfare regarding the creation and use of genetically engineered animals.

#### **Ethical issues related to genetically modified food:**

There are a number of ethical concerns over genetically modified (GM) foods and these have all affected public support of the products. The issues have also triggered controversy and regulations around GM foods and any company that produces these crops or products. Concerns range from the environment to risks to our food web or issues concerning disease, allergies and contamination. A key ethical concern about GM foods is their potential to trigger allergies or disease in humans. Given that a gene could be extracted from an allergenic organism and placed into another one that typically does not cause allergies; a person may unknowingly be exposed to an allergen. In turn, this could lead to an allergic reaction. There is also the fear that new allergies could occur from the mixing of genes from two organisms. Disease is a major health worry with regards to GM foods. Given that some of the crops modified are done so with DNA from a bacterium or virus, there is concern that a new disease may occur in humans who consume the GM food. With some GM crops having antibiotic-resistant marker genes, there is also the worry that these genes could be passed on to microbes that cause disease and health problems in humans. With widespread antibiotic resistance currently already occurring, any new resistance could prove disastrous.

Damage to the environment is another ethical fear with regards to GM crops. Unfortunately, the technology is still new enough that there is much we do not know about the effect of GM crop production on the environment. Long-term studies take decades to complete and most studies of GM crop production involve short-term effects

of the technology. Another ethical issue around GM crops is our ability to contain them in a specific area. There are fears that if these crops do negatively impact the environment, they will spread in an out-of-control fashion and we will not be able to stop their damaging effects. For instance, one type of sugar beet that had been engineered to be resistant to a specific herbicide ended up unintentionally having the genes to resist a different herbicide. When farmers went to eliminate the crop, they still found that a small percentage had survived. Cross-pollination is a challenge for any crop growth but it can typically be managed if care is taken to use good growing practices. There is the possibility of genes from GM foods spreading to other plants and crops, which could create overzealous weeds that can't be contained at all.

Risks to the food web are a very real ethical concern around GM technology. Any pesticide or herbicide from the crop could harm animals and other organisms in the environment. For example, GM sugar beets that were produced to be resistant to herbicides did successfully reduce weeds. However, Skylark birds that consume the seeds from this particular weed would now be required to find a new food source, thereby endangering their existence. An animal could also consume the GM crop itself, which means that if the crop has been engineered to produce a pesticide, the animal may become ill and die. In one North American study, caterpillars of the monarch butterfly were killed when they fed on pollen from GM corn crops. Unfortunately, the controversy and fears around GM foods and any company that produces these products still continue to persevere, although this could be viewed as a positive movement because it will challenge GM technology and help to make it safer and more regulated. In one public opinion poll, it was found that the more people read about GM foods, the more concerned they became about the technology.

Studies are ongoing into the many ethical concerns around GM foods but these are not conclusive and have thus far shown very mixed results. It is also very difficult to assess the long-term impact, thereby leaving many of the public fearing for the long-term safety of humans and the environment. For now, it is hoped that people will become more educated on the ethical concerns about GM foods, which will ideally fuel further research and accountability in the field. One of the main controversies around GM foods is the potential of these products to affect biodiversity. This is somewhat of a confusing area in the sense that it is a difficult one to assess and the effects tend to be long-term ones, rather than consequences that can be observed and measured in the short-term. As such, it is challenging because a GM crop may be approved but problems relating to biodiversity will not be evident for some time afterwards. By that time, restoring biodiversity is a difficult if not impossible task.

### **Risk factors of GM foods:**

There are four health risks related to GM food and these are allergies, antibiotic resistance, pesticide exposure and unpredictable/ unknown exposures. Perhaps the number one health concern over GM technology is its capacity to create new allergens in our food supply. Allergic reactions typically are brought on by proteins. Nearly every transfer of genetic material from one host into a new one results in the creation of novel proteins. Genetic engineering can increase the levels of a naturally occurring allergen already present in a food or insert allergenic properties into a food that did not previously contain them. It can also result in brand new allergens we've never before known. Genetic engineers rely heavily on antibiotics to guide experiments. It works like this: Not all host cells will take up foreign genes, so engineers attach a trait for a particular type of antibiotic resistance to the gene they introduce into host cells. After they've introduced the gene into the cells, they douse all the cells with the antibiotic to see which ones survive. The surviving cells are antibiotic-resistant, and therefore engineers know they have taken up the foreign gene. Overuse of antibiotics can potentially cause the development of antibiotic-resistant pathogens. Several health organizations, including the World Health Organization and the American Medical Association, have spoken out about the need for the use of these antibiotics to be phased out of the process of making GM foods. Food Patriot Sam Spitz' harrowing story provides a scary, precautionary warning of how antibiotic-resistant "superbugs" can affect your health.

The majority of GM crops in cultivation are engineered to contain a gene for pesticide resistance. Most are "Roundup Ready," meaning they can be sprayed with Monsanto's glyphosate herbicide Roundup without being harmed. The idea is that if the crop itself is immune to Roundup, you can spray it to kill any weeds endangering the plant without worrying about harming your crop. Sound like a good thing? Only if increased human exposure to pesticides is a good thing. Glyphosate has been linked to numerous health problems in animal studies, among them birth defects, reproductive damage, cancer and endocrine disruption. Foreign genetic material in a host can cause other genetic material in that host to behave erratically. Genes can be suppressed or over expressed, causing a wide variety of results. One consequence of over expression, for example, can be cancer. Nutritional problems can also result from the transfer. In one example, cows that ate Roundup Ready

soybeans produced milk with more fat in it. In another example, milk from cows injected with a genetically engineered growth hormone was found by a number of researchers, including those published in the journal *Lancet*, to have substantially higher levels of a compound known as insulin-like growth factor-1, which is linked to human breast, colon and prostate cancers. The milk also has higher levels of bovine growth hormones in it, along with pus and sometimes antibiotics. GM crops have been linked to health problems as diverse as reproductive damage, cancer, Alzheimer's disease and diabetes. Concerned scientists have been outspoken about these risks. DNA is complex, and we have yet to understand all the potential complex interactions. The potential hazards are difficult to predict and identify immediately. Additionally, the United States regulatory system is set up to deal with problems occurring with GM foods only after they occur. But what if, instead, we invoked the precautionary principle, an international agreement that calls for intelligent caution when it comes to new science and technologies? Thankfully, you can protect yourself and your family by taking action against GMO foods. Choose organic foods wherever possible, support farms that refuse to grow GMO foods, and pressure your lawmakers to force agriculture companies to label GMOs. The right to know is one we must be outspoken to protect.

### **Genetic modification of animals and their uses:**

The genetic engineering of animals has increased significantly in recent years, and the use of this technology brings with it ethical issues, some of which relate to animal welfare defined by the World Organisation for Animal Health as "the state of the animal...how an animal is coping with the conditions in which it lives". These issues need to be considered by all stakeholders, including veterinarians, to ensure that all parties are aware of the ethical issues at stake and can make a valid contribution to the current debate regarding the creation and use of genetically engineered animals. In addition, it is important to try to reflect societal values within scientific practice and emerging technology, especially publicly funded efforts that aim to provide societal benefits, but that may be deemed ethically contentious. As a result of the extra challenges that genetically engineered animals bring, governing bodies have started to develop relevant policies, often calling for increased vigilance and monitoring of potential animal welfare impacts. Veterinarians can play an important role in carrying out such monitoring, especially in the research setting when new genetically engineered animal strains are being developed.

Genetic engineering technology has numerous applications involving companion, wild, and farm animals, and animal models used in scientific research. The majority of genetically engineered animals are still in the research phase, rather than actually in use for their intended applications, or commercially available. By inserting genes from sea anemone and jellyfish, zebrafish have been genetically engineered to express fluorescent proteins — hence the commonly termed "GloFish." GloFish began to be marketed in the United States in 2003 as ornamental pet fish; however, their sale sparked controversial ethical debates in California — the only US state to prohibit the sale of GloFish as pets. In addition to the insertion of foreign genes, gene knock-out techniques are also being used to create designer companion animals. For example, in the creation of hypoallergenic cats some companies use genetic engineering techniques to remove the gene that codes for the major cat allergen. Companion species have also been derived by cloning. The first cloned cat, "CC," was created in 2002. At the time, the ability to clone mammals was a coveted prize, and after just a few years scientists created the first cloned dog, "Snuppy". With the exception of a couple of isolated cases, the genetically engineered pet industry is yet to move forward. However, it remains feasible that genetically engineered pets could become part of day-to-day life for practicing veterinarians, and there is evidence that clients have started to enquire about genetic engineering services, in particular the cloning of deceased pets.

The primary application of genetic engineering to wild species involves cloning. This technology could be applied to either extinct or endangered species; for example, there have been plans to clone the extinct thylacine and the woolly mammoth. Holt et al point out that, "As many conservationists are still suspicious of reproductive technologies, it is unlikely that cloning techniques would be easily accepted. Individuals involved in field conservation often harbour suspicions that hi-tech approaches, backed by high profile publicity would divert funding away from their own efforts." However, cloning may prove to be an important tool to be used alongside other forms of assisted reproduction to help retain genetic diversity in small populations of endangered species. As reviewed by Laible, there is "an assorted range of agricultural livestock applications [for genetic engineering] aimed at improving animal productivity; food quality and disease resistance; and environmental sustainability." Productivity of farm animal species can be increased using genetic engineering. Examples include transgenic pigs and sheep that have been genetically altered to express higher levels of growth hormone.

Genetically engineered farm animals can be created to enhance food quality. For example, pigs have been genetically engineered to express the  $\Delta 12$  fatty acid desaturase gene (from spinach) for higher levels of omega-3, and goats have been genetically engineered to express human lysozyme in their milk. Such advances may add to the nutritional value of animal-based products. Farm species may be genetically engineered to create disease-resistant animals. Specific examples include conferring immunity to offspring via antibody expression in the milk of the mother; disruption of the virus entry mechanism (which is applicable to diseases such as pseudorabies); resistance to prion diseases; parasite control and mastitis resistance (particularly in cattle). Genetic engineering has also been applied with the aim of reducing agricultural pollution. The best-known example is the Enviropig<sup>TM</sup>; a pig that is genetically engineered to produce an enzyme that breaks down dietary phosphorus (phytase), thus limiting the amount of phosphorus released in its manure. Despite resistance to the commercialization of genetically engineered animals for food production, primarily due to lack of support from the public, a recent debate over genetically engineered AquAdvantage<sup>TM</sup> Atlantic salmon may result in these animals being introduced into commercial production.

Effort has also been made to generate genetically engineered farm species such as cows, goats, and sheep that express medically important proteins in their milk. According to Dyck et al, “transgenic animal bioreactors represent a powerful tool to address the growing need for therapeutic recombinant proteins.” In 2006, ATryn<sup>®</sup> became the first therapeutic protein produced by genetically engineered animals to be approved by the Food and Drug Administration (FDA) of the United States. This product is used as a prophylactic treatment for patients that have hereditary antithrombin deficiency and are undergoing surgical procedures. Biomedical applications of genetically engineered animals are numerous, and include understanding of gene function, modeling of human disease to either understand disease mechanisms or to aid drug development, and xenotransplantation. Through the addition, removal, or alteration of genes, scientists can pinpoint what a gene does by observing the biological systems that are affected. While some genetic alterations have no obvious effect, others may produce different phenotypes that can be used by researchers to understand the function of the affected genes. Genetic engineering has enabled the creation of human disease models that were previously unavailable. Animal models of human disease are valuable resources for understanding how and why a particular disease develops, and what can be done to halt or reverse the process. As a result, efforts have focused on developing new genetically engineered animal models of conditions such as Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), Parkinson’s disease, and cancer. However, as Wells points out: “these genetically engineered animal models do not always accurately reflect the human condition, and care must be taken to understand the limitation of such models.”

The use of genetically engineered animals has also become routine within the pharmaceutical industry, for drug discovery, drug development, and risk assessment. As discussed by Rudmann and Durham: “Transgenic and knock out mouse models are extremely useful in drug discovery, especially when defining potential therapeutic targets for modifying immune and inflammatory responses...Specific areas for which may be useful are in screening for drug induced immunotoxicity, genotoxicity, and carcinogenicity, and in understanding toxicity related drug metabolizing enzyme systems.” Perhaps the most controversial use of genetically engineered animals in science is to develop the basic research on xenotransplantation that is, the transplant of cells, tissues, or whole organs from animal donors into human recipients. In relation to organ transplants, scientists have developed a genetically engineered pig with the aim of reducing rejection of pig organs by human recipients. This particular application of genetic engineering is currently at the basic research stage, but it shows great promise in alleviating the long waiting lists for organ transplants, as the number of people needing transplants currently far outweighs the number of donated organs. However, as a direct result of public consultation, a moratorium is currently in place preventing pig organ transplantation from entering a clinical trial phase until the public is assured that the potential disease transfer from pigs to humans can be satisfactorily managed. According to Health Canada, “xenotransplantation is currently not prohibited in Canada. However, the live cells and organs from animal sources are considered to be therapeutic products (drugs or medical devices)...No clinical trial involving xenotransplantation has yet been approved by Health Canada”.

### **Genetic modification of animals and their ethical issues:**

Ethical issues, including concerns for animal welfare, can arise at all stages in the generation and life span of an individual genetically engineered animal. The following sections detail some of the issues that have arisen during the peer-driven guidelines development process and associated impact analysis consultations carried out by the CCAC. The CCAC works to an accepted ethic of animal use in science, which includes the principles of the Three Rs (Reduction of animal numbers, Refinement of practices and husbandry to minimize pain and distress, and Replacement of animals with non-animal alternatives wherever possible). Together the Three Rs

aim to minimize any pain and distress experienced by the animals used, and as such, they are considered the principles of humane experimental technique. However, despite the steps taken to minimize pain and distress, there is evidence of public concerns that go beyond the Three Rs and animal welfare regarding the creation and use of genetically engineered animals. The generation of a new genetically engineered line of animals often involves the sacrifice of some animals and surgical procedures (for example, vasectomy, surgical embryo transfer) on others. These procedures are not unique to genetically engineered animals, but they are typically required for their production.

During the creation of new genetically engineered animals (particularly mammalian species) oocyte and blastocyst donor females may be induced to superovulate via intraperitoneal or subcutaneous injection of hormones; genetically engineered embryos may be surgically implanted to female recipients; males may be surgically vasectomized under general anesthesia and then used to induce pseudopregnancy in female embryo recipients; and all offspring need to be genotyped, which is typically performed by taking tissue samples, sometimes using tail biopsies or ear notching. However, progress is being made to refine the genetic engineering techniques that are applied to mammals (mice in particular) so that less invasive methods are feasible. For example, typical genetic engineering procedures require surgery on the recipient female so that genetically engineered embryos can be implanted and can grow to full term; however, a technique called non-surgical embryo transfer (NSET) acts in a similar way to artificial insemination, and removes the need for invasive surgery. Other refinements include a method referred to as “deathless transgenesis,” which involves the introduction of DNA into the sperm cells of live males and removes the need to euthanize females in order to obtain germ line transmission of a genetic alteration; and the use of polymerase chain reaction (PCR) for genotyping, which requires less tissue than Southern Blot Analysis.

Many of the embryos that undergo genetic engineering procedures do not survive, and of those that do survive only a small proportion (between 1% to 30%) carry the genetic alteration of interest. This means that large numbers of animals are produced to obtain genetically engineered animals that are of scientific value, and this contradicts efforts to minimize animal use. In addition, the advancement of genetic engineering technologies in recent years has led to a rapid increase in the number and varieties of genetically engineered animals, particularly mice. Although the technology is continually being refined, current genetic engineering techniques remain relatively inefficient, with many surplus animals being exposed to harmful procedures. One key refinement and reduction effort is the preservation of genetically engineered animal lines through the freezing of embryos or sperm (cryopreservation), which is particularly important for those lines with the potential to experience pain and distress.

Number of research projects creating and/or using genetically engineered animals worldwide has increased in the past decade. In Canada, the CCAC’s annual data on the numbers of animals used in science show an increase in procedures with the potential to cause moderate to severe pain and distress at present the creation of a new genetically engineered animal line is a Category D procedure. The data also show an increase in the use of mice, which are currently the most commonly used species for genetic engineering, making up over 90% of the genetically engineered animals used in research and testing. This rise in animal use challenges the Three Rs principle of Reduction. It has been reasoned that once created, the use of genetically engineered animals will reduce the total number of animals used in any given experiment by providing novel and more accurate animal models, especially in applications such as toxicity testing. However, the greater variety of available applications, and the large numbers of animals required for the creation and maintenance of new genetically engineered strains indicate that there is still progress to be made in implementation of the Three Rs principle of Reduction in relation to the creation and use of genetically engineered animals.

Little data has been collected on the net welfare impacts to genetically engineered animals or to those animals required for their creation, and genetic engineering techniques have been described as both unpredictable and inefficient. The latter is due, in part, to the limitations in controlling the integration site of foreign DNA, which is inherent in some genetic engineering techniques. In such cases, scientists may generate several independent lines of genetically engineered animals that differ only in the integration site, thereby further increasing the numbers of animals involved. This conflicts with efforts to adhere to the principles of the Three Rs, specifically Reduction. With other, more refined techniques that allow greater control of DNA integration (for example, gene targeting), unexpected outcomes are attributed to the unpredictable interaction of the introduced DNA with host genes. These interactions also vary with the genetic background of the animal, as has frequently been observed in genetically engineered mice. Interfering with the genome by inserting or removing fragments of DNA may result in alteration of the animal’s normal genetic homeostasis, which can be manifested in the behavior and well-being of the animals in unpredictable ways. For example, many of the early transgenic

livestock studies produced animals with a range of unexpected side effects including lameness, susceptibility to stress, and reduced fertility.

A significant limitation of current cloning technology is the prospect that cloned offspring may suffer some degree of abnormality. Studies have revealed that cloned mammals may suffer from developmental abnormalities, including extended gestation; large birth weight; inadequate placental formation; and histological effects in organs and tissues (for example, kidneys, brain, cardiovascular system, and muscle). One annotated review highlights 11 different original research articles that documented the production of cloned animals with abnormalities occurring in the developing embryo, and suffering for the newborn animal and the surrogate mother. Genetically engineered animals, even those with the same gene manipulation, can exhibit a variety of phenotypes; some causing no welfare issues, and some causing negative welfare impacts. It is often difficult to predict the effects a particular genetic modification can have on an individual animal, so genetically engineered animals must be monitored closely to mitigate any unanticipated welfare concerns as they arise. For newly created genetically engineered animals, the level of monitoring needs to be greater than that for regular animals due to the lack of predictability. Once a genetically engineered animal line is established and the welfare concerns are known, it may be possible to reduce the levels of monitoring if the animals are not exhibiting a phenotype that has negative welfare impacts. To aid this monitoring process, some authors have called for the implementation of a genetically engineered animal passport that accompanies an individual animal and alerts animal care staff to the particular welfare needs of that animal. This passport document is also important if the intention is to breed from the genetically engineered animal in question, so the appropriate care and husbandry can be in place for the offspring. With progress in genetic engineering techniques, new methods may substantially reduce the unpredictability of the location of gene insertion. As a result, genetic engineering procedures may become less of a welfare concern over time.

As pointed out by Lassen et al, “Until recently the main limits [to genetic engineering] were technical: what it is *possible* to do. Now scientists are faced with ethical limits as well: what it is *acceptable* to do” (emphasis theirs). Questions regarding whether it is acceptable to make new transgenic animals go beyond consideration of the Three Rs, animal health, and animal welfare, and prompt the discussion of concepts such as intrinsic value, integrity, and naturalness. When discussing the “nature” of an animal, it may be useful to consider the Aristotelian concept of *telos*, which describes the “essence and purpose of a creature”. Philosopher Bernard Rollin applied this concept to animal ethics as follows: “Though [*telos*] is partially metaphysical (in defining a way of looking at the world), and partially empirical (in that it can and will be deepened and refined by increasing empirical knowledge), it is at root a moral notion, both because it is morally motivated and because it contains the notion of what about an animal we *ought* to at least try to respect and accommodate. Rollin has also argued that as long as we are careful to accommodate the animal’s interests when we alter an animal’s *telos*, it is morally permissible. He writes, “...given a *telos*, we should respect the interests which flow from it. This principle does not logically entail that we cannot modify the *telos* and thereby generate different or alternative interests”. Views such as those put forward by Rollin have been argued against on the grounds that health and welfare (or animal interests) may not be the only things to consider when establishing ethical limits. Some authors have made the case that genetic engineering requires us to expand our existing notions of animal ethics to include concepts of the intrinsic value of animals, or of animal “integrity” or “dignity”. Veerhoog argues that, “we misuse the word *telos* when we say that human beings can ‘change’ the *telos* of an animal or create a new *telos*” — that is to say animals have intrinsic value, which is separate from their value to humans. It is often on these grounds that people will argue that genetic engineering of animals is morally wrong. For example, in a case study of public opinion on issues related to genetic engineering, participants raised concerns about the “nature” of animals and how this is affected (negatively) by genetic engineering.

An alternative view put forward by Schicktanz argues that it is the human-animal relationship that may be damaged by genetic engineering due to the increasingly imbalanced distribution of power between humans and animals. This imbalance is termed “asymmetry” and it is raised alongside “ambivalence” as a concern regarding modern human-animal relationships. By using genetically engineered animals as a case study, Schicktanz argues that genetic engineering presents “a troubling shift for all human-animal relationships.” Opinions regarding whether limits can, or should, be placed on genetic engineering are often dependent on people’s broader worldview. For some, the genetic engineering of animals may not put their moral principles at risk. For example, this could perhaps be because genetic engineering is seen as a logical continuation of selective breeding, a practice that humans have been carrying out for years; or because human life is deemed more important than animal life. So if genetic engineering creates animals that help us to develop new human medicine then, ethically speaking, we may actually have a moral obligation to create and use them; or because of an expectation that genetic engineering of animals can help reduce experimental animal numbers, thus implementing the accepted Three Rs framework. For others, the genetic engineering of animals may put their

moral principles at risk. For example costs may always be seen to outweigh benefits because the ultimate cost is the violation of species integrity and disregard for the inherent value of animals. Some may view *telos* as something that cannot or should not be altered, and therefore altering the *telos* of an animal would be morally wrong. Some may see genetic engineering as exaggerating the imbalance of power between humans and animals, whilst others may fear that the release of genetically engineered animals will upset the natural balance of the ecosystem. In addition, there may be those who feel strongly opposed to certain applications of genetic engineering, but more accepting of others. For example, recent evidence suggests that people may be more accepting of biomedical applications than those relating to food production. Such underlying complexity of views regarding genetic engineering makes the setting of ethical limits difficult to achieve, or indeed, even discuss. However, progress needs to be made on this important issue, especially for those genetically engineered species that are intended for life outside the research laboratory, where there may be less careful oversight of animal welfare. Consequently, limits to genetic engineering need to be established using the full breadth of public and expert opinion.

Genetic engineering also brings with it concerns over intellectual property, and patenting of created animals and/or the techniques used to create them. Preserving intellectual property can breed a culture of confidentiality within the scientific community, which in turn limits data and animal sharing. Such limits to data and animal sharing may create situations in which there is unnecessary duplication of genetically engineered animal lines, thereby challenging the principle of Reduction. Indeed, this was a concern that was identified in a recent workshop on the creation and use of genetically engineered animals in science. It should be noted that no matter what the application of genetically engineered animals, there are restrictions on the methods of their disposal once they have been euthanized. The reason for this is to restrict the entry of genetically engineered animal carcasses into the natural ecosystem until the long-term effects and risks are better understood. As genetically engineered animals begin to enter the commercial realm, it will become increasingly important for veterinarians to inform themselves about any special care and management required by these animals. As animal health professionals, veterinarians can also make important contributions to policy discussions related to the oversight of genetic engineering as it is applied to animals, and to regulatory proceedings for the commercial use of genetically engineered animals. It is likely that public acceptance of genetically engineered animal products will be an important step in determining when and what types of genetically engineered animals will appear on the commercial market, especially those animals used for food production. Veterinarians may also be called on to inform the public about genetic engineering techniques and any potential impacts to animal welfare and food safety. Consequently, for the discussion regarding genetically engineered animals to progress effectively, veterinarians need to be aware of the current context in which genetically engineered animals are created and used, and to be aware of the manner in which genetic engineering technology and the animals derived from it may be used in the future.

Genetic engineering techniques can be applied to a range of animal species, and although many genetically engineered animals are still in the research phase, there are a variety of intended applications for their use. Although genetic engineering may provide substantial benefits in areas such as biomedical science and food production, the creation and use of genetically engineered animals not only challenge the Three Rs principles, but may also raise ethical issues that go beyond considerations of animal health, animal welfare, and the Three Rs, opening up issues relating to animal integrity and/or dignity. Consequently, even if animal welfare can be satisfactorily safeguarded, intrinsic ethical concerns about the genetic engineering of animals may be cause enough to restrict certain types of genetically engineered animals from reaching their intended commercial application. Given the complexity of views regarding genetic engineering, it is valuable to involve all stakeholders in discussions about the applications of this technology.

### **Molecular Genetics and Human Genome Project:**

The idea of the HGP was initiated in 1977, when simple and efficient methods for sequencing DNA were described. Before that time the possibility of sequencing the entire human genome was no more than extreme wishful thinking. In the 1980's it was becoming increasingly apparent to many scientists that an understanding of basic biology would be greatly enhanced if the detailed structure of DNA was understood. Over the last two decades, automated DNA sequencers have made the process of obtaining the base-by-base sequence of DNA easier. In 1984, for the first time a meeting was sponsored by the Department of Energy (DOE) to address the problem of detecting extremely low levels of very rare changes in DNA (mutations) in humans exposed to radiation and other environmental hazards. At that time, it was realized that the level of effort including the

automation of DNA analysis techniques would be similar to the requirements for sequencing the human genome. Several other meetings followed until the first formal proposal appeared in 1986 published by Renato Dulbecco who focused on potential benefits to cancer research from the availability of the complete genomic sequence. The immediate public response was considerable skepticism about the possibility and economical feasibility of the HGP, the value of the results, its impact on the rest of biological research, goal definitions, funding, and potential risks of information abuse.

The HGP formally began in the fall of 1990 as a \$3 billion, 15-year effort to find the estimated 80,000-100,000 human genes and determine the sequence of the 3-billion chemical bases that make up human DNA and underlies all life's diversity. Despite voices of concern in the scientific community, the U.S. National Human Genome Research Institute (NHGRI) started allocating funding for the creation of the HGP in 1988 and delegated \$17.2 million to the National Institute of Health (NIH) and \$10.7 million for DOE, based on the agency's interest and experience with genetic research related to radiation effects and its background in computer science. James D. Watson, Ph.D., the famous co-discoverer of the DNA double helix, was recruited to direct the NIH effort. Watson has been enthusiastic about the prospect of creating a complete catalogue of the three billion base pairs in the human genome - the straightforward concept of sequencing the entire human genome and mapping, all to be achieved within the lifetime of one scientist. In response to widespread concern about possible negative consequences of increased knowledge of the human genome, between 2 and 5% of the total budget have been set aside for a program on ethical, legal and social implications. An international Human Genome Organization (HUGO) was founded in April, 1988 by an independent group of scientists initially for the purpose of assisting with coordinating national efforts, facilitating exchange of research resources, encouraging public debate, and providing information on the implications of human genome research. HUGO now has primary responsibility for organizing workshops on individual human chromosomes. It will also coordinate projects on sequencing and mapping cDNAs.

The major goals defined in the HGP are: (1) construction of a high resolution genetic map of the human genome; (2) production of a variety of physical maps of all human chromosomes and the chromosomes of selected organisms; (3) determination of the complete sequence of human DNA and of the DNA of selected model organisms; (4) development of the capabilities for collecting, storing, distributing, and analyzing the data produced, and (5) creation of appropriate technologies necessary to achieve these objectives.

Rapid technological advances have accelerated and shifted the expected completion date to 2003. In 1998, new 5-year goals were published including identifying regions of the human genome that differ from person to person since it is believed that these DNA sequence variations play a major role on how individuals respond to diseases, and environmental insults such as bacteria, viruses, and toxins, and drugs. Additional goals of the new plan focus on comparing human DNA sequences with those from organisms such as the laboratory mouse and yeast, addressing the ethical, legal, and social issues surrounding genetic tools and data, developing the computational capability to collect, store, and analyze DNA data, and developing interdisciplinary training programs for future genomics scientists. One goal of sequencing the genome is to identify, in the proper order, the three billion base pairs that make up human DNA. The other goal of the HGP is to map the human genome and create landmarks throughout the genome that can be used as reference points or as unique sequences of DNA that locate genes in their vicinity. Landmarks are an ordered collection of overlapping cloned DNA segments that together span a given region of the genome and help develop physical maps. Such landmarks can be identified by the use of genetic tests. Once a physical map is constructed, each gene on a chromosome can be located in terms of its position relative to a marker. Physical maps in addition with linkage maps are helpful in identifying genes responsible for diseases and are also necessary for sequencing. However, only a tiny fraction of human DNA is known to code for protein or RNA, the rest (95% or more) either is non-functional or has some function that has not yet been identified. Such an effort would begin with cDNA localization of most or all of the 50,000 genes, followed by base-sequence determination of the entire genome. Analyses of base sequences are also being conducted, but these are concentrated on currently identifiable genes, such as those implicated in genetic diseases. Automation is making the task of sequencing less laborious and costly, and powerful computer programs manage and analyze the data. Based on experience gained from pilot projects, an international consortium predicts they will produce at least 90 percent of the human genome sequence in a "working draft" form already by the spring of 2000.

The ultimate goal of the HGP is exploiting the knowledge gained from this project for a truly, profound molecular-level understanding of how we develop from embryo to adult, what makes us work and what causes things to go wrong. The project also includes the genomic analysis of organisms other than the human.

Comparative mapping studies are being carried out simultaneously in a number of other organisms, especially in the laboratory mouse (*Mus musculus*), the fruitfly (*Drosophila melanogaster*), a nematode worm (*Caenorhabditis elegans*), yeast (*Saccharomyces cerevisiae*), and *Escherichia coli*. Comparisons of DNA sequences and the chromosomal organization of related genes and clusters of genes from different organisms are powerful tools for identifying the elements essential for their functions. The information gained from the comparative mapping studies of other organisms will add greatly to human's understanding of evolutionary relationships due to the extensive homologies among different genomes and conservative nature of evolution, but they also significantly increase the scope and cost of the overall project.

The project has been controversial for many reasons. A great deal of variety remains in the approaches available to sequencing the human genome. It is not yet clear which will prove the most efficient and most cost effective way to read long stretches of DNA. Major questions and considerations included whether the sequence of the human genome should be done randomly, in the expectation that all the pieces would fit together eventually, or whether to sequence portions of the genome that are already known to be of biochemical interest and responsible for common genetic diseases. Should one chromosome being studied at a time and should any massive sequencing be done with present technology or delayed until more rapid, automated techniques will become available. Some scientist have argued that the conventional approach of first identifying an important gene, then cloning and studying it, is scientifically more interesting and more cost-effective over the long term. Supporters of the project argue that many important genes that might be very difficult to identify will be uncovered in the course of the investigation. Even apparently nonfunctional DNA ("junk DNA") may turn out to be important. There is considerable debate about whether wholesale sequencing is worth the billions of dollars it is likely to cost, especially since other projects will necessarily go unfunded to allow this initiative, and it will mean a huge redirection of talent from other genetic engineering projects. Keeping in mind that the human genome contains three billion gene pairs it was estimated in 1986 that one skilled person could sequence 100,000 base pairs per year at an average cost of \$1/base pair. Many genes known to be responsible for genetic diseases are being studied, and many more already being uncovered appear to be associated with predispositions to diseases such as heart disease and cancer. In the long run, however, there seems little doubt that the human gene project, if fully carried out, will make possible many kinds of therapeutic intervention, and cast considerable light on chromosomal organization and evolution (Gottesman and Collins 1994).

Our knowledge about human genetics clearly expand at a great rate over the coming years. This fundamental understanding will permit control over many biological processes, and biological control will transform medicine, agriculture, animal husbandry, and pharmaceutical production. The project has already stimulated significant investment by large corporations and lead to the creation of new companies hoping to capitalize on the project's profound and inestimable implications. Great desire exists among biotechnology companies to acquire efficient technologies such as the genome-driven drug discovery. An understanding of human DNA certainly will be an important key in understanding a host of human diseases. Cancers, in particular, are now being understood as genetic diseases, since cancerous growths arise from either acquired or hereditary changes in cellular DNA. Once we know how altered DNA induces cancer development, effective tools can be developed to prevent or treat malignant growths. It is important that this knowledge will be used well, and not to stigmatize or discriminate, but to improve human health.

The HGP should illuminate fundamental functions of the body and become invaluable basis for genomic technology; however it will primarily open a fascinating area for exploration. A large portion of the value of the projects rests on the expansion of our basic understanding of biological life in general and the explicit promise of the relief of suffering from the more than 4,000 genetic hereditary diseases (i.e. Huntington disease and cystic fibrosis) either through prevention or cure. Understanding of the human genome will have an enormous impact on the ability to assess risk posed to individuals by exposure to toxic agents and scientists know that genetic differences make some people more susceptible and others more resistant to such agents. Far more research work will be needed to determine the genetic basis of variability. This knowledge addresses the DOE's goal to understand the effects of low level exposures to radiation and other energy-related agents, especially in terms of cancer risk.

The advantage of the Human Genome Project has been the recognition that it attracted extra funding to the work, raised the profile of the effort within the scientific communities, and provided elements of organization

and cooperation that would not have occurred with individual scientists pursuing projects based on their personal interest. Scientists have begun to complete mapping of the total informational content of the human genome, a major coordinated international effort and challenge with the United States taking the leading role so far. Mapping is the process of determining the position and spacing of genes, or other genetic landmarks, on the chromosomes relative to one another. There are basically two types of maps, genetic and physical, which differ in the methods used to construct them and in the metric that is used to measure the distance between genes. The introduction of DNA markers, such as restriction fragment length polymorphisms (RFLPs) to detect genetic variation among individuals. Such markers are relatively easy to find in large numbers and have been used to construct genetic maps. A complete map of the human genome was completed in 1994 with additional work still being necessary to identify more markers. Emphasis is now on sequencing the human genome. The HGP's continued emphasis is on obtaining a complete and highly accurate reference sequence (1 error in 10,000 bases) that is largely continuous across each human chromosome. Scientists believe that knowing this sequence is critically important for understanding human biology and for applications in other fields.

Craig Venter is the president of Celera Genomics that is on its way of becoming one of the largest DNA sequencing center in the world. He claims that his team will finish the DNA sequence of the entire human genome in just 18 months, finishing it by the end of 2001 instead of 2005 and at a cost ten times less than the publicly funded project. Celera does not plan to make all its sequence data immediately available, although Venter has said scientists will have free access to parts of it. Celera plans to patent several hundred human genes and a large set of human single nucleotide polymorphisms for use in individually tailored medicine by pharmaceutical companies.

Large-scale human DNA sequencing was not initiated until 1996, after preliminary mapping had been accomplished. Genetic DNA sequencing had been a tremendously labor intense process until now. What sets Venter's business apart is its scale and promised high speed sequencing robots that determine the precise order of nucleotide bases in DNA in a steady flow of data-signals representing the DNA bases A, C, G, and T. However, opponents of Venter's promises believe that such "whole-genome shotgun" would leave over 100,000 serious gaps in Venter's human genome project. This type of cloning ignores mapping the genome-defining molecular landmarks that will allow sequence data to be assembled correctly. Venter's technique breaks the genome in millions of overlapping fragments and determines part of the sequence of chemical units within each fragment. Computer programs then put these pieces together to recreate the sequence of the genome. Some scientists believe that the whole genome shotgun cloning could degrade the quality of data, and that the publicly funded HGP would reduce standards in accuracy and completion to keep pace. Unlike Venter's process, the public consortium's approach is to break a chromosome down into large overlapping fragments which then will be studied to find out the region on the chromosome from which each fragment comes. This process is known as mapping. The number of mapped human genes is rapidly increasing. About one-fifth of all protein-coding genes in our genome, most of them associated with specific diseases or predispositions, were defined, usually by positional cloning. Even after the HGP is completed and all the genes are mapped and sequenced, it will take years of intense and careful work to understand the interaction of multiple genes in producing complex, polygenic conditions and traits.

Significant information about the content of the human genome and differential expression in various tissues has been derived from partial cDNA sequences, called expressed sequenced tags (ESTs). Analysis of EST sequences in the public domain now indicates that over 40,000 unique cDNAs have been sequenced, which represents a significant number of the estimated 50,000-100,000 human genes. Until the human genome is completed, EST databases will be an important drug discovery tool to identify and clone disease genes and to study gene expression. Many scientists felt that mapping and sequencing should be an international effort since there is only one human species and the results of analyzing human genome will be useful for all of us. In Germany, there is a widespread opposition to learning a lot about human genetics before regulations have been established to prevent misuse of the information. The Hitler Nazi regime in Germany between 1933 and 1945 killed millions of Jews, Gypsies, mental patients, and disabled people in concentration camps in the name of the pseudoscience eugenics. Any suggestion that eugenic improvements may be feasible, as a result of gained knowledge from the HGP, are alarming signs and create strong objections to the sequencing of human genome. That eugenics philosophy which lead to the horrors of National Socialism in Germany have made many people appropriately sensitive to the potential abuses of genetic science. Some people fear that once we have the tools to "play around" with our genes, we may be tempted to use them to design a "super" race of human beings. Beyond abuses, there are basic problems in the application of genetic knowledge in medicine and society related to the benefits and harms of testing and screening, issues of privacy and confidentiality issues of regulation, and issues of justice in access to the powerful new tools.

The HGP will provide knowledge, which will offer a new era of molecular medicine characterized not by treating symptoms, but rather looking to the deepest causes of diseases. Rapid and more accurate diagnostic tests (genetic screening) will make possible earlier treatment for countless diseases. Even more promising, insight into genetic susceptibilities to disease and to environmental impacts coupled with preventive gene therapy will become possible and in some cases actually "fix" genetic errors before they can trigger the disease. A technique that uses short strands of genetic material, known as DNA probes, will be used to detect normal and abnormal genes for diagnostic and screening purposes, and gene therapy will be used to transfer genes into cells to repair, alter or enhance their function. The ability of exploiting such genetic technologies to diagnose, cure and alter the course of diseases results from the identification of all human genes and understanding of their specific functions.

A great deal of the work to date on the ethical, legal, and social implications of the HGP has focused on genetic testing. Patients who can afford the expenditure for genetic testing can simply buy the service they desire even if it is not covered by their public or private insurance plan. This would classify people and benefit only those people who can afford wealth-based access. Genetic information can be complex and difficult to understand, leading people to misunderstand the results. Therefore genetic testing and its predictive power must be supported by careful counseling. Insurers may require applicants for insurance to be tested to determine their susceptibility to genetic disorders. Positive results can lead health insurers to refuse to insure the individual, to charge prohibitively high premiums. Positive test results also can prevent the individual from obtaining life insurance, or at least from being able to purchase a policy at an affordable price. Employers may show interests in genetic information similar to those to health insurers. Employers may refuse to hire people with genetic tendency to develop disease in order to avoid having to pay the cost of the future treatment. For the same reason, a positive genetic test result may cause an employer to try to fire a current employee. Employers also may fear that an affected employee may create safety risks for customers or other employees, if the disorder is one that, like Huntington's disease, can diminish coordination and judgement. Family members may seek another member's test results in order to learn if they themselves are at risk. This information can be beneficial to the family or can destroy family relationships. Young couples (prospective mates) may insist on genetic testing before they will agree to become married in the first place. But one must not overlook the tremendous benefits that genetic testing potentially can provide. Even if the genetic disorder cannot be treated, knowledge of one's risk can enable an individual to make important decisions in areas of family planning, reproduction, financial planning, and life-style choices.

### **Thoughts on eugenics:**

Eugenics is a movement that is aimed at improving the genetic composition of the human race. Historically, eugenicists advocated selective breeding to achieve these goals. Today we have technologies that make it possible to more directly alter the genetic composition of an individual. However, people differ in their views on how to best (and ethically) use this technology. In 1883, Sir Francis Galton, a respected British scholar and cousin of Charles Darwin, first used the term eugenics, meaning "well-born." Galton believed that the human race could help direct its future by selectively breeding individuals who have "desired" traits. This idea was based on Galton's study of upper class Britain. Following these studies, Galton concluded that an elite position in society was due to a good genetic makeup. While Galton's plans to improve the human race through selective breeding never came to fruition in Britain, they eventually took sinister turns in other countries. The eugenics movement began in the U.S. in the late 19<sup>th</sup> century. However, unlike in Britain, eugenicists in the U.S. focused on efforts to stop the transmission of negative or "undesirable" traits from generation to generation. In response to these ideas, some US leaders, private citizens, and corporations started funding eugenical studies. This led to the 1911 establishment of The Eugenics Records Office (ERO) in Cold Spring Harbor, New York. The ERO spent time tracking family histories and concluded that people deemed to be unfit more often came from families that were poor, low in social standing, immigrant, and/or **minority**. Further, ERO researchers "demonstrated" that the undesirable traits in these families, such as pauperism, were due to genetics, and not lack of resources.

Committees were convened to offer solutions to the problem of the growing number of "undesirables" in the U.S. population. Stricter immigration rules were enacted, but the most ominous resolution was a plan to sterilize "unfit" individuals to prevent them from passing on their negative traits. During the 20<sup>th</sup> century, a total of 33 states had sterilization programs in place. While at first sterilization efforts targeted mentally ill people exclusively, later the traits deemed serious enough to warrant sterilization included alcoholism, criminality chronic poverty, blindness, deafness, feeble-mindedness, and promiscuity. It was also not uncommon for

African American women to be sterilized during other medical procedures without consent. Most people subjected to these sterilizations had no choice, and because the program was run by the government, they had little chance of escaping the procedure. It is thought that around 65,000 Americans were sterilized during this time period. The eugenics movement in the U.S. slowly lost favor over time and was waning by the start of World War II. When the horrors of Nazi Germany became apparent, as well as Hitler's use of eugenic principles to justify the atrocities, eugenics lost all credibility as a field of study or even an ideal that should be pursued.

According to Richard Lynn, eugenics may be divided into two main categories based on the ways in which the methods of eugenics can be applied.<sup>[65]</sup>

## 1. Classical Eugenics

### 1. Negative eugenics by provision of information and services, i.e. reduction of unplanned pregnancies and births.

1. "Just say no" campaigns
2. Sex education in schools
3. School-based clinics
4. Promoting the use of contraception
5. Emergency contraception
6. Research for better contraceptives
7. Sterilization
8. Abortion

### 2. Negative eugenics by incentives, coercion and compulsion

1. Incentives for sterilization
2. The Denver Dollar-a-day program, i.e. paying teenage mothers for not becoming pregnant again
3. Incentives for women on welfare to use contraceptions
4. Payments for sterilization in developing countries
5. Curtailment of benefits to welfare mothers
6. Sterilization of the "mentally retarded"
7. Sterilization of female criminals
8. Sterilization of male criminals

### 3. Licences for parenthood

### 4. Positive eugenics

1. Financial incentives to have children
2. Selective incentives for childbearing
3. Taxation of the childless
4. Ethical obligations of the elite
5. Eugenic immigration.

## 2. New Eugenics

1. Artificial insemination by donor.
2. Egg donation.
3. Prenatal diagnosis of genetic disorders and pregnancy terminations of defective fetuses.
4. Embryo selection.
5. Genetic engineering
6. Gene therapy
7. Cloning.

A common criticism of eugenics is that "it inevitably leads to measures that are unethical". Historically, this statement is evidenced by the obvious control of one group imposing its agenda on minority groups. This includes programs in England, Germany, and America targeting various groups, including Jews, homosexuals, Muslims, Romani, the homeless, and those with intellectual disabilities.

Many of the ethical concerns from eugenics arise from the controversial past, prompting a discussion on what place, if any, it should have in the future. Advances in science have changed eugenics. In the past, eugenics has had more to do with sterilization and enforced reproduction laws (i.e. no inter-racial marriage and marriage restrictions based on land ownership). Now, in the age of a progressively mapped genome, embryos can be tested for susceptibility to disease, gender, and genetic defects, and alternative methods of reproduction such as in vitro fertilization are becoming more common. In short, eugenics is no longer ex post facto regulation of the living but instead preemptive action on the unborn. With this change, however, there are ethical concerns which lack adequate attention, and which must be addressed before eugenic policies can be properly implemented in the future. Sterilized individuals, for example, could volunteer for the procedure, albeit under incentive or duress, or at least voice their opinion. The unborn fetus on which these new eugenic procedures are performed cannot speak out, as the fetus lacks the voice to consent or to express his or her opinion. The ability to manipulate a fetus and determine who the child will be is something questioned by many of the opponents of, and even proponents for, eugenic policies.

Societal and political consequences of eugenics call for a place in the discussion on the ethics behind the eugenics movement. Public policy often focuses on issues related to race and gender, both of which could be controlled by manipulation of embryonic genes; eugenics and political issues are interconnected and the political aspect of eugenics must be addressed. Laws controlling the subjects, the methods, and the extent of eugenics will need to be considered in order to prevent the repetition of the unethical events of the past. Most of the ethical concerns about eugenics involve issues of morality and power. Decisions about the morality and the control of this new science (and the subsequent results of the science) will need to be made as eugenics continue to influence the development of the science and medical fields. Eugenic policies could also lead to loss of genetic diversity, in which case a culturally accepted "improvement" of the gene pool could very likely—as evidenced in numerous instances in isolated island populations (e.g., the dodo, *Raphus cucullatus*, of Mauritius)—result in extinction due to increased vulnerability to disease, reduced ability to adapt to environmental change, and other factors both known and unknown. A long-term species-wide eugenics plan might lead to a scenario similar to this because the elimination of traits deemed undesirable would reduce genetic diversity by definition.

Edward M. Miller claims that, in any one generation, any realistic program should make only minor changes in a fraction of the gene pool, giving plenty of time to reverse direction if unintended consequences emerge, reducing the likelihood of the elimination of desirable genes. Miller also argues that any appreciable reduction in diversity is so far in the future that little concern is needed for now. While the science of genetics has increasingly provided means by which certain characteristics and conditions can be identified and understood, given the complexity of human genetics, culture, and psychology there is at this point no agreed objective means of determining which traits might be ultimately desirable or undesirable. Some diseases such as sickle-cell disease and cystic fibrosis respectively confer immunity to malaria and resistance to cholera when a single copy of the recessive allele is contained within the genotype of the individual. Reducing the instance of sickle-cell disease genes in Africa where malaria is a common and deadly disease could indeed have extremely negative net consequences.

However, some genetic diseases such as haemochromatosis can increase susceptibility to illness, cause physical deformities, and other dysfunctions, which provides some incentive for people to re-consider some elements of eugenics. Autistic people have advocated a shift in perception of autism spectrum disorders as complex syndromes rather than diseases that must be cured. Proponents of this view reject the notion that there is an "ideal" brain configuration and that any deviation from the norm is pathological; they promote tolerance for what they call neurodiversity. Baron-Cohen argues that the genes for Asperger's combination of abilities have operated throughout recent human evolution and have made remarkable contributions to human history. The possible reduction of autism rates through selection against the genetic predisposition to autism is a significant political issue in the autism rights movement, which claims that autism is a part of neurodiversity.

Many culturally Deaf people oppose attempts to cure deafness, believing instead deafness should be considered a defining cultural characteristic not a disease. Some people have started advocating the idea that deafness brings about certain advantages, often termed "Deaf Gain". The heterozygote test is used for the early detection

of recessive hereditary diseases, allowing for couples to determine if they are at risk of passing genetic defects to a future child. The goal of the test is to estimate the likelihood of passing the hereditary disease to future descendants. Recessive traits can be severely reduced, but never eliminated unless the complete genetic makeup of all members of the pool was known, as aforementioned. As only very few undesirable traits, such as Huntington's disease, are dominant, it could be argued from certain perspectives that the practicality of "eliminating" traits is quite low. There are examples of eugenic acts that managed to lower the prevalence of recessive diseases, although not influencing the prevalence of heterozygote carriers of those diseases. The elevated prevalence of certain genetically transmitted diseases among the Ashkenazi Jewish population (Tay-Sachs, cystic fibrosis, Canavan's disease, and Gaucher's disease), has been decreased in current populations by the application of genetic screening

Pleiotropy occurs when one gene influences multiple, seemingly unrelated phenotypic traits, an example being phenylketonuria, which is a human disease that affects multiple systems but is caused by one gene defect. Andrzej Pękalski, from the University of Wrocław, argues that eugenics can cause harmful loss of genetic diversity if a eugenics program selects for a pleiotropic gene that is also associated with a positive trait. Pekalski uses the example of a coercive government eugenics program that prohibits people with myopia from breeding but has the unintended consequence of also selecting against high intelligence since the two go together. Among institutions, the Catholic Church was an opponent of state-enforced sterilizations. Attempts by the Eugenics Education Society to persuade the British government to legalise voluntary sterilisation were opposed by Catholics and by the Labour Party. The American Eugenics Society initially gained some Catholic supporters but Catholic support declined following the 1930 papal encyclical *Casti connubii*. In this, Pope Pius XI explicitly condemned sterilization laws: "Public magistrates have no direct power over the bodies of their subjects; therefore, where no crime has taken place and there is no cause present for grave punishment, they can never directly harm, or tamper with the integrity of the body, either for the reasons of eugenics or for any other reason.

#### **Uses of human genetic information:**

Unprecedented progress in identifying and understanding the 50,000 to 100,000 or so genes that make up the human genome provides an opportunity for scientists to develop strategies to prevent or reduce the effects of genetic disease. Scientists have shown that straightforward inherited errors in our genes are responsible for an estimated 3,000 to 4,000 diseases, including Huntington's disease, cystic fibrosis, neurofibromatosis, and Duchenne muscular dystrophy. More complex inheritance of multiple genetic errors also can increase an individual's risk of developing common disorders such as cancer, heart disease, and diabetes. Genetic technologies, such as simple DNA tests, increasingly are becoming available to identify people who might have an increased likelihood of developing a disorder. The majority of diseases Americans encounter, however, do not result solely from genetic predisposition but from the interaction of genes with environmental factors, including occupation, diet, and lifestyle. Consequently, genetic tests alone cannot predict with certainty whether a person with a particular genetic error will in fact develop a disease. With tools from the Human Genome Project, a new gene discovery is reported nearly every week. For example, scientists recently reported the discovery of a genetic alteration that, in early studies, appears to double a person's risk of colon cancer. The genetic alteration, which can be identified with a \$200 blood test, is most prevalent among Jews of Eastern European descent. Once identified, people who carry this mutation can use regular colon examinations to detect cancer growth early when it is most easily treated.

Where effective means of early detection and treatment have been established, knowledge of genetic alterations can help a person prevent or reduce the likelihood of illness, and in some instances actually reduce health care costs. For example, genetic testing for hemochromatosis, glaucoma, and some cancers can alert the individual to begin preventive measures before the disease causes harm. There are several ways to gather genetic information. It can be deduced from a family's medical history or during a physical examination. Routine laboratory tests that measure the body's output of specific substances might also suggest the genetic make-up of the individual. But the most direct approach to obtaining genetic information is through analysis of DNA, the material that makes up genes. Such genetic tests identify specific DNA features in people who have already developed a disease, in healthy people who may be at risk of developing a genetic disorder later in life, or in people who are at risk of having a child with an inherited disorder. Thus, genetic information includes information about genes, gene products, and inherited characteristics that may derive from individuals or their family members.

While genetic technology increases the ability to detect and prevent health disorders, it can also be misused to discriminate against or stigmatize individuals. A 1996 survey of individuals at risk of developing a genetic condition and parents of children with specific genetic conditions identified more than 200 cases of genetic discrimination among the 917 people who responded. The cases involved discrimination by insurance companies, employers, and other organizations that use genetic information. Another recent survey of genetic counselors, primary care physicians, and patients, identified 550 people who had been denied employment or insurance based on their genetic predisposition to an illness. In addition, because an individual's genetic information has implications for his or her family members and future generations, misuse of genetic information could have intergenerational effects that are far broader than any individual incident of misuse. Many Americans are reluctant to take advantage of new breakthroughs in genetic testing for fear that the results will not be used to improve their health but rather to deny them jobs or health insurance. A 1995 Harris poll of the general public found that over 85 percent of those surveyed indicated they were very concerned or somewhat concerned that insurers or employers might have access to and use genetic information. Sixty-three percent of the participants in a 1997 national telephone survey of more than 1000 people reported that they would not take genetic tests for diseases if health insurers or employers could get access to the results. Eighty-five percent felt that employers should be prohibited from obtaining information about an individual's genetic conditions, risks, and predispositions.

Researchers conducting a multi-year Pennsylvania study designed to understand how to keep women with breast cancer gene mutations healthy reported that nearly one-third of the high-risk women invited to participate in the study refused because they feared discrimination or a loss of privacy. Another study of 332 people who belonged to support groups for families with genetic disorders found that fear of genetic discrimination resulted in 17 percent of the participants not revealing genetic information to employers. In addition, people have hidden genetic information about themselves due to fear of the effects of disclosure. For example, an 18-year-old man, at risk for inheriting Huntington's disease from one of his parents, who wished to enlist in the Marines to serve in the Persian Gulf War, believed that knowledge of his risk status would disqualify him from service, even though it was unlikely that he would become symptomatic during his tour of duty. He therefore answered "no" to questions regarding hereditary disorders on his application and did not include Huntington's disease in his family medical history. Another individual whose parent died of Huntington's disease also chose to hide the truth from his employer. Fearing adverse consequences at work if this cause of death was known, the individual arranged for the diagnosis of asphyxiation to be reported as the cause of death to avoid mention of the disease in an obituary. Fear of genetic discrimination and the consequences of this fear have been reported in both the scientific literature and the popular press.

Genetic changes are not always heritable such as chromosomal damage have been associated with exposure to radiation and some chemical mutagens or carcinogens, little is known about which changes are predictive of subsequent disease risk. Much more research is required to establish the relationship, if any, between those changes and subsequent disease risk for affected populations and individuals. For this reason, use of genetic monitoring results to make employment decisions is rarely justifiable. In addition, some employers may seek to use genetic tests to discriminate against workers - even those who have not yet or who may never show signs of disease-because the employers fear the cost consequences. Based on genetic information, employers may try to avoid hiring workers who they believe are likely to take sick leave, resign, or retire early for health reasons, file for workers' compensation, or use health care benefits excessively. A 1989 survey of large businesses, private utilities, and labor unions found that 5 percent of the 330 organizations responding conducted genetic screening or monitoring of its workers. Another 1989 survey of 400 firms, conducted by Northwestern National Life Insurance, found that 15 percent of the companies planned, by the year 2000, to check the genetic status of prospective employees and their dependents before making employment offers. Thus, there is evidence that genetic information continues to be used to discriminate against qualified workers. The economic incentive to discriminate based on genetic information is likely to increase as genetic research advances and the costs of genetic testing decrease.

Genetic predisposition or conditions can lead to workplace discrimination, even in cases where workers are healthy and unlikely to develop disease or where the genetic condition has no effect on the ability to perform work. As a result, real people are denied employment opportunities. One individual was screened and learned he was a carrier of a single mutation for Gaucher's disease. His carrier status indicates that he might pass this mutation to his children, but not that he would develop Gaucher's disease himself. He revealed this information when applying for a job and was denied the job because of his genetic mutation, even though it had no bearing on his present or future ability to perform a job. A 53-year-old man at a job interview with an insurance company revealed that he had hemochromatosis but was asymptomatic. During the second interview, he was told that the company was interested in hiring him but would not be able to offer him health insurance because

of his genetic condition. He agreed to this arrangement. During his third interview, the company representative told him that they would like to hire him, but were unable to do so because of his genetic condition.

An employee's parent developed Huntington's disease-indicating that the employee had a 50 percent chance of inheriting the mutated gene that would cause her to develop the disease. She decided to be tested. A genetic counselor advised her to secure life and health insurance before testing, because a positive test result would not only mean that she would get the disease but would probably prevent her from obtaining insurance as well. A co-worker who overheard her making arrangements to be tested reported the employee's conversations to their boss. Initially, the boss seemed empathetic and offered to help. When the employee eventually shared the news that her test results indicated that she did carry the mutated gene, she was fired from her job. In the 8-month period prior to her termination, she had received three promotions and outstanding performance reviews. Frightened by their sister's experience, none of her siblings are willing to undergo genetic testing for fear of losing health insurance or jobs. Consequently, they must live with the uncertainty of not knowing whether they have inherited the genetic trait that leads to Huntington's disease. There is no scientific evidence to substantiate a relationship between unexpressed genetic factors and an individual's ability to perform his or her job. Thus, most expert groups recommend prohibiting or severely restricting the use of genetic testing and access to genetic information in the workplace. The American Medical Association's (AMA) Council on Ethical and Judicial Affairs concludes that it is inappropriate to exclude workers with genetic risks for disease from the workplace because of that risk. In the future, however, the AMA Council acknowledges there may be an appropriate but limited role for genetic testing in certain situations to protect workers who have a genetic susceptibility to occupational illness when health risks can be accurately predicted by the test. The National Action Plan on Breast Cancer (NAPBC) and the National Institutes of Health-Department of Energy Working Group on Ethical, Legal and Social Implications of Human Genome Research also has drafted recommendations for state and federal policy makers to protect against genetic discrimination in the workplace. Generally, the recommendations limit the collection, disclosure, and use of genetic information and support strong enforcement of these limitations through governmental agencies or private right of action. Exceptions are made for possible situations in the future that may arise if testing is shown to be scientifically valid to predict occupational risk and situations where an individual is unable to meet the performance requirements of a job.

There are no federal laws that directly and comprehensively protect against abuses in the gathering or use of genetic information in the workplace. A few protections exist incidentally under federal laws enacted to address other types of workplace discrimination. The incidental federal protections against workplace discrimination based on genetic information that do exist are narrow in scope and, in large measure, not well established. They are not sufficient to provide Americans with adequate protection against genetic discrimination in the workplace. States continue to enact legislation in response to growing concern over the specter of genetic discrimination in the workplace. Existing state laws, however, differ in coverage, protections afforded, and enforcement schemes. Federal leadership is necessary to ensure that all workers are protected against discrimination based on genetic information. The only federal law that directly addresses the issue of genetic discrimination is the 1996 Health Insurance Portability and Accountability Act (HIPAA). HIPAA prohibits group health plans from using any health status-related factor, including genetic information, as a basis for denying or limiting eligibility for coverage or for charging an individual more for coverage. In addition, the Administration has worked closely with Congress on legislation that would prevent an insurance company or HMO from disclosing genetic information or charging an entire plan or group more for health insurance on the basis of genetic information. These efforts, however, do not address the larger problems of the gathering or use of genetic information in the workplace outside of the health insurance context.

The most likely current source of protection against genetic discrimination in the workplace is provided by laws prohibiting discrimination based on disability. Title I of the Americans with Disabilities Act (ADA), enforced by the Equal Employment Opportunity Commission (EEOC), and similar disability-based anti-discrimination laws, such as the Rehabilitation Act of 1973, do not explicitly address genetic information, but they provide some protections against disability-related genetic discrimination in the workplace. Under the ADA, individuals with symptomatic genetic disabilities have the same protections against discrimination as individuals with other disabilities. However, as we make new advances in genetics, this protection will not be sufficient. More and more people will be vulnerable to genetic discrimination based on unexpressed genetic conditions that do not fall within the clear disability-based discrimination prohibitions of the ADA. Protection against discrimination based on genetic information for those who do not currently have a symptomatic genetic disability is not well established. Individuals who do not currently have a symptomatic genetic disorder and, therefore, may not be protected against discrimination as a currently disabled person include unaffected carriers of a disease who may never get the disease themselves, individuals with late-onset genetic disorders who may be identified through

genetic testing as being at high risk of developing the disease, and others who are identified through family history as being at high risk of developing the disease.

The EEOC has tried to provide ADA protection to individuals who do not have symptomatic genetic disabilities but who may be subject to discrimination based on genetic information. In 1995 the EEOC issued enforcement guidance advising that an employer who takes adverse action against an individual on the basis of genetic information relating to illness, disease, or other disorders regards that individual as having a disability within the meaning of the ADA. The ADA prohibits discrimination against a person who is regarded as having a disability. The guidance, however, is limited in scope and legal effect. It is policy guidance that does not have the same legally binding effect on a court as a statute or regulation and has not been tested in court. Moreover, many cases based on the argument that an employer has discriminated against workers by regarding them as disabled have not been well-received by the courts. In addition, the ADA does not protect workers from requirements or requests to provide genetic information to their employers. Under the ADA, an employer generally may not make medical inquiries about a job applicant prior to extending a conditional offer of employment. However, once a conditional offer of employment has been extended, but before the individual begins work, the employer may obtain extensive medical information about the applicant, including genetic information. During this period an employer could, for example, obtain and store genetic samples of job applicants, require genetic screening as a condition of employment, or purchase genetic information about applicants from a genetic information data bank. In addition, once the applicant is hired the employer may request medical information that is job related and consistent with business necessity.

It is difficult to ensure that medical information is not used to discriminate. Detecting discrimination based on genetic information, which indicates a risk rather than a manifestation of disease, is particularly difficult. As a result, genetic information could be used to deny workers employment or opportunities regardless of their ability to do the job. This concern is especially significant because of the rapid advances in genetic research. For instance, genetic information obtained today may, in the future, be found to indicate a risk factor that could be the basis for discrimination. Moreover, this information also could be used to predict the health risks of an individual's family members - creating the potential that genetic information could be used to discriminate against future generations of workers. Another federal law that may incidentally provide protection against some forms of genetic discrimination is Title VII of the Civil Rights Act of 1964. An argument could be made that genetic discrimination based on racially or ethnically linked genetic disorders constitutes unlawful race or ethnicity discrimination. Protection under Title VII, however, is only available where an employer engages in discrimination against a particular racial or ethnic group based on a genetic trait that is substantially related to a race or ethnic group. Since a strong nexus between race or national origin has been established for only a few diseases, Title VII will not be an effective tool for combating most forms of genetic discrimination. Thus, it is clear that current anti-discrimination laws would not adequately address the issue of genetic-based discrimination in employment.

A number of states have addressed the issue of genetic discrimination in employment through state legislation. As of October 1997, 14 states had enacted laws to provide protections against various forms of genetic discrimination in the workplace. There are wide variations among these state laws. Some of the first state laws enacted to address this issue prohibited discrimination against individuals with specific genetic traits or disorders, such as the sickle-cell trait (Florida and Louisiana) or the hemoglobin trait (North Carolina). Later laws cover broader categories of genetic traits and disorders. For example, a 1981 New Jersey statute (later broadened) prohibits discrimination in employment based on an "atypical hereditary cellular or blood trait," and a New York law prohibits employers from denying equal employment opportunities based on "unique genetic disorders." Other state laws regulate both the use of genetic testing in employment decisions and the disclosure of genetic test results. These state laws generally prohibit employers from requiring workers and applicants to undergo genetic testing as a condition of employment. For example, Oregon state law prohibits employers from using genetic information to distinguish between or discriminate against applicants and employees and prohibits employers from subjecting applicants and employees to genetic testing. A recently enacted Texas law prohibits employers, labor organizations, licensing agencies, and employment agencies from discriminating against any individual on the basis of the results of a genetic test or because of the individual's refusal to submit to genetic testing. Some states permit genetic testing when it is requested by the worker or applicant for the purpose of investigating a worker's compensation claim or determining the workers' susceptibility to potentially toxic chemicals in the workplace. These statutes often require the worker to provide informed written consent for such testing and contain specific restrictions governing disclosure and prevent the employer from taking adverse action against the employee.

Given the substantial gaps in state and federal protections against employment discrimination based on genetic information, comprehensive federal legislation is needed to ensure that advances in genetic technology and research are used to address the health needs of the nation-and not to deny individuals employment opportunities and benefits. Federal legislation would establish minimum protections that could be supplemented by state laws. The need for federal protection has been recognized by Congress with the introduction of numerous bills with bipartisan support. Three stand-alone bills have been introduced that amend existing civil rights or labor laws to protect workers against employment discrimination based on genetic information. Two additional bills have been introduced that include worker protections against discrimination based on genetic information, as part of broader proposals addressing the use of genetic information. Federal legislation is needed to ensure that knowledge gained from genetic research is fully utilized to improve the health of Americans and not to discriminate against workers. This legislation should provide a floor or minimum level of protection and allow existing state laws to provide greater protection. Workers should not be forced to avoid tests that can help prevent disease because of fear of discrimination. At the same time, we must preserve the ability of scientists to continue the research, including studies of occupational health and safety that is so vital to expanding our knowledge of genetics and health. The Administration proposes that Congress pass a law to ensure that discoveries made possible by the Human Genome Project are used to improve health and not to discriminate against workers or their families. Legislation generally should include the following basic protections against misuse of genetic information in the workplace.

Employers should not require or request that employees or potential employees take a genetic test or provide genetic information as a condition of employment or benefits. Employers should not use genetic information to discriminate against, limit, segregate, or classify employees in a way that would deprive them of employment opportunities. Employers should not obtain or disclose genetic information about employees or potential employees under most circumstances. Genetic testing and the use of genetic information by employers should be permitted in the following situations to ensure workplace safety and health and to preserve research opportunities. However, in all cases where genetic information about employees is obtained, the information should be maintained in medical files that are kept separate from personnel files, treated as confidential medical records, and protected by applicable state and federal laws. An employer should be permitted to monitor employees for the effects of a particular substance found in the workplace to which continued exposure could cause genetic damage under certain circumstances. Informed consent and assurance of confidentiality should be required. In addition, employers may only use the results to identify and control adverse conditions in the workplace and to take action necessary to prevent significant risk of substantial harm to the employee or others. The statutory authority of a federal agency or contractor to promulgate regulations, enforce workplace safety and health laws, or conduct occupational or other health research should not be limited. An employer should be able to disclose genetic information for research and other purposes with the written, informed consent of the individual.

These recommendations should apply to public and private-sector employers, unions, and labor-management groups that conduct joint apprenticeship and other training programs. Employment agencies and licensing agencies that issue licenses, certificates, and other credentials required to engage in various professions and occupations also should be covered. Individuals who believe they have been subjected to workplace discrimination based on genetic information should be able to file a charge with the Equal Employment Opportunity Commission, Department of Labor or other appropriate federal agency for investigation and resolution. The designated agency should be authorized to bring lawsuits in the federal courts to resolve those issues that would not settle amicably. The courts should have the authority to halt the violations and order relief, such as hiring, promotion, back pay and compensatory and punitive damages, to the individual. Alternatively, an individual should be able to elect to bring a private lawsuit in federal or state court to obtain the same type of relief plus reasonable costs and attorney's fees. In order to enforce these protections, the designated enforcement agency must be given sufficient additional resources to investigate and prosecute allegations of discrimination.

### **Genetic Diagnosis:**

Genetic testing is a type of medical test that identifies changes in chromosomes, genes, or proteins. This test helps in the diagnosis of various genetic diseases. The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person's chance of developing or passing on a genetic disorder. More than 1,000 genetic tests are currently in use, and more are being developed. Several methods can be used for genetic testing:

- Molecular genetic tests (or gene tests) study single genes or short lengths of DNA to identify variations or mutations that lead to a genetic disorder.

- Chromosomal genetic tests analyze whole chromosomes or long lengths of DNA to see if there are large genetic changes, such as an extra copy of a chromosome, that cause a genetic condition.
- Biochemical genetic tests study the amount or activity level of proteins; abnormalities in either can indicate changes to the DNA that result in a genetic disorder.

Genetic testing is voluntary. Because testing has benefits as well as limitations and risks, the decision about whether to be tested is a personal and complex one. A geneticist or genetic counsellor can help by providing information about the pros and cons of the test and discussing the social and emotional aspects of testing.

### **Genetic screening:**

Genetic testing is "the analysis of chromosomes (DNA), proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes." It can provide information about a person's genes and chromosomes throughout life. Available types of testing include:

Newborn screening is used just after birth to identify genetic disorders that can be treated early in life. A blood sample is collected with a heel prick from the newborn 24-48 hours after birth and sent to the lab for analysis. Newborn screening varies state by state, but all states by law test for at least 21 disorders. If abnormal results are obtained, it does not necessarily mean the child has the disorder. Diagnostic tests must follow the initial screening to confirm the disease. The routine testing of infants for certain disorders is the most widespread use of genetic testing, millions of babies are tested each year in the United States. All states currently test infants for phenylketonuria (a genetic disorder that causes mental illness if left untreated) and congenital hypothyroidism (a disorder of the thyroid gland). People with PKU do not have an enzyme needed to process the amino acid phenylalanine, which is responsible for normal growth in kids and normal protein use throughout their lifetime. If there is a build up of too much phenylalanine, brain tissue can be damaged, causing developmental delay. Newborn screening can detect the presence of PKU, allowing kids to get put on a special diet right away to avoid the effects of the disorder.

Diagnostic testing is used to diagnose or rule out a specific genetic or chromosomal condition. In many cases, genetic testing is used to confirm a diagnosis when a particular condition is suspected based on physical mutations and symptoms. Diagnostic testing can be performed at any time during a person's life, but is not available for all genes or all genetic conditions. The results of a diagnostic test can influence a person's choices about health care and the management of the disease. For example, people with a family history of polycystic kidney disease (PKD) who experience pain or tenderness in their abdomen, blood in their urine, frequent urination, pain in the sides, a urinary tract infection or kidney stones may decide to have their genes tested and the result could confirm the diagnosis of PKD. Carrier testing is used to identify people who carry one copy of a gene mutation that, when present in two copies, causes a genetic disorder. This type of testing is offered to individuals who have a family history of a genetic disorder and to people in ethnic groups with an increased risk of specific genetic conditions. If both parents are tested, the test can provide information about a couple's risk of having a child with a genetic condition like cystic fibrosis.

Genetic testing procedures that are performed on human embryos prior to the implantation as part of an in vitro fertilization procedure. Pre-implantation testing is used when individuals try to conceive a child through in vitro fertilization. Eggs from the woman and sperm from the man are removed and fertilized outside the body to create multiple embryos. The embryos are individually screened for abnormalities, and the ones without abnormalities are implanted in the uterus.

Prenatal testing is used to detect changes in a fetus's genes or chromosomes before birth. This type of testing is offered to couples with an increased risk of having a baby with a genetic or chromosomal disorder. In some cases, prenatal testing can lessen a couple's uncertainty or help them decide whether to abort the pregnancy. It cannot identify all possible inherited disorders and birth defects, however. One method of performing a prenatal genetic test involves an amniocentesis, which removes a sample of fluid from the mother's amniotic sac 15 to 20

or more weeks into pregnancy. The fluid is then tested for chromosomal abnormalities such as Down syndrome (Trisomy 21) and Trisomy 18, which can result in neonatal or fetal death. Test results can be retrieved within 7–14 days after the test is done. This method is 99.4% accurate at detecting and diagnosing fetal chromosome abnormalities. Although there is a risk of miscarriage associated with an amniocentesis, the miscarriage rate is only 1/400. Another method of prenatal testing is Chorionic Villus Sampling (CVS). Chorionic villi are projections from the placenta that carry the same genetic makeup as the baby. During this method of prenatal testing, a sample of chorionic villi is removed from the placenta to be tested. This test is performed 10–13 weeks into pregnancy and results are ready 7–14 days after the test was done. Another test using blood taken from the fetal umbilical cord is percutaneous umbilical cord blood sampling.

Predictive and presymptomatic types of testing are used to detect gene mutations associated with disorders that appear after birth, often later in life. These tests can be helpful to people who have a family member with a genetic disorder but who have no features of the disorder themselves at the time of testing. Predictive testing can identify mutations that increase a person's chance of developing disorders with a genetic basis, such as certain types of cancer. For example, an individual with a mutation in *BRCA1* has a 65% cumulative risk of breast cancer. Hereditary breast cancer along with ovarian cancer syndrome is caused by gene alterations in the genes *BRCA1* and *BRCA2*. Major cancer types related to mutations in these genes are female breast cancer, ovarian, prostate, pancreatic, and male breast cancer. Li-Fraumeni syndrome is caused by a gene alteration on the gene *TP53*. Cancer types associated with a mutation on this gene include breast cancer, soft tissue sarcoma, osteosarcoma, leukemia and brain tumors. In the Cowden syndrome there is a mutation on the *PTEN* gene, causing potential breast, thyroid or endometrial cancer. Presymptomatic testing can determine whether a person will develop a genetic disorder, such as hemochromatosis, before any signs or symptoms appear. The results of predictive and presymptomatic testing can provide information about a person's risk of developing a specific disorder, help with making decisions about medical care and provide a better prognosis.

Type of genetic testing that determines the influence of genetic variation on drug response is known as pharmacogenomics. When a person has a disease or health condition, pharmacogenomics can examine an individual's genetic makeup to determine what medicine and what dosage would be the safest and most beneficial to the patient. In the human population, there are approximately 11 million single nucleotide polymorphisms (SNPs) in people's genomes, making them the most common variations in the human genome. SNPs reveal information about an individual's response to certain drugs. This type of genetic testing can be used for cancer patients undergoing chemotherapy. A sample of the cancer tissue can be sent in for genetic analysis by a specialized lab. After analysis, information retrieved can identify mutations in the tumor which can be used to determine the best treatment option.

Non-diagnostic testing includes:

- Forensic testing: Forensic testing uses DNA sequences to identify an individual for legal purposes. Unlike the tests described above, forensic testing is not used to detect gene mutations associated with disease. This type of testing can identify crime or catastrophe victims, rule out or implicate a crime suspect, or establish biological relationships between people (for example, paternity).
- Paternity testing: This type of genetic test uses special DNA markers to identify the same or similar inheritance patterns between related individuals. Based on the fact that we all inherit half of our DNA from the father, and half from the mother, DNA scientists test individuals to find the match of DNA sequences at some highly differential markers to draw the conclusion of relatedness.
- Genealogical DNA test: To determine ancestry or ethnic heritage for genetic genealogy
- Research testing: Research testing includes finding unknown genes, learning how genes work and advancing our understanding of genetic conditions. The results of testing done as part of a research study are usually not available to patients or their healthcare providers.

### **The possibility of genetic discrimination:**

Genetic discrimination occurs when people are treated differently by their employer or insurance company because they have a gene mutation that causes or increases the risk of an inherited disorder. Fear of discrimination is a common concern among people considering genetic testing. Several laws at the federal and state levels help protect people against genetic discrimination. In particular, a federal law called the Genetic Information Nondiscrimination Act (GINA) is designed to protect people from this form of discrimination. GINA has two parts: Title I, which prohibits genetic discrimination in health insurance, and Title II, which prohibits genetic discrimination in employment. Title I makes it illegal for health insurance providers to use or require genetic information to make decisions about a person's insurance eligibility or coverage. This part of the law went into effect on May 21, 2009. Title II makes it illegal for employers to use a person's genetic information when making decisions about hiring, promotion, and several other terms of employment. This part of the law went into effect on November 21, 2009. GINA and other laws do not protect people from genetic discrimination in every circumstance. For example, GINA does not apply when an employer has fewer than 15 employees. It does not cover people in the U.S. military or those receiving health benefits through the Veterans Health Administration or Indian Health Service. GINA also does not protect against genetic discrimination in forms of insurance other than health insurance, such as life, disability, or long-term care insurance.

### **The burden of genetic information:**

Genetic information raises highly sensitive-raise unique social issues, it also provide information about family members and relatives and lead to breaches of confidentiality. Patient will face emotional challenges. Thus there is a greater impact of a genetic diagnosis. Couple who are the carriers of genetic diseases has to face family planning decisions and special reproductive challenges. So one of the burdens of genetic information is the segregation of the communities In a children's hospital, genetic diseases are common, not rare. The public appears to have a strong interest in understanding the impact of new knowledge of genetics and molecular biology on their lives and their illnesses. The current workforce of specialty-trained genetics providers seems insufficient to meet the expected increasing need. In addition to a larger genetic workforce, every person providing care to children, and to adults, will need to be fluent in the language of molecular biology and genetics, able to grasp the complexities of genetic information when applied to health and disease, competent to explain these complexities to an anxious public and to discuss their implications with affected families, knowledgeable about the power and potential pitfalls of genetic testing and the implications of the results for the individual and the family, informed about the promises and actualities of therapies for genetic disorders, including gene transfer and progenitor cell transfer approaches, and cognizant of the complex legal, ethical, and privacy issues raised by the characterization of an individual's genetic makeup. This will require significant changes in the processes of medical education at all levels of training and a real commitment from health care providers to make the effort to become conversant in genetic concepts. In the not-so-distant future, medical practitioners will need to be as comfortable discussing SNPs and proteomics as they now are discussing germs and antibiotics. There are number of coping mechanism like mother has to focus on the child's overall well-being. Parents must provide realistic expectations for the future and models for coping. There is need to explain condition to a child in an understandable way. These are only parents who can cope with the stress of caring.

Furthermore, species with large ecological amplitudes are equipped with high genetic diversities. In contrast, more specialised species with narrow ecological amplitudes show low levels of genetic diversity. Generalist species are mostly rather marginally affected by recent land-use changes; specialist can be supported by specific conservation measures. In the light of Conservation Genetics, species being ecologically intermediate between these two extremes are the most seriously affected ones by recent environmental changes. Such species which formerly occurred in large population networks have to sustain their high level of genetic variability via gene flow. Today, species from the latter group are negatively affected by rapid habitat collapses causing sudden lacks of population interconnectivity. Therefore, species with intermediate habitat demands and originally high genetic diversity might be at highest risk due to inbreeding depressions.

## **Genetic modifications of humans: Fact or fiction**

Humans have been manipulating the genes of crops for millennia by selectively breeding plants with desirable traits. Virtually all of food crops have been genetically modified in some way. In that sense, GMOs are not radical at all. But the technique does differ dramatically from traditional plant breeding. Scientists extract a bit of DNA from an organism, modify or make copies of it, and incorporate it into the genome of the same species or a second one. They do this by either using bacteria to deliver the new genetic material, or by shooting tiny DNA-coated metal pellets into plant cells with a gene gun. While scientists can't control exactly where the foreign DNA will land, they can repeat the experiment until they get a genome with the right information in the right place. That process allows for greater precision.

**"With GMOs, we know the genetic information we are using, we know where it goes in the genome, and we can see if it is near an allergen or a toxin or if it is going to turn [another gene] off," says Peggy G. Lemaux, a plant biologist at the University of California, Berkeley. "That is not true when you cross widely different varieties in traditional breeding."**

It depends on how you define new. Genetically engineered plants first appeared in the lab about 30 years ago and became a commercial product in 1994. Since then, more than 1,700 peer-reviewed safety studies have been published, including five lengthy reports from the National Research Council, that focus on human health and the environment. The scientific consensus is that existing GMOs are no more or less risky than conventional crops. So-called terminator genes, which can make seeds sterile, never made it out of the patent office in the 1990s. Seed companies do require farmers to sign agreements that prohibit replanting in order to ensure annual sales, but Kent Bradford, a plant scientist at the University of California, Davis, says large-scale commercial growers typically don't save seeds anyway. Corn is a hybrid of two lines from the same species, so its seeds won't pass on the right traits to the next generation. Cotton and soy seeds could be saved, but most farmers don't bother.

**"The quality deteriorates—they get weeds and so on—and it's not a profitable practice," Bradford says.**

GMOs alone probably won't solve the planet's food problems. But with climate change and population growth threatening food supplies, genetically modified crops could significantly boost crop output. "GMOs are just one tool to make sure the world is food-secure when we add two billion more people by 2050," says Pedro Sanchez, director of the Agriculture and Food Security Center at Columbia University's Earth Institute. "It's not the only answer, and it is not essential, but it is certainly one good thing in our arsenal."

Many people worry that genetic engineering introduces hazardous proteins, particularly allergens and toxins, into the food chain. It's a reasonable concern: Theoretically, it's possible for a new gene to express a protein that provokes an immune response. That's why biotech companies consult with the Food and Drug Administration about potential GMO foods and perform extensive allergy and toxicity testing. Those tests are voluntary but commonplace; if they're not done, the FDA can block the products. One frequently cited study, published in 2012 by researchers from the University of Caen in France, claimed that one of Monsanto's corn GMOs caused tumors in lab rats. But the study was widely discredited because of faulty test methods, and the journal retracted it in 2013. More recently, researchers from the University of Perugia in Italy published a review of 1,783 GMO safety tests; 770 examined the health impact on humans or animals. They found no evidence that the foods are dangerous.

This simply isn't true. Over the past decade, hundreds of independent researchers have published peer-reviewed safety studies. At least a dozen medical and scientific groups worldwide, including the World Health Organization and the American Association for the Advancement of Science, have stated that the GMOs currently approved for market are safe. This claim requires a little parsing. Two relevant GMOs dominate the market. The first enables crops to express a protein from the bacterium *Bacillus thuringiensis* (Bt), which is toxic to certain insects. It's also the active ingredient in pesticides used by organic farmers. Bt crops have dramatically reduced reliance on chemical insecticides in some regions, says Bruce Tabashnik, a University of

Arizona entomologist. The second allows crops to tolerate the herbicide glyphosate so that farmers can spray entire fields more liberally yet kill only weeds. Glyphosate use has skyrocketed in the U.S. since these GMOs were introduced in 1996. But glyphosate is among the mildest herbicides available, with toxicity 25 times less than caffeine. Its use has decreased reliance on more toxic alternatives, such as atrazine. If farmers rely too heavily on Bt or glyphosate, then pesticide resistance is inevitable, says Tabashnik. That's evolution at work, and it's analogous to antibiotics creating hardier bacteria. It is an increasing problem and could lead to the return of harsher chemicals. The solution, he says, is to practice integrated pest management, which includes rotating crops. The same goes for any type of farming.

This has been partly debunked. Bt insecticides attach to proteins found in some insects' guts, killing select species. For most insects, a field of Bt crops is safer than one sprayed with an insecticide that kills indiscriminately. But monarch butterflies produce the same proteins as one of Bt's target pests, and a 1999 Cornell University lab experiment showed that feeding the larvae milkweed coated in Bt corn pollen could kill them. Five studies published in 2001, however, found that monarchs aren't exposed to toxic levels of Bt pollen in the wild. A 2012 paper from Iowa State University and the University of Minnesota suggested glyphosate-tolerant GMOs are responsible for monarchs' recent population decline. The herbicide kills milkweed (the larvae's only food source) in and near crops where it's applied. The first part could certainly be true: Plants swap genetic material all the time by way of pollen, which carries plant DNA—including any genetically engineered snippets. According to Wayne Parrott, a crop geneticist at the University of Georgia, the risk for neighboring farms is relatively low. For starters, it's possible to reduce the chance of cross-pollination by staggering planting schedules, so that fields pollinate during different windows of time. (Farmers with adjacent GMO and organic fields already do this.) And if some GMO pollen does blow into an organic field, it won't necessarily nullify organic status. Even foods that bear the Non-GMO Project label can be 0.5 percent GMO by dry weight. As for a GMO infiltrating wild plants, the offspring's survival partly depends on whether the trait provides an adaptive edge. Genes that help wild plants survive might spread, whereas those that, say, boost vitamin A content might remain at low levels or fizzle out entirely.

### **Genes-the wider issues:**

The emergence of genetic medicine as well as advancements in biotechnology have been accompanied by a significant proliferation in the number of patents granted over biological materials. Recent debates in Australia regarding the patenting of such substances, in particular human genomic materials, have raised concerns about the ethical and practical implications of patenting in the biotechnology sector. On 13 June 2013, the Supreme Court of the United States handed down its long awaited decision in *Association for Molecular Pathology vs Myriad Genetics*. The biotechnology firm Myriad Genetics discovered the precise location and sequence of the BRCA1 and BRCA2 genes, mutations of which are associated with a greater risk of breast and ovarian cancer. The company obtained several patents based upon these findings, which provided it with the exclusive right to isolate an individual's BRCA1 and BRCA2 genes and perform medical tests for detecting these mutations. However, the Supreme Court found Myriad's patents over isolated human DNA sequences to be invalid.

Moral duty exists to treat all human beings as ends in themselves and not solely as a means to other ends. It can be argued that this fundamental principle should be considered in guiding the legally mandated uses of new biotechnological inventions, to eschew practices that undermine humans' inherent worth. However, these ethical arguments may be criticised on the basis that assigning an economic value to individual human biological components does not necessarily equate to the commodification of an individual. In this respect, it is important to differentiate between complete and incomplete commodification. David Resnik observes that for several years, scientists have patented complex molecules that occur within the human body, such as proteins, hormones and lipids, without particularly strong moral opposition being voiced. This process merely represents an 'incomplete commodification' of human substances. The patenting of human genetic material, Resnik argues, similarly constitutes an 'incomplete commodification' that will not inexorably lead to the 'complete commodification' of humans as a whole. In any event, human beings are already commonly defined by market rhetoric without significant objection. Putting a price on human life through insurance policies, negligence suits

or even wages and salaries as compensation for human labour are examples of current practices that apply market rhetoric to human beings. A common related argument that also criticises the relegation of humans to a quasi chattel-like status under the Patents Act asserts that because patents over human biological materials confer proprietary rights on patentees, gene patenting promotes a system of ownership over human beings. However, this argument confuses intangible intellectual property rights with physical property rights. The intellectual property rights that patents grant over isolated genetic material under the Patents Act do not necessarily grant positive physical property rights over parts of each person's human body. Rather, they confer a right upon the patentee to exclude others from the manipulation and manufacture of certain genetic sequences for a specified period of time. In this respect, ethical arguments based on the notion that patents reduce human life to the property of patentees, which have been recently put forward by supporters of the applicants in Myriad Genetics, do not necessarily offer an entirely convincing argument against patenting. As a consequence, the argument that patents reduce human life to a commodity may possess moral resonance in the context of patenting entire living organisms, however, this argument loses some force in respect of patenting only genes. On this view, it may be argued that patenting of 'human beings and the biological processes for their generation' may be justified, however, excluding a wider range of biological substances, such as human genetic material, may not be as compelling.

Genes make the (wo)man? A further concern that arises is that permitting the patenting of human genetic material under current case law and legislation fails to recognise the uniqueness and sui generis nature of the human genome and its centrality in forming the essence of a human being. Many divergent opinions exist regarding the meaning of personhood and its precise relationship with an individual's genetic composition. What constitutes 'humanness' is essentially a metaphysical question? In the Cartesian tradition, a dichotomy between the material body and the immaterial human essence was traditionally assumed to exist. However, 21st century phenomenology presents a different image that places greater emphasis on the unity of body and mind 'in which all structures and functions of the body are modes of the person and there is no sharp duality between the person and the body.' This theory of genetic essentialism seeks to challenge the metaphysical separation of the human body and the human person by suggesting that genes intrinsically constitute the very essence of human existence. Genetic material is accordingly not only closely linked to an individual's physicality, emotional and intellectual composition, but also to his or her personhood and sense of self. In this respect, Rogeer Hoedemaekers and Wim Dekkers suggest that the human genome has assumed the position of a cultural symbol, commenting that 'the gene is not just another part of the body ... but rather is an entity with an unprecedented social power to completely change humans.' This view suggests that the human genome sequence codes the human essence and that no individual or corporation should retain control over human genetic material. However, this genocentric approach essentially equates genetic identity with personal identity. Yet it may be contended that a human is more than the sum of his or her genealogical composition, an argument that renders the metaphysical conflation of the human genetic makeup and human essence somewhat tenuous. Under this view, genes are not inherently tied to the essence of an individual; it should be noted, for example, that fruit flies share 60 per cent of their DNA with humans,<sup>73</sup> bonobos 98.7%,<sup>74</sup> and chimpanzees more than 99%.

'Is There A Unique Moral Status of The Human DNA that Prevents Patenting?' From a purely chemical perspective, human genes may therefore be considered merely another arrangement of complex molecular structures that is shared by several other living organisms, and as such they are not necessarily solely responsible for creating the unique nature of humans. In fact, suggesting that humans may be reduced to a piece of code may itself constitute a very affront to human dignity to which opponents of gene patenting claim to strongly object. Common heritage of humankind Opponents of human gene patenting have also argued that the current patentable status of human genes is ethically unacceptable because the human genome constitutes the common heritage of humankind. The United Nations has traditionally applied the common heritage doctrine to areas such as the deep seabed and the Antarctic, declaring under Article 37(2) of the United Nations Convention on the Law of the Sea that such areas cannot be subject to alienation by any one state. In characterising the status of the human genome, an analogy may similarly be drawn to the concept of *res communis humanitatis*, which may provide the basis for an ethical argument against permitting solely private control over the manipulation of human genomic material. According to this reasoning, it may be argued that the 'privatisation' of genetic sequence information, which it can be contended is a product of human evolutionary processes, should not belong to a single patentee, but rather to all of humankind. This argument finds support in Article 1

of the Universal Declaration on the Human Genome and Human Rights, which states that ‘the human genome underlies the fundamental unity of all members of the human family ... in a symbolic sense, it is the heritage of humanity.’ In fact, one of the primary purposes of the Human Genome Project was to identify all human genes and render them freely available within the public domain to encourage research and development and to maximise their benefit to society. These sentiments find expression in the Bilbao Declaration, an international statement on the legal implications of the Human Genome Project, which proclaims that the human gene sequence does not belong to any specific individual. From this concept, it can be extrapolated that human genetic information constitutes a shared resource that exists for a common benefit and should not be monopolised for the advantage of one single entity. This is arguably a practice that may be permitted under current gene patent law.

### **Gene patents in agriculture and livestock:**

Patents give the holder the right to prevent others from using the genes in the ways specified in the patent, but only in the countries where the patent is valid. Not only do different countries have different standards over what can be patented, patenting is expensive, so most companies only apply for a patent in countries where they can sell a product for a profit. Many developing countries do not have a system which allows patenting of genes, but sometimes the techniques or the final products may be protected in the context of the national law relating to intellectual property protection. The idea of patents is to reward inventors not just for having the idea, but for making it public. A requirement of granting a patent is the publication of all of the information needed for someone to repeat the work. It also recognizes that there is a lot of investment needed to make a product out of an invention. A patent is granted for a limited period of time so that the inventor can get a return on that investment. In particular, GE plants take many years to reach the market because of lengthy regulatory approval processes and the time it takes to breed varieties even after new genes have been introduced. It is hard to see how companies would make the long-term investments necessary for research and development related to GE technology if they could not expect a return.

No, plant varieties are often protected under a different mechanism referred to as Plant Variety Protection (PVP) or Plant Breeders’ Rights (PBR). This isn’t as strict as a patent in terms of needing to be an invention – any plant variety can be protected as long as it is distinguishable from other registered varieties and has not been registered previously, but there are also some limitations to the protection this gives. There is an exemption for farmers to retain seed for re-planting and there is also an exemption for another breeder to use the variety in a breeding program. The idea is to give breeders some return for their time and effort in breeding, but at the same time to encourage more breeding and wide use of new varieties if farmers think they are better. The early protection of intellectual property rights can be traced back to Venice in the Middle Ages when master craftsmen in guilds prohibited competition from former apprentices for a period of 20 years. Such laws had considerably different economic effects for the master craftsman, the apprentice and the general public. For livestock, early breed societies were developed and monitored pedigrees to protect the IP of the master breeders.

The first modern patent act is often thought of as The US Patent Act of 1790. There was similar legislation in France in 1791. Patents related to living matter are relatively new. One of the earliest patents for living matter was granted to L. Pasteur for a yeast strain but this was done under the belief that it was an inanimate object and not living. The first specialized patent law applied to living organisms was that of the Plant Protection Act of 1930 in the US and provided what is commonly referred to as Plant Breeders Rights (PBR) to propagate new varieties by asexual methods. In 1961, a similar law was passed in France called the UPOV (International Union for the Protection of New Varieties). Protection in the US was expanded in 1970 with the Plant Variety Protection Act to include sexually reproduced plants. The UPOV was revised in Europe in 1991. Under these laws two principles, “breeder’s rights” which allows breeders to use protected varieties without permission of the owner and “farmer’s privilege” which allows farmers to collect seeds from their crops and use them, were developed. For years many seed companies have attempted to halt this latter practice by asking farmers to sign contracts prohibiting it. Recent technology, like the “terminator” technology, biologically prohibits the practice.

### **Gene patents and medical genetics:**

"Gene patenting" is a broad term referring to the patenting of genetic sequences such as DNA and RNA, and to alternative forms of DNA such as cDNA (complementary DNA). After it was announced in June 2000 that the human genome was almost completely mapped, private and public entities unleashed a flood of patent requests for genes and small pieces of gene sequences. The total number of human genes is estimated to be about 30,000,

and it is estimated that up to 20 percent of genes are patented by private companies, the government and even individuals. The American Medical Association is opposed to gene patenting because it has the potential to inhibit access to genetic testing for patients and hinder research on genetic disease. Others believe that gene patents provide incentives for private company investment in education. Human gene patents give rise to more than usual controversy; significant public, medical, and academic opposition to these patents exists. A certain amount of this opposition stems from principled objections to the patenting of human genetic material; a feeling that this amounts to the patenting of human life or is contrary to human dignity. In addition, many are concerned that patents on human genes will have a negative impact on patient access to medical care and diagnostic services. Thousands of patent applications relating to human DNA have been filed in patent offices around the world in the past 15 years. Some relate to the gene sequence as a compound per se, and others claim methods of diagnosis. A significant number of these applications have been granted, and many are still pending. Although many of the initial concerns about the potential negative impact of biotechnology patents have subsequently declined, concerns persist about the impact of gene patents in the field of genetic diagnostics. The recent Secretary's Advisory Committee on Genetics, Health and Society Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests again highlighted the difficulties of patents in the area of genetic testing and made controversial recommendations. Recent and pending patent law decisions in the United States and Europe may also have important implications for gene patents and their application to genetic testing. All these decisions and reports evidence the controversy and uncertain state of the law in this area.

The existence of gene patents gives rise to certain key potential difficulties for those conducting diagnostic testing. There is the possibility that "patent thickets" may arise in genetic testing. A patent thicket arises where a multitude of patents required for a particular innovative product or process is held by a multitude of owners and may be horizontal or vertical. Vertical thickets arise where narrower and more specific gene patents, for example, for individual causative mutations are granted. Horizontal thickets may increase as genetic tests for more complex genetic disorders are developed, in which many different mutations in many different genes will need to be tested. A related problem that arises from patent thickets is "royalty stacking." If many patents need to be licensed and each requires the payment of a royalty, then the resulting test may become very expensive. Finally, the transaction costs of investigating freedom to operate, including identifying relevant patents, determining whether the test falls within the scope of the claims, and then negotiating necessary licenses, or defending infringement proceedings, are high, even for individual patents. When multiple patents are held by multiple owners, the costs are likely to increase accordingly. In the public sector, or smaller companies, there tends to be little infrastructure support for investigating freedom to operate. In the United Kingdom, the existence of an experimental use defense to infringement means that research to develop new genetic tests is unlikely to constitute patent infringement, but the limits of the defense have not been fully tested. At the very least, it seems clear that tests that have clinical relevance to individual patients will not fall within the scope of the defense and, thus, could constitute patent infringement. A significant proportion of the genetic tests conducted in genetics laboratories around the world are likely to fall within the scope of existing gene patents, especially if no attempt is made to invent around any existing patents. These are significant potential problems that could have a considerable impact on the delivery of genetic tests to patients. Despite the fact that little empirical evidence of impact actually exists, some commentators continue to contend that gene patents impede patient access to genetic diagnostic testing. Other commentators conclude that lack of empirical evidence correlates to lack of negative impact on patients. In the United Kingdom, however, with the notable exception of Myriad Genetics and breast cancer genetic testing, there have been few controversies about access to genetic testing. As gene patent disputes have resulted in very few legal cases, the traditional means of legal analysis of case law will not provide illumination of the way in which gene patents influence practice. Other methods of investigation, most usefully empirical research into practice, are required. Although there are some important differences between patent law in different jurisdictions and there are also differences in the health care context within which gene tests are delivered, lessons can be learned from the way in which different jurisdictions address the common challenges that patents pose for genetic testing.

Despite the potential for gene patents to have significant negative consequences for genetic testing, this study found that, on the whole, human gene patents have little or no impact on practice for those developing genetic tests in the public sector in the United Kingdom. This is not because patents are managed optimally; rather, gene patents are essentially ignored. Genetics centers have not reduced services or failed to conduct testing because of patents. With very few exceptions, those developing and carrying out genetic tests did not conduct freedom to operate searches and did not license patents. They did not experience any negative consequences of this failure to take account of existing intellectual property (IP) rights, they had not been approached by patent holders either informally or formally, and they had not been sued for patent infringement. There were many nuanced factors that influenced the noncompliant behavior, but these factors fall under two broad types. First, stakeholders had limited awareness of the legal framework. Second, stakeholders perceived the balance of costs

and benefits of compliance and noncompliance with the legal framework to be weighted in favor of noncompliance.

Awareness is an important precondition to compliance with a legal framework. If someone is unaware that the law might impose particular obligations or restraints on their conduct, then they will not take action to ensure that their conduct is in compliance with those obligations or restraints. Generally, interviewees did recognize that the rules of IP law, and more specifically patent law, could have relevance for their practice. Most were, however, relatively uninformed as to the specific nature of any obligations that they might have under such law. The controversy surrounding the breast cancer gene patents held by Myriad Genetics has been extremely influential in informing interviewees about gene patents more generally. Myriad Genetics holds patents in many countries around the world for breast cancer genes. These patents were highly controversial in Europe and were challenged in highly publicized opposition proceedings at the European Patent Office. The Myriad case has galvanized awareness in the United Kingdom of some of the controversial issues of gene patenting. Many interviewees had some knowledge of the issues arising from the Myriad case, and their views and beliefs about gene patents had to some extent been shaped by this controversy. Interviewees reported that they knew that breast cancer testing continued in the United Kingdom without negative impact from the Myriad patents, and this fact was also highly influential. The data used to develop the home-brew tests, which are the predominant type of genetic test in the United Kingdom, are freely available on the internet to all, and there is, in most cases, nothing to alert those looking at such data to the fact that the gene sequences in question could be the subject of patent rights. Researchers and clinicians in particular seemed to be influenced by the fact that gene sequence information was “open access” in failing to enquire further or believing that gene patents would not influence their work.

Generally, those developing home-brew tests did not carry out any program of freedom to operate searches. This lack of due diligence was partly due to the fact that such programs can be costly, especially if it must be carried out for a number of genes. However, apart from concerns about the cost, there also seemed to be general ignorance that due diligence was necessary; most respondents did not seem to have considered that due diligence was something that they should do. Apart from due diligence, direct contact from a patent holder may serve to make a laboratory aware of a potentially relevant patent. In the United States, cease and desist letters have been sent to genetic testing laboratories, and many laboratories have reported refraining from offering a test for which there is a patent on the basis of receiving a cease and desist letter. This was not mirrored in the NHS laboratories contacted for this research. Very few respondents reported having had any direct contact from patent holders. Some laboratory managers also mentioned that direct contact had been made over the cystic fibrosis patents, although they were very vague over details as this was a considerable number of years previously. Patents had not been enforced against those interviewed. Interviewees reported that patent holders generally had not contacted possible infringers in the NHS, had not made approaches about licensing, and had not sent cease letters.

The attitude of many interviewees to gene patents could perhaps best be characterized as “willful blindness.” They had some degree of awareness that gene patents could, or should, influence their practice. Despite this awareness, they believed that if they refused to acknowledge the realities of gene patents, then they would not become an issue in day-to-day practice. Most saw gene patents as a potential problem, which they would prefer not to address if possible. As a result of this willful blindness, respondents often did not engage in any lengthy consideration of patents and did not conduct due diligence or freedom to operate searches, or undertake licensing negotiations. If asked, most denied that they would knowingly infringe a patent and indicated that they would take steps to comply with the law should they be informed that they were infringing a valid patent. Despite these claims, these people in reality took few or no steps to ensure that they actually complied with the law, which meant that it was possible that they were (perhaps unknowingly) infringing patents. When considering whether to comply with patent law, interviewees engaged in a balancing of the perceived costs and benefits of compliance against the perceived costs and benefits of noncompliance. What they characterized as being a “cost” or a “benefit” was very broad, and it encompassed not only monetary costs but also time and effort, as well as moral issues. This balancing exercise tended to result in general noncompliance. It was clear that very little due diligence was carried out. This was partly not only due to ignorance that it was necessary but also due to the fact that it was perceived to be difficult and costly, as well as unnecessary. The fact that due diligence was not conducted in the past, with few negative consequences, was influential in this respect. The balancing of the relative costs and benefits of compliance versus noncompliance also took account of some complicated moral considerations.

### **Genetic piracy:**

From 16<sup>th</sup> to 17<sup>th</sup> Century, piracy means robbery at sea-sailors wearing long boots and striped jerseys. This is a romantic image but robbery at sea is still robbery. In some parts of the world, piracy is still a hazard. What has piracy to do with genes? Can genes be the subject of robbery at sea? Piracy is using something without permission e.g., running a radio station, CD copyright without permission is a piracy. The patient's cells, for the sake of lesions they exhibit are used by the physicians without permission, brought gain to the user. For example physician has done Spleenectomy for the sake of patient's health but later physician is using that spleen for research purpose without permission. In USA, once the organ has been removed during surgery it is no longer belong to the patient. Permission is required in cases of -live donor of a kidney, post-mortem research. Number of arguments has been raised like genetic piracy has no ownership rights, one feels uncomfortable, and injustice has been done.

If medicinal plants are used for pain relieving then is this an intellectual property? Do wild plants belong to anyone? The answer is no. Laws prevent removal of plants only from the private owner land. In case of research progress, nothing is illegal. Initiating research and development program, patents must be registered of intellectual property as a result of which there is a profit for the company. Central America has done agreement with transnational biotechnology company. USA has allowed company to exploit gene pool of the rain forest. This is of company interest to protect asset/ commercial potential of forest plants.

### **Ethical issues related to cloning of sheep and frog:**

From the production of vaccines to organ regrowth for transplantation, cloning from stem cells can improve people's health. In regards to the cloning of whole organisms, however, the benefits are largely found in increasing nutrition derived from food. In the United States, you frequently see whole organism cloning in the genetically modified foods you eat, which are FDA approved and not limited to plants but also to animals such as cloned pigs modified to be a source of omega-3 fatty acids that usually come from fish and certain seeds. Additionally, the replacement of dead or dying household pets and children with genetic disorders, termed "reproductive cloning," has become a social argument in favor of cloning. In fact, in 2004 a company devoted solely to the cloning of household pets opened, and though it closed after only a short, two-year stint, some people continue to see this as a valuable route for cloning research.

From a religious standpoint, many argue that the act of cloning makes humans God, an equality not viewed as appropriate as humans lack omniscience. Morally, the arguments are broader. The ethics of animal research come into play, where many, such as the moral philosopher Peter Singer, believe that all animals are created equal; suggesting animal testing in science should be completely eliminated. The possibilities of unforeseen health risks in cloned organisms and potential negative effects of decreased genetic variation on the human gene pool are seen as ethical causes for concern in addition to the mixed ethical and social consideration of increasing population sizes when worldwide resource availability is a problem.

The social issues of cloning tend to focus on human clones in terms of both availability of cloning technology and integration of clones into society. Reproductive cloning raises the question of cost and who should have access. However, the biggest social argument is that cloning negates a person's right to individuality and ignores the potential psychological effects of such a parentless and de-individualized identity.

Legally, funding has always been a concern for cloning research. Many believe the government and taxpayer money should not support research not agreed upon by a clear majority and in this respect, the U.S. Congress has continued to prohibit use of taxpayer dollars for any research that may result in the death of human embryos. However, reproductive animal cloning continues not just in the U.S., but around the world. The biggest legal issues concerning animal clones are who should be responsible for and at what depth there should be oversight and accountability, as well as the legal right to patent live organisms.

### **The ethics of human cloning: an overview**

The word clone derived from the Greek Klonos, which means branch. Semantic implication is obvious. Human cloning is the main process by which a genetically identical copy of a certain bacteria, plant or animal is produced by asexual reproduction. The term "clone" was coined by JBS Holdone, an eminent Scottish biologist and used in his speech titled "Biological Possibilities for the Human species of the next-Thons and Ten Years" in 1963. Cloning is defined as the production of genetically identical organisms. Somatic cell nuclear transfer

refers to the process by which a somatic cell nucleus is transferred into the existing body of an oocyte from which the nucleus was removed. In other words, cloning is a method of producing a child who has exactly the same genes or parent. I take an egg and remove the nucleus that contains DNA genes. Then take DNA from an adult cell and placed in the egg, the adult cell is merged with the enucleated egg, or by a sophisticated nuclear transfer. Then the egg is stimulated electrically or chemically reconstructed and tries to make it to divide and become an embryo. However, many groups have used a broader definition of cloning. They include production of tissues and organs by increasing cell or tissue cultures, with current production of embryos. This occurs by creating stem cells. When an egg / ovum are fertilized and begin dividing, stem cells are all alike. As cells divide, some cells differentiate and become stem cells that produce specific tissues and then organs. We must understand that cloning does not produce an exact copy of the person cloned. What is cloning is that it copies itself and creates duplicate DNA/genes. The person will not be a Xerox copy. He or she will grow in an environment different from that of the clone, with different experiences and opportunities. Genetics does not define a person or personality in its entirety.

The history of human cloning is undoubtedly one of the most fascinating chapters of our lives. Essential question to be discussed to understand the ramifications of human cloning is when human life begins? C. Ward Kischer, a famous American embryologist, wrote in a recent article: "Since 1973 when Roe vs. Wade was won there were many socio-legal issues related to human embryo. Abortion, fertilization in vitro research on human embryos, research on stem cells, cloning and genetic engineering are substantive issues of human embryology". The answer is clear embryology that life begins at fertilization of the egg by a sperm (sexual reproduction) or if the SCNT cloning, implantation and activation when the donor somatic cell nucleus into an egg recipient (asexual reproduction). Although non-mammalian cloning was achieved in 1952, mankind had to wait another 44 years until he was finally cloned the first mammal. The first cloned mammal, Dolly the sheep was born on July 5, 1996. In this fascinating history of cloning, there has been a major setback in 2003 when Dolly died at the age of 6 years. Death of the first cloned mammal was followed by a lively debate related issues / ethical aspects of cloning, debate that continues today. Besides the successful attempts to clone the different species of animals, XX century was marked by several important moments in the development of the genealogy. Deciphering the success of DNA code in 1968 came as an enormous progress around much desired human clone. With nearly 20 years later, by 1988 the human genome, that genome Homosapiens stored in 23 pairs of chromosomes has been released. As things were headed becoming better by the appearance of a human clone, a major problem has become "human cloning prohibition act" in 2009, which has labelled as cloning illegal, immoral, not unethical activity. Since 2009, human cloning is illegal in 23 countries. So far, experiments were undertaken with five species of animals and the high rate of failure has given rise to many questions about human cloning success. Only 1% of animal cloning made so far has had a positive result, but most of them have suffered serious disorders. The conclusion of experts is that the current level of technology, human cloning is very dangerous. I discussed two types of human cloning: therapeutic cloning and reproductive cloning. Therapeutic cloning involves cloning cells from an adult for medicinal use and is an active research area, while reproductive cloning would involve the creation of human clones. Therapeutic cloning could provide unique ways to cure diseases until now considered incurable: diabetes, Parkinson's, Alzheimer's, heart disease. The third type of cloning called replacement cloning is a possibility in theory and would be a combination of therapeutic cloning and reproductive cloning. Higher probability of achieving a therapeutic cloning is more accessible in terms of technique, but also less morally problematic.

There are many medical benefits and disadvantages of cloning and its technology. They include the following potential health benefits: - the possibility of cloning technology to learn to renew activity damaged tissues and grow new cells to replace them; - people's ability to create genetically identical to donor organs such as: kidney, bone marrow transplant; - the benefit of studying cell differentiation at the same time as the study and development of cloning; - sterile couples will be able to have children who will have the genetic information of the mother or the father's. Potential risks or disadvantages: cloning creates identical genes. It is a process of replication of genetic constitution, so preventing gene diversity. Reducing the diversity of genes, weaken the ability to adapt. Cloning is also detrimental to the beauty that comes from diversity. While human cloning to allow genetic mixing with humans, also makes the reproduction characteristics likely to be undesirable. The cloning of human organs and their use for transplantation or cloning human beings must be taken into account technical and economic barriers. Cloning organs will be more efficient and cost? Cloning techniques will really reach the ordinary people? Further cloning of human rights and animals will play. Cloning technology is not yet well developed. It has a low fertility rate. The cloning of Dolly has been used 277 eggs, 30 began to divide, nine induced pregnancy, and only one survived to term. Clones may be treated as second class citizens, which are only created as organ donors. If people will be cloned, and clones will hopefully receive the same rights as any other human being. Some ethicists fear the clones' rights will be broken. Paul Billings, co-founder of Genebase was involved in drafting an international document that would ban reproductive cloning and genetic engineering

of microbial limits. As arguments against human cloning, he quoted: "Nobody has the right to have a genetically related child, cloning is not safe, cloning is not legally required medical.

Ethical issues of human cloning have become an important issue in recent years. Many ethical arguments against human cloning are based on misconceptions. Many people think that these clones will have the same characteristics / personalities as the person cloned. Although clone and cloned individual have the same genes, traits and personalities are different. People think that a clone is physically identical to the donor and her behaviour, but this is not true because although there is a physical identity, living environment shapes an individual's ongoing behaviour and psychology. Many people believe that cloning will lead to loss of individuality eventually, but people have their own personality cloned which personality is similar to those in which they were created. Lawrence Nelson, associate professor of philosophy at UCS, said that embryos can be used for research if: - the purpose of research cannot be achieved by other methods; - the embryos have reached more than 14-18 days of development; - those who use forbid you to consider or treat as personal property. One of the most serious problems of cloning of human embryos for therapeutic purposes is that with harvesting stem cells, the embryo is formed by cloning practical killed. We cannot reduce the existence of a human embryo to "a cell" as long as after both science and teaching of the Church, the human embryo is a carrier of life. For a few years, the legalization of human cloning is in the centre of global debate, which was also attended not only scientists but also politicians, philosophers, theologians, psychologists. For example, American Association of Pro Life Obstetricians and Gynecologists (AAPLOG) has spoken out against cloning, drawing attention that some business people might think of trading a human life. What is harder is that it could reach the reproduction of living people without them knowing, to be involved in this process or to give consent. Questions appeared on the social status of any clone. What will be their status in society? In the U.S. House of Representatives issued a ruling that human cloning is illegal, but the Senate has yet to rule on the matter. The opinions are still leaning toward accepting only therapeutic cloning. Legalization of therapeutic cloning has been proposed as the only way to investigate, the chances of success, the basic criterion for funding such programs as the primary objective should be finding cures for incurable diseases. A coalition of states, including Spain, Italy, Philippines, USA, Costa Rica and the "Holy Land" have tried to expand the debate on all forms of human cloning, noting that in their view, therapeutic cloning violates human dignity. Costa Rica proposed the adoption of an international convention to combat any form of cloning. Australia has banned human cloning in December 2006, but therapeutic cloning is now legal in some parts of Australia. European Union - European Convention on Human Rights prohibits human cloning in an additional protocol, but the protocol has been ratified only by Greece, Spain and Portugal. England - The British government introduced legislation to allow therapeutic cloning in a debate on January 14, 2001. Hope that parliament will pass the law was prohibitive. Roman Catholic Church under Pope Benedict XVI has condemned the practice of human cloning, saying it represents "a grave offense against human dignity and equality among the people." Human cloning is prohibited in Islam at the Tenth Conference in Jeddah. Saudi Arabia has decided on June 28, 1997-July 3, 1997 as the beginning of human cloning is forbidden by the faith-sin. Jesse Rainbow explain why there is an aversion to human cloning - a clone would not be a "real person" - cloning is "playing the God" - cloning is not "natural" mention in closing some of the conditions proposed in a provisional list yet, so research on therapeutic human cloning (reproductive one is illegal) to proceed lawfully: it is necessary for embryos to be used only in the early stages of their development, without being allowed to grow further, all programs research must be supervised by government organizations dealing with fertilization and genetic techniques, various research programs will receive funding and approval only if it is scientifically demonstrated that there is no other way of obtaining the same results conventional, will not be permitted to research on human genetic material can be combined with that of animals, there must be a permanent state of public information on research undertaken and to be postulated that the limitations may be required to report the experiences and suffering of animals used for human benefit.

### **Ethical status of early human embryo;**

Embryonic stem cells offer hope for new therapies, but their use in research has been hotly debated. Different countries have chosen to regulate embryonic stem cell research in very different ways. Mention embryonic stem cells in the pub and the topic still divides opinion. But what exactly are the ethical arguments and why are they so tricky to resolve? Embryonic stem cell research poses a moral dilemma. It forces us to choose between two moral principles; the duty to prevent or alleviate suffering; the duty to respect the value of human life.

In the case of embryonic stem cell research, it is impossible to respect both moral principles. To obtain embryonic stem cells, the early embryo has to be destroyed. This means destroying a potential human life. But embryonic stem cell research could lead to the discovery of new medical treatments that would alleviate the suffering of many people. So which moral principle should have the upper hand in this situation? The answer hinges on how we view the embryo. Does it have the status of a person?

The moral status of the embryo is a controversial and complex issue. Either the embryo is viewed as a person whilst it is still an embryo, or it is seen as a potential person. The criteria for 'personhood' are notoriously unclear; different people define what makes a person in different ways. Development from a fertilized egg into to baby is a continuous process and any attempt to pinpoint when personhood begins is arbitrary. A human embryo is a human being in the embryonic stage, just as an infant is a human being in the infant stage. Although an embryo does not *currently* have the characteristics of a person, it *will become* a person and should be given the respect and dignity of a person. Argument against this view is that an early embryo that has not yet implanted into the uterus does not have the psychological, emotional or physical properties that we associate with being a person. It therefore does not have any interests to be protected and we can use it for the benefit of patients. The embryo cannot develop into a child without being transferred to a woman's uterus. It needs external help to develop. Even then, the probability that embryos used for in vitro fertilization will develop into full-term successful births is low. Something that *could* potentially become a person should not be treated as if it actually *were* a person. Some people argue that a human embryo deserves special protection from around day 14 after fertilization because after 14 days the embryo can no longer split to form twins. Before this point, the embryo could still be split to become two or more babies, or it might fail to develop at all. Before day 14, the embryo has no central nervous system and therefore no senses. If we can take organs from patients who have been declared brain dead and use them for transplants, then we can also use hundred-cell embryos that have no nervous system. Fertilization is itself a process, not a 'moment'. An embryo in the earliest stages is not clearly defined as an individual.

An embryo deserves some protection from the moment the sperm fertilizes the egg, and its moral status increases as it becomes more human-like. There are several stages of development that could be given increasing moral status like implantation of the embryo into the uterus wall around six days after fertilization, appearance of the primitive streak – the beginnings of the nervous system – at around 14 days, the phase when the baby could survive if born prematurely and birth. If a life is lost, we tend to feel differently about it depending on the stage of the lost life. A fertilized egg before implantation in the uterus could be granted a lesser degree of respect than a human fetus or a born baby. More than half of all fertilized eggs are lost due to natural causes. If the natural process involves such loss, then using some embryos in stem cell research should not worry us either. Argument against this view is we protect a person's life and interests not because they are valuable from the point of view of the universe, *but* because they are important to the person concerned. *Whatever moral status the human embryo has for us, the life that it lives has a value to the embryo itself.* If we judge the moral status of the embryo from its age, then we are making arbitrary decisions about who is human. For example, even if we say formation of the nervous system marks the start of personhood, we still would not say a patient who has lost nerve cells in a stroke has become less human. If we are not sure whether a fertilized egg should be considered a human being, then we should not destroy it. A hunter does not shoot if he is not sure whether his target is a deer or a man.

An embryo is organic material with a status no different from other body parts. Fertilized human eggs are just parts of other people's bodies until they have developed enough to survive independently. The only respect due to blastocysts is the respect that should be shown to other people's property. If we destroy a blastocyst before implantation into the uterus we do not harm it because it has no beliefs, desires, expectations, aims or purposes to be harmed. Arguments against this view are by taking embryonic stem cells out of an early embryo, we prevent the embryo from developing in its normal way. This means it is prevented from becoming what it was programmed to become – a human being. Different religions view the status of the early human embryo in different ways. For example, the Roman Catholic, Orthodox and conservative Protestant Churches believe the embryo has the status of a human from conception and no embryo research should be permitted. Judaism and Islam emphasize the importance of helping others and argue that the embryo does not have full human status before 40 days, so both these religions permit some research on embryos. Other religions take other positions.

### **Therapeutic cloning:**

The advancement in biotechnologies and stem cell research, although encountering many scientific difficulties, legal constraints and ethical roadblocks, offers a tremendous potential in regenerative medicine and in the treatment of genetic defects. Therapeutic cloning is the transfer of nuclear material isolated from a somatic cell into an enucleated oocyte in the goal of deriving embryonic cell lines with the same genome as the nuclear donor. Somatic cell nuclear transfer (SCNT) products have histological compatibility with the nuclear donor, which circumvents, in clinical applications, the use of immunosuppressive drugs with heavy side-effects. While the goal of reproductive cloning is the creation of a person, the purpose of therapeutic cloning is to generate and direct the differentiation of patient-specific cell lines isolated from an embryo not intended for transfer in utero.

Therapeutic cloning, through the production of these autologous nuclear-transfer embryonic stem cells (ntESC), offers great promises for regenerative and reproductive medicine, and in gene therapy, as a vector for gene-delivery. This review focuses on the recent breakthroughs in research based on therapeutic cloning, their feasibility, and their potential applications in medicine. The second part of this review discusses current roadblocks of therapeutic cloning, both in science and biomedical ethics, as well as the main alternatives to therapeutic cloning. Laws regarding biomedicine are generally formulated in vague terms that do not distinguish reproductive from therapeutic cloning. The Convention on Human Rights and Biomedicine, formulated by the Council of Europe in 1997, is counterintuitive. Article 13 declares that “an intervention seeking to modify the human genome may be only undertaken for preventive, diagnostic or therapeutic purposes” and stipulates in Article 18 that “the creation of human embryos for research is prohibited.” The Protocol on Cloning, put forward in 1998 and signed by 19 European nations, bans reproductive cloning and was paradoxically signed by France and Germany, which both have permissive policies regarding the generation of human ntESC lines.

Committees are formed in different countries to debate and regulate cloning, such as the President’s Council on Bioethics, created in the USA in 2002, which is a much less permissive group than the UK’s Human Fertilization and Embryology Authority (HFEA). The legitimacy of the latter is being questioned by the ProLife movement under the pretext that they were not democratically elected. Canada’s Assisted Human Reproduction Act, in vigor since 2004, allows stem cell research only on unimplanted embryos obtained from fertility clinics but forbids SCNT. Asia has the highest legal permissibility since the generation of human ntESC lines through SCNT is legal. Australia is currently reviewing its existing laws to follow the Asian trend in Singapore, China and South Korea, and to legalize the generation of chimeras using human DNA. Since both reproductive and therapeutic cloning require the in vitro generation of a human embryo, prohibiting reproductive cloning is likely to result in severely hindering medically important research based on therapeutic cloning. A worldwide ban on reproductive human cloning was proposed by France and Germany to the UN in 2001 and effective since September 2006. A breakthrough in reproductive cloning was published a month earlier by Zavos and Illmensee, who injected a skin fibroblast nucleus from an infertile man into an oocyte provided by his wife. One out of three SCNT attempts was successful, and although the four-celled embryo failed to implant in utero, this is the “first evidence of the creation and transfer of a human cloned embryo for reproductive purposes.” One may infer, from the rigidity of the current legislature regarding therapeutic cloning and stem cell research, that legal constraints are motivated by the fear that scientific development will be faster than the legislative debate, which was almost the case with Zavros and Illmensee’s breakthrough, and lead to the unregulated reproductive cloning of human beings.

SCNT in the context of therapeutic cloning holds a huge potential for research and clinical applications including the use of SCNT product as a vector for gene delivery, the creation of animal models of human diseases, and cell replacement therapy in regenerative medicine. Furthermore, SCNT might, in the future, allow in vitro organogenesis and counteract senescence. The combination of therapeutic cloning and gene therapy offers a great potential for patient-specific rescue of a genetic mutation of the loss-of-function type, resulting in lowered or eliminated activity of a particular protein. Therapeutic cloning used in cell replacement therapy has the potential to create various types of tissues such as osteoblasts to counteract osteoporosis, and spinal cord regeneration following trauma, as shown by Deshpande et al, who transferred motor neurons derived from ESC to rats with a severed spinal cord. The resulting recovery of motility could lead to clinical applications for paralysis in humans through therapeutic cloning. Therapeutic cloning constitutes a promising tool in tissue engineering and might offer the possibility of synthesizing organs de novo, which would solve the problems of immune rejection and organ shortage for transplantation. The assembly of patient-specific cardiomyocytes, blood vessels and skin pieces fixed on a scaffold holds great hope in the treatment of infarctus, atherosclerosis and severe burns, respectively. Consequently, the feasibility of de novo organogenesis based on SCNT depends on the elucidation of the tissue-specific molecular pathways mediating differentiation as well as the improvement of current SCNT and tissue engineering methods in order to recreate in vitro the complex three-dimensional organization and different intercellular interactions in organogenesis.

D’Amour et al designed in 2006 a five-step protocol enabling human embryonic stem cells to differentiate into endocrine cells producing most pancreatic hormones, including glucagon and insulin, with implications for use in cell replacement therapy for the treatment of diabetes mellitus. The combination of growth factors and differentiation markers added at each stage of the method were designed to duplicate pancreatic organogenesis in vivo, a breakthrough which could concretize the hope of generating organs using therapeutic cloning. According to this protocol, patient-specific ntESC lines would be differentiated into successive cell-type intermediates representative of pancreatic organogenesis, from endoderm to the terminally differentiated  $\beta$ -cell that would then be transplanted into the patient’s pancreas to treat diabetes-related hyperglycemia.

The recent success of therapeutic cloning in a mouse model of Parkinson's disease foreshadows clinical applicability in humans to treat neurodegenerative diseases and conditions involving demyelination. Parkinson's disease is characterized by the deterioration of dopaminergic neurons resulting in constant tremor and muscular stiffness impairing motility. Barberi et al derived, by SCNT with somatic nuclei from mouse cumulus and tail-tip cells, two ntESC lines which were induced to differentiate into motor, GABAergic, serotonergic and dopaminergic neurons (11) forming synapses and displaying normal electrophysiological properties in vitro. The dopaminergic neurons were directly injected into the cortical striatum of mice with Parkinson-like lesions induced by 6-hydroxydopamine. Long-term behavioral rescue was observed, and 80% of the ntESC derived neurons were alive 8 week post-transplantation, contrary to only 40% for stem cell-derived neurons. Hence, the therapeutic cloning approach was shown to be more permanent as a cell replacement therapy and could eventually be extended to the treatment of cortical atrophy resulting from stroke or Alzheimer's disease.

It has been observed that the SCNT of the nucleus of a cell close to reaching senescence resets the lifespan of the cell, as seen by the ability of the resulting embryo to carry 31 rounds of division, compared to 33 for a wild-type embryo of the same developmental stage. The rejuvenating potential conferred by SCNT can be paradoxically thwarted by telomere shortening, which reflects both the biological age of the nuclear donor and the time during which the ntESC lines were grown, leading to premature aging also observed in cloned animals. However, the addition of a transgene containing the two coding regions needed for the production of telomerase could restore telomere lengths and thus increase the survival of the transplanted cells, which would increase the success rate of therapeutic cloning for regenerative medicine. This strategy needs more investigation to be feasible because, while telomere length would not trigger tumorigenesis, Stampfer et al showed that, knockout p16INK4a epithelial cells with no endogenous telomerase activity do not respond to the proapoptotic signals of the growth factor TGF- $\beta$  following the addition of high levels of hTERT, the telomerase catalytic subunit.

Animal models of human diseases can be designed through therapeutic cloning for research purposes. Although a viable nonhuman primate has not yet been produced by SCNT, the success of Mitalipov and Wolf in creating a monkey by embryonic cloning from the nucleus of an allogenic blastomere supported the possibility that, through gene targeting, genetic defects can be reproduced in a wild-type genome to express a loss of function. Hence, we are getting one step closer to patient-specific genetic engineering of animal models of human disease. With improved SCNT protocol, the nucleus of a patient's skin biopsy could be introduced into a primate or mouse enucleated oocyte so that the resulting clone expresses the condition in a patient-specific way. Hence, clinical testing would be done on the animal model to find an optimal treatment, such as the drug combination to treat epigenetically-triggered cancer, highly variable among instances. SCNT has applications in cancer research to identify whether a particular type of cancer arises from a genetic or an epigenetic defect, such as the demethylation of a tumor suppressor gene. The epigenetic modifications of chromatin structure in cancerous cells involve altered histone methylation, phosphorylation and deacetylation, as well as DNA methylation, which are reversible unlike genetic mutations. Supportive evidence for oncogenesis resulting from epigenetic features includes studies where normal mice blastula were obtained through SCNT from a skin malignancy and a medullar tumor. These studies could lead to clinical applications for cancer diagnosis in humans since nuclear reprogramming signals from the host ooplasm variably reset the epigenetic profile of the nuclear donor DNA. The derivation through SCNT of a healthy patient-specific stem line would show that cancer onset was triggered by epigenetic alterations. Anti-methylation drug, such as 5-aza-2'-deoxycytidine inhibiting DNA methyltransferases that inactivate apoptotic genes in cancerous cells and histone deacetylase inhibitors against oncogene overexpression are currently under clinical trial as a potential anti-cancer therapy.

However, epigenetic resetting following SCNT is likely to disrupt normal phenotype of the embryo-derived cell lines and the adult clone, the latter displaying an abnormally low body weight and expression level of MUP encoding genes (Major Urinary Proteins) as shown by Reik et al in the mouse. The epigenetic pattern of imprinted genes that was established during gametogenesis is lost through SCNT and the inactivation of early genes directing embryogenesis can explain low embryo viability and poor efficiency in the derivation of autologous ntESC lines. Blelloch et al found out, from studies on neurons, that stem cells used as the nuclear donor have a higher success rate than fully differentiated cells in the derivation of autologous embryonic cells. The introduction of a genetic mutation to reduce the function of DNA methyltransferase-1, as investigated by the same team, improved the production of ntESC due to resulting "global hypomethylation" of genomic nuclear DNA. SCNT from genetically modified nuclei obtained from a patient's skin biopsy, for example, is an efficient strategy to restore normal expression of a missing factor or to facilitate in vivo survival of the graft generated. For instance, patient-specific cardiomyocytes produced through SCNT will not integrate into the scarred heart tissue resulting from myocardial infarction. A proposed strategy would be the genomic integration of an exogenous gene, prior to transplantation, encoding an anti-scarring factor such as TGF- $\beta$  (transforming

growth factor- $\beta$ ). In the case of haemophilia, characterized by a deficit in functional clotting factor IX and XIII, the addition of the genetically engineered missing DNA sequence, or the replacement of the dysfunctional gene through homologous recombination in a patient's biopsy prior to SCNT could produce patient-specific cell lines with a correction for the defect.

For instance, Duchenne Muscular Dystrophy (DMD) is an inheritable X-linked condition characterized by reduced intramuscular dystrophin levels, causing cellular necrosis and weakening. Being a single-gene disorder, DMD can be treated by therapeutic cloning in combination with gene therapy to restore normal dystrophin production. In the case where ntESC are transplanted without prior differentiation in vitro, the insertion of a transgene encoding MyoD, a transcription factor responsible for commitment to the myogenic lineage, may promote muscle regeneration. The combination of gene therapy and therapeutic cloning has exciting potential for the genetic rescue of missing alleles in heritable genetic disorders such as severe combined immunodeficiency (SCID), in which genetic mutations of specific genes such as RAG-1 and 2, essential for the DNA recombination allowing immunoglobulin and lymphocyte polymorphism, render the immune system completely inefficient. Hochedlinger et al took a somatic nucleus from the tail-tip of an SCID mouse-model, created through the double-knockout of the Rag-2 gene (recombination-activating gene 2), and rescued the genetic defect through the insertion of two copies of the Rag-2 gene by homologous recombination. SCNT was performed to clone viable Rag-2 (+/+) mice with a normal immune system, from which embryonic stem cells were differentiated in vitro into hematopoietic stem cells normally found in the bone marrow. Three weeks following transplantation into the Rag-2(-/-) knockout mouse model, partial rescue of immune function was observed, as well as the presence of lymphocyte precursors and functional antibodies. However, mature T lymphocytes were not observed, suspected to be due to selective differentiation of the transplanted stem cells into myeloid cells (bone marrow precursors) instead. Although more work needs to be done to elucidate the pathways leading to preferential differentiation in vivo, the combination of gene therapy for the rescue of a loss of function and therapeutic cloning to bypass graft rejection holds the potential to eventually cure other immune disorders. Oncogenic activation following transduction constitutes a major drawback to this approach. In 2002, the insertion of the transgene to treat X-linked SCID in the LMO2 oncogene caused the onset of leukemia in two out of seven patients recently treated. Repeated graft rejection, even when derived through SCNT, remains an unsolved problem in the case of autoimmune disorders such as pernicious anemia and multiple sclerosis. Legislative constraints and the subsequent lack of funding constitute a major impediment to the advancement of therapeutic cloning.

### **Designer babies:**

Advanced reproductive technologies allow parents and doctors to screen embryos for genetic disorders and select healthy embryos. The fear is that in the future we may be able to use genetic technologies to modify embryos and choose desirable or cosmetic characteristics. A designer baby is a term used by journalists to describe this frightening scenario. Designer babies are children-genetically engineered in the womb to have desired qualities. They are produced through in vitro fertilization. First embryo is removed-manipulated for desired qualities and is then placed back into mother's womb. The major disadvantage is that it is expensive not 100% save. This curiosity for better looking can create gap in the society. This affect the gene pool as genes can have more than one use e.g., genes of intelligence may be associated with the genes of anger. The major disadvantage is that infants cannot give the consent. However number of advantage are there like it increases human life span up to 30 years, prevent genetic disorders, infertile women can have children, parents set their own limits for genetically engineered babies. Many religious scholars and philosophers believe that this is unethical and unnatural, morally wrong. Most of the times, parents get upset when trait didn't pay off. On later stages, problems may arise in the child/parent relationships. Recently scientists have made rapid advances in our knowledge of the human genome and in our ability to modify and change genes. In the future we may be able to "cure" genetic diseases in embryos by replacing faulty sections of DNA with healthy DNA. This is called germ line therapy and is carried out on an egg, sperm or a tiny fertilised embryo. Such therapy has successfully been done on animal embryos but at present it is illegal to do this in humans. However, it is legal to modify the faulty genes in the cells of a grown child or an adult to cure diseases like cystic fibrosis - this is called body cell gene therapy.

### **Case study 1:**

Donated gametes-sperm and ova are used in fertility treatments for patients who are unable to produce their own. It is much easier to donate sperm than ova because donated ova are very scarce. During fetal development, females lay down a lifetime's supply of oocytes. It is therefore suggested that aborted female fetus may be used

to supply oocytes for fertility treatments. Do you approve or disapprove of this idea. ANSWER: Dr. Roger Gosden, pioneer-reproductive biology and of infertility treatment proposed this way. what people want is the ultimate measure of right and wrong. This depends on the public opinion, which at present doesn't support this use.

#### **Case study 2:**

A small less developed country in South America is deep in debt. Its main source is its rain forest. The land has been cleared used for cattle ranching to raise beef in the US market. The government has also granted a license to transnational biotechnology company to exploit the forest's gene pool. The company has agreed to pay royalties on income generated from discoveries based on rain forest gene pool. What are the issues in dealing with this situation?

Answer: There are deleterious effects on biodiversity. You have a right to exploit any living organism or any ecological community only if you have license. This agreement might create a genuine commercial flow of money from the richer to some of the poorer nations. It's a wealth of local knowledge on biodiversity. This is an effort to bring traditional knowledge under an extended intellectual property umbrella. It appears that an imbalance of power is being corrected within this general area of exploiting exotic gene pools.

#### **Case study 3:**

In which of the following cases, would you grant permission?

- a. normal fertile couples undergo in vitro fertilization in order to produce a baby that can be a stem cell donor for an older sibling
- b. The older sibling suffers from genetic disorder and the embryo created in vitro would be tested for the absence of mutation and is the positive tissue match to the older sibling
- c. The condition suffered by the older sibling is not genetic but the child still needs donated stem cells.

Answer: In this case, in vitro embryo would be selected solely as a tissue match. There should be clear cut regulations surrounding these concepts. HFE 1990 Act, creation of saviour sibling - enable the identification of a tissue match for an older sibling suffer from life-threatening disease. There are some true examples, elder sister suffered from promyelotic leukemia - Anna selected an embryo to provide umbilical cord stem cell. Similarly, Nash family elder daughter suffered from Fanconi's anemia. In 2000, Adam was born a suitable match for her sister. But most of the people say "If you use one of your children to save the life of another, are you being a good mother or a very bad one"

#### **Case study 4:**

A small biotechnology company in Mexico has discovered a gene that encodes a protein in the network of resistance to oxidative stress in plants. Laboratory experiments have shown that when the gene is transferred by genetic modification techniques to crop species, they show enhanced capacity to grow under conditions where water supply is limiting. The company has not published its data because it is filing a patent on the gene. If the patent is granted, the company plans to license it out to a major trans-national agri-chemical company. Should the patent be granted?

Answer: Yes, the term oxidative stress is used-comprising all kind of biotic and abiotic stress conditions. This will be helpful in reducing the damaging of crops caused by stress conditions.

#### **Case study 5:**

If you are the head of biology department and university promotion committee has asked you to select any one of the academic staff. Candidate A is 37, working on the ecology of plant-insect relations. His research on the evolution of pollination mechanisms is widely respected. The research has steady flow of grant. Candidate B is 34, working on the regulation of gene expression in programmed cell death, especially in relation to cancer. This work is of great interest in the biomedical community. The work is supported by extensive funds. What should be the criteria of selecting according to research?

Answer: As a head of the department you must look at the particular research goals as well as candidate aspirations and world-view. Also look whether his or her research is beneficial for the public or not.

#### **Case study 6:**

Employing science to sell a product either the modernist or post-modernist version is acceptable or not. For example, a female actor told viewers about shampoo on UK TV in 2004. She told hair is 96% amino acids. Shampoo should be rich in amino acids to nourish hair or not?

Analysis: Yes, hair has amino acids which are joined together in a long protein chain called keratin. Protein cannot be repaired by direct uptake of amino acids as hair takes up small amount of amino acids from the shampoo. Another view is that the process of protein synthesis takes place in the hair cell at the base of the hair not in the hair itself. Shampoo cannot deliver amino acids because detergents can disrupt the protein synthesis.

The term “amino” should be used rather than amino acids because it gives negative impact. This is not a comment on the shampoo efficacy; we are sure that modern shampoos clean the hair and scalp and leave the hair shiny and manageable. Rather this is a comment on the dishonest use of scientific terminology to imply things that cannot happen. Advertisers’ said that they will continue to use the jargon of science, it is classic post-modern triumph of style over substance.

#### **Case study 7:**

- a. Because of the family history I know I am likely to be an unaffected carrier of a gene that causes a serious and so far untreatable condition. Do I request a test for that gene? If the test is positive should I tell my spouse?
- b. Family history informs me that I have 50-50 chance of possessing a gene that at the age of 40 cause serious neuro-degenerative diseases for which there is no treatment. Do I want the test? if the test is positive should I tell my spouse or children
- c. Currently I am healthy but I know I have a gene that is very likely to cause serious health problems and possibly death in the middle age. Who else should know?

Answer: Sometimes the knowledge that one is certain to suffer a serious and distressing condition is a burden too heavy to bear thus ignorance is bliss. There is also a problem of social stigma if the disease is running in the family. Such situation emphasize the importance of genetic counseling; both in the phase of deciding whether to take test and if the test is taken when the results are available.

#### **Case study 8:**

A man presents with symptoms representing cancer and as part of his treatment spleen should be removed. The pathology department use it to establish a cultured cell line in order to study the rare cancer. The cell line performs so well that the scientists collaborate with Biotechnology Company to patent it. They start to earn royalties from other laboratories and organizations that wish to use the cell line. When patient find all this he was amazed; nobody has taken the consent from him nor he has been informed by anyone about these developments. Analyze the ethical issues?

Answer: In terms of medical ethics, removal of the spleen was an act of doing good-beneficence. Patient’s personal autonomy had been respected. It was for the sake of his health that spleen has been removed. In UK, there is great sensitivity concerning the fate of organ removed. Under new legislation, if there is no pre-death consent then kin permission must be taken to retain any organs from dead bodies. In USA, once the organ is removed during surgery, it is no longer belonging to the patient. What is the purpose of keeping their appendix or diseased kidney in a jar in their office? In such situations, donor cannot claim on the income gained as a result of research. Anyone who donates a kidney makes a gift not an investment in the recipient.

### **The stem cell debate:**

Opponents of embryonic stem cell research compare the destruction of an embryo to an abortion. They believe that the embryo constitutes life because it has the potential to fully develop into a human being. Those against embryonic stem cell use believe that it is immoral and unethical to destroy one life to save another. By using stem cells and discarding the embryo, it is thought that human life is ultimately de-valued by this act and is paving a slippery slope for further scientific procedures that similarly de-value life. In particular, many religious groups who are adamantly pro-life have condemned embryonic stem cell research and all of its applications. Other arguments against embryonic stem cells cite the fact that adult stem cells are the ones currently being used in therapies and thus, there is no need to even venture into embryonic stem cell territory. Those who support embryonic stem cell research believe that an embryo is not equivalent to human life because it is inside the womb. Supporters also contend that the societal costs of many diseases and conditions, both in monetary and suffering aspects, means that the ethical concerns regarding embryonic stem cell usage are not sufficient to warrant discontinuation of this promising therapy.

Another argument for embryonic stem cell research is that the embryos are leftover from in-vitro fertilisation and would otherwise be destroyed, so they should instead be put to greater use. Even further down the line in development is the belief that those embryos from legal abortions, which have already been destroyed, would be better used to advance human health rather than simply discarded. Fortunately, there are alternatives but they are far from perfect and they do still require further research before they can be used with an acceptable level of success. Two new embryonic stem cell treatments avoid the foetal destruction by either deriving embryonic stem cells without destructing the foetus or obtaining embryonic stem cells without actually creating a foetus.

In altered nuclear transfer (ANT), an embryo is not created. A derivative of somatic cell nuclear transfer (SCNT), the nucleus of the somatic cell is altered, or genetically reprogrammed, prior to being transferred into the egg. The alteration consequence is that the somatic cell DNA still produces stem cells but does not generate an embryo. In blastomere extraction, an embryo is created but not destroyed. This procedure is performed on a two-day old embryo, following the division of the fertilised egg into eight blastomeres or cells. Previously, the techniques used for harvesting involving the derivation of embryonic stem cells at a later developmental stage, when the embryo is made up of approximately 150 cells. When these cells were harvested, the embryo was destroyed. Embryonic stem cells can instead be extracted from blastomeres, therefore preventing embryo destruction and allowing use of stem cells for research and therapeutic treatment of disease. The other alternative is to strictly use adult stem cells because these are derived from adult tissues. The therapeutic potential is lower, however, because adult stem cells can't differentiate into as many different types of cells as can embryonic stem cells. They are also more likely to have developed genetic abnormalities over time and they don't tend to replicate as efficiently. It is unlikely that a comprehensive solution will be found for the embryonic stem cell debate anytime soon. In the meantime, both national and international policies along with collective public views will likely guide the research and therapy efforts for Embryonic Stem Cells. There is no doubt that stem cells have great potential for treating disease but there unfortunately still remain doubts as to the ethical and moral ramifications of pursuing this potential.

### **Conclusion of cloning controversy:**

The fact that human beings can be cloned is a scientific triumph, but it is also an ethical earthquake. Because these experiments offer the potential to advance scientific knowledge, they will tempt us—always for “the best” reasons—to set aside our convictions about the intrinsic dignity of all human life.

### **Genetic counselling:**

Genetic counselling is the process by which the patients or relatives at risk of an inherited disorder are advised of the consequences and nature of the disorder, the probability of developing or transmitting it, and the options open to them in management and family planning. This complex process can be separated into diagnostic (the actual estimation of risk) and supportive aspects. The National Society of Genetic Counsellors (NSGC) officially defines genetic counselling as the understanding and adaptation to the medical, psychological and familial implications of genetic contributions to disease. This process integrates:

- Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence.
- Education about inheritance, testing, management, prevention, resources

- Counselling to promote informed choices and adaptation to the risk or condition.

A genetic counsellor is an expert with a Master of Science degree in genetic counselling. Genetic counsellors work as members of a health care team and act as a patient advocate as well as a genetic resource to physicians. Any person may seek out genetic counselling for a condition they may have inherited from their biological parents. A woman, if pregnant, may be referred for genetic counselling if a risk is discovered through prenatal testing. Some clients are notified of having a higher individual risk for chromosomal abnormalities or birth defects. Testing enables women and couples to make a decision as to whether or not to continue with their pregnancy, and helps provide information that can be used to prepare for the birth of a child with medical issues. A person may also undergo genetic counselling after the birth of a child with a genetic condition. In these instances, the genetic counsellor explains the condition to the patient along with recurrence risks in future children. In all cases of a positive family history for a condition, the genetic counsellor can evaluate risks, recurrence and explain the condition itself.

The goals of genetic counselling are to increase understanding of genetic diseases, discuss disease management options, and explain the risks and benefits of testing. Counselling sessions focus on giving vital, unbiased information and non-directive assistance in the patient's decision-making process. Seymour Kessler, in 1979, first categorized sessions in five phases: an intake phase, an initial contact phase, the encounter phase, the summary phase, and a follow-up phase. The intake and follow-up phases occur outside of the actual counselling session. The initial contact phase is when the counsellor and families meet and build rapport. The encounter phase includes dialogue between the counsellor and the client about the nature of screening and diagnostic tests. The summary phase provides all the options and decisions available for the next step. If counselees wish to go ahead with testing, an appointment is organized and the genetic counsellor acts as the person to communicate the results.

### **Responding to trafficking and HIV/AIDs:**

The average age of girls trafficked from Nepal to India dropped from 14-16 years in the 80's to 10-14 years in 1994, according to a report by the Human Rights Watch. The notion that young girls are 'virginal' less sexually experienced and hence 'disease-free' and safe, has fuelled increases in the demand for younger sex workers. Gender-based discrimination is compounded by discrimination based on forms of "otherness" such as race, ethnicity, religion and economic status. This forces the vast majority of women into precarious marginalisation. Their undocumented status and lack of access to official papers is one of the factors impeding their free and informed movement across borders. TAsia is home to some of the world's most affluent. It is also home to two-thirds of the world's poor. The increasing feminisation of the region's poverty makes the situation complex. Two-thirds of the region's poor are women and about 20 to 40 percent of the households are led by them. In addition, the number of women living in poverty has increased disproportionately over the last decade. Growing landlessness and lack of work in the village are pushing tens of thousands to move to towns and cities with breakdown of communities and traditional knowledge. Factors that compound such movements also lie in what can be termed, 'socially sanctioned violations'. Situations of conflict and calamities are additional 'push' factors. Even for those who live in cities, employment options in the formal sector are severely limited. As the economy undergoes rapid changes, there are new opportunities. But for those without education or the 'right' connections, it means growing inequalities. For many people, mobility is an important survival mechanism and a freedom. But people on the move can be particularly vulnerable to HBV exposure due to long periods of separation from family, removal from familiar behavioural norms and expectations, social and cultural; isolation and lack of access to information and services. Many who start out as migrants end up being trafficked route.

Globally, there exists a new protocol, 'The UN Protocol to Prevent, Suppress and Punish Trafficking in Persons, especially Women and Children (2000)', which contains the first international definition of 'trafficking in persons'. It is a step forward from the 1949 UN Convention that focused only on sex work and considered all sex works, voluntary and forced, to be trafficking. Much work needs to be undertaken however and there remains no room for complacency. Progress in movements against trafficking and HIV/AIDS is evidenced in the formulation of a human rights standard to deal with trafficked persons. The result of concerted efforts by GAATW and several NGOs, 'The Human Rights Standards for the Treatment of Trafficked Persons and Recommendations' is a lobbying tool at the national, regional and international level for human rights protection for trafficked persons and to promote their basic rights.

There were door-to-door campaigns and street plays to get across the anti-trafficking message. Conducting awareness programmes in villages was, however, risky during the early stages. The poor recognition of the rights of women in that social milieu has, over time, led to aberrations. Their devalued existence often exposes

them to various exploitative practices, be it sexual abuse or gender-based discrimination and neglect. This is also manifested in legal lacunae: women are not entitled to inherit property, and, until recently, the law did not acknowledge marital rape. Such gender inequality makes Nepali women and girls particularly vulnerable to both trafficking and HIV/AIDS.

### **Responding to disasters:**

Natural disasters can be especially traumatic for children and youth. Experiencing a dangerous or violent flood, storm, wildfire, or earthquake is frightening even for adults, and the devastation to the familiar environment (i.e., home and community) can be long lasting and distressing. Often an entire community is impacted, further undermining a child's sense of security and normalcy. These factors present a variety of unique issues and coping challenges, including issues associated with specific types of natural disasters, the need to relocate when home and/or community have been destroyed, the role of the family in lessening or exacerbating the trauma, emotional reactions, and coping techniques. Children look to the significant adults in their lives for guidance on how to manage their reactions after the immediate threat is over. Schools can help play an important role in this process by providing a stable, familiar environment. Through the support of caring adults school personnel can help children return to normal activities and routines and provide an opportunity to transform a frightening event into a learning experience. Immediate response efforts should emphasize teaching effective coping strategies, fostering supportive relationships, and helping children understand the disaster event. Collaboration between the school crisis response team and an assortment of community, state, and federal organizations and agencies is necessary to respond to the many needs of children, families, and communities following a natural disaster. Healing in the aftermath of a natural disaster takes time; however, advanced preparation and immediate response will facilitate subsequent coping and healing.

**Hurricanes:** Usually hurricanes are predicted days to weeks in advance, giving communities time to prepare. These predictions give families time to gather supplies and prepare. At the same time, however, these activities may generate fear and anxiety. Although communities can be made aware of potential danger, there is always uncertainty about the exact location of where the hurricane will impact. When a hurricane strikes, victims experience intense thunder, rain, lightning, and wind. Consequently, startle reactions to sounds may be acute in the months that follow. Among a few children subsequent storms may trigger panic reactions. Immediate reactions to hurricanes can include emotional and physical exhaustion. In some instances children may experience survivor guilt. Research indicates that greater symptomatology in children is associated with more frightening experiences during the storm and with greater levels of damage to their homes.

**Earthquakes:** Aftershocks differentiate earthquakes from other natural disasters. Since there is no clearly defined endpoint, the disruptions caused by continued tremors may increase psychological distress. Unlike other natural disasters, earthquakes occur with virtually no warning. This fact limits the ability of disaster victims to make the psychological adjustments that can facilitate coping. This relative lack of predictability also significantly lessens feelings of controllability. While one can climb to higher ground during a flood, or install storm shutters before a hurricane, there is usually no advance warning or immediate preparation with earthquakes. Survivors may have to cope with reminders of the destruction.

**Tornadoes:** Like earthquakes, tornadoes can bring mass destruction in a matter of minutes, and individuals typically have little time to prepare. Confusion and frustration often follow. Similar to a hurricane, people experience sensations during tornadoes that may generate coping challenges. It can be difficult to cope with the sights and smells of destruction. Given the capricious nature of tornadoes, survivor guilt has been observed to be an especially common coping challenge. For instance, some children may express guilt that they still have a house to live in while their friend next door does not. In addition, a study following a tornado that caused considerable damage and loss of life revealed significant associations between children's disturbances and having been in the impact zone, been injured, and having experienced the death of relatives.

**Floods:** These events are one of the most common natural disasters. Flash floods are the most dangerous as they occur without warning; move at intense speeds; and can tear out trees, destroy roads and bridges, and wreck buildings. In cases of dam failure the water can be especially destructive. Research has reported that many children who survive a destructive flood experience psychological distress. The two most significant predictors of impairment are the degree of disaster exposure and perceptions of family reactions. Sensations that may generate coping challenges include desolation of the landscape, the smell of sludge and sodden

property, coldness and wetness, and vast amounts of mud. Most floods do not recede overnight, and many residents have to wait days or weeks before they can begin the cleanup.

**Wildfires:** Unlike other natural disasters such as earthquakes, there is often some warning of an advancing wildfire. However, depending upon the wind and terrain the direction and spread of a wildfire can change abruptly. The amount of warning can vary from one neighborhood to the next. While some people may have hours (or even days) to evacuate, others will have only a few minutes to gather their belongings and leave their homes. Even if evacuation is not ultimately necessary, preparing for the possibility can be frightening for children, particularly if they are seeing images of homes burning nearby on television. Reactions immediately following a wildfire may include emotional and physical exhaustion. In some instances children may experience survivor guilt (e.g., that their home was left unharmed, while others were completely destroyed). In general it might be expected that greater symptomatology in children will be associated with more frightening experiences during the wildfire and with greater levels of damage to their community and homes. The sights, sounds, and smells of a wildfire often generate fear and anxiety. Consequently, similar sensations (e.g., the smell of smoke) may generate distress among children in the months that follow. Given the scale of most wildfires, individuals living outside the ravages of the fires may still feel exposed to the danger from drifting clouds of smoke, flames on the horizon, and television reports. Some children may also react to follow-up news coverage, and even weather reports that talk about dry fire conditions after the fact.

It is important to acknowledge that although a given natural disaster may last for only a short period; survivors can be involved with the disaster aftermath for months or even years. In attempts to reconstruct their lives following such a natural disaster, families are often required to deal with multiple people and agencies (e.g., insurance adjustors, contractors, electricians, roofers, the Red Cross, the Federal Emergency Management Agency (FEMA), and the Salvation Army). Most children will be able to cope over time with the help of parents and other caring adults. However, some children may be at risk of more extreme reactions. The severity of children's reactions will depend on their specific risk factors. These include exposure to the actual event, personal injury or loss of a loved one, dislocation from their home or community, level of parental support, the level of physical destruction, and pre-existing risks, such as a previous traumatic experience or mental illness. Symptoms may differ depending on age but can include:

- **Preschoolers**—thumb sucking, bedwetting, clinging to parents, sleep disturbances, loss of appetite, fear of the dark, regression in behaviour, and withdrawal from friends and routines.
- **Elementary School Children**—irritability, aggressiveness, clinginess, nightmares, school avoidance, poor concentration, and withdrawal from activities and friends.
- **Adolescents**—sleeping and eating disturbances, agitation, increase in conflicts, physical complaints, delinquent behaviour, and poor concentration.

A minority of children may be at risk of post-traumatic stress disorder (PTSD). Symptoms can include those listed above, exhibited over an extended period of time. Other symptoms may include re-experiencing the disaster during play and/or dreams; anticipating or feeling that the disaster is happening again; avoiding reminders of the disaster; general numbness to emotional topics; and increased arousal symptoms such as inability to concentrate and startle reactions. Although rare, some adolescents may also be at increased risk of suicide if they suffer from serious mental health problems like PTSD or depression. Students who exhibit these symptoms should be referred for appropriate mental health evaluation and intervention. Risk factors are outlined in the above section on children's reactions. Interventions may include individual counselling, small group counselling, or family therapy. From group crisis interventions, and by maintaining close contact with teachers and parents, the school crisis response team can determine which students need supportive crisis intervention and counselling services. A mechanism also needs to be in place for self-referral and parental-referral of students.

Provide staff members with information on the symptoms of children's stress reactions and guidance on how to handle class discussions and answer children's question. As indicated, offer to help conduct a group discussion. Reinforce that teachers should pay attention to their own needs and not feel compelled to do anything they are not comfortable doing. Suggest that administrators provide time for staff to share their feelings and reactions on a voluntary basis as well as help staff develop support groups. In addition, teachers who had property damage or personal injury to themselves or family members will need leave time to attend to their needs. La Greca and colleagues have developed a manual for professionals working with elementary school children following a natural disaster. Activities in this manual emphasize three key components supported by the empirical

literature: (a) exposure to discussion of disaster-related events, (b) promotion of positive coping and problem-solving skills, and (c) strengthening of children's friendship and peer support. Specifically:

- **Encourage children to talk about disaster-related events.** Children need an opportunity to discuss their experiences in a safe, accepting environment. Provide activities that enable children to discuss their experiences. These may include a range of methods (both verbal and nonverbal) and incorporate varying projects (e.g., drawing, stories, audio and video recording). Again provide teachers specific suggestions or offer to help with an activity.
- **Promote positive coping and problem-solving skills.** Activities should teach children how to apply problem-solving skills to disaster-related stressors. Children should be encouraged to develop realistic and positive methods of coping that increase their ability to manage their anxiety and to identify which strategies fit with each situation.
- **Strengthen children's friendship and peer support.** Children with strong emotional support from others are better able to cope with adversity. Children's relationships with peers can provide suggestions for how to cope with difficulties and can help decrease isolation. In many disaster situations, friendships may be disrupted because of family relocations. In some cases parents may be less available to provide support to their children because of their own distress and their feelings of being overwhelmed. It is important for children to develop supportive relationships with their teachers and classmates. Activities may include asking children to work cooperatively in small groups in order to enhance peer support.

Focus on their competencies in terms of their daily life and in other difficult times. Help children identify what they have done in the past that helped them cope when they were frightened or upset. Tell students about other communities that have experienced natural disasters and recovered. All crisis response team members need an opportunity to process the crisis response. Providing crisis intervention is emotionally draining. This is likely to include teachers and other school staff if they have been serving as crisis caregivers for students. Although more than enough caregivers are often willing to provide support during the immediate aftermath of a natural disaster, long-term services may be lacking. School psychologists and other school mental health professionals can help provide and coordinate mental health services, but it is important to connect with community resources in order to provide such long-term assistance. Ideally these relationships would be established in advance. The frequent need for disaster survivors to relocate creates unique crisis problems. For example, it may contribute to the social, environmental, and psychological stress experienced by disaster survivors. Research suggests that relocation is associated with higher levels of ecological stress, crowding, isolation, and social disruption.

Parents' adjustment is an important factor in children's adjustment, and the adjustment of the child in turn contributes to the overall adjustment of the family. Altered family functions, separation from parents after natural disaster, and ongoing maternal preoccupation with the trauma are more predictive of trauma symptomatology in children than is the level of exposure. Thus, parents' reactions and family support following a natural disaster are important considerations in helping children's cope. Preliminary findings suggest that children who tend to be anxious are those most likely to develop post-trauma symptomatology following a natural disaster. Research suggests that children who had a pre-existing anxiety disorder prior to a natural disaster are at greater risk of developing PTSD symptoms. It is important to examine children's coping following a natural disaster because coping responses appear to influence the process of adapting to traumatic events. Research suggests that the use of blame and anger as a way of coping may create more distress for children following disasters. Research suggests that long term difficulties following a natural disaster (e.g., PTSD), are most likely to be seen among children who experienced any of the following:

- Had threats to their physical safety.
- Thought they might die during the disaster.
- Report that they were very upset during the disaster.
- Lost their belongings or house as a result of the disaster.
- Had to relocate in the aftermath.
- Attended schools following the disaster that had multiple schedule changes, double sessions or a lot of disruptions.

Consequently, crisis response team members need to identify students who experience these risk factors and closely monitor their status. These students may require long-term coping assistance.

**Biosafety:**

Biosafety is the prevention of large-scale loss of biological integrity, focusing both on ecology and human health. These prevention mechanisms include conduction of regular reviews of the biosafety in laboratory settings, as well as strict guidelines to follow. Biosafety is used to protect us from harmful incidents. High security facilities are necessary when working with Synthetic Biology as there are possibilities of bioterrorism acts or release of harmful chemicals and or organisms into the environment. A complete understanding of experimental risks associated with synthetic biology is helping to enforce the knowledge and effectiveness of biosafety. Biosafety is related to several fields like with ecology, agriculture, medicine, chemistry, exobiology, synthetic biology.

The international Cartagena Protocol on Biosafety deals primarily with the agricultural definition but many advocacy groups seek to expand it to include post-genetic threats: new molecules, artificial life forms, and even robots which may compete directly in the natural food chain. Biosafety in agriculture, chemistry, medicine, and exobiology and beyond will likely require application of the precautionary principle and a new definition focused on the biological nature of the threatened organism rather than the nature of the threat. When biological warfare or new, currently hypothetical, threats (i.e., robots, new artificial bacteria) are considered, biosafety precautions are generally not sufficient. The new field of biosecurity addresses these complex threats. Biosafety level refers to the stringency of biocontainment precautions deemed necessary by the Centres for Disease Control and Prevention (CDC) for laboratory work with infectious materials. Typically, institutions that experiment with or create potentially harmful biological material will have a committee or board of supervisors that is in charge of the institution's biosafety. They create and monitor the biosafety standards that must be met by labs in order to prevent the accidental release of potentially destructive biological material.

**Biosecurity:**

Biosecurity has multiple meanings and is defined differently according to various disciplines. The original definition of biosecurity started out as a set of preventive measures designed to reduce the risk of transmission of infectious diseases in crops and livestock, quarantined pests, invasive alien species, and living modified organisms. The term was first used by the agricultural and environmental communities. Starting from the late 1990s in response to the threat of biological terrorism, biosecurity encompasses the prevention of the intentional removal of biological materials from research laboratories. These preventative measures are a combination of systems and practices put into its place at bioscience laboratories to prevent the use of dangerous pathogens and toxins for malicious use, as well as by customs agents and agricultural and natural resource managers to prevent the spread of these biological agents.

Advances in technology have meant that many civilian research projects in medicine have the potential to be used in military applications (dual-use research) and biosecurity protocols are used to prevent dangerous biological materials from falling into the hands of malevolent parties. The National Academies of Science define biosecurity as "security against the inadvertent, inappropriate, or intentional malicious or malevolent use of potentially dangerous biological agents or biotechnology, including the development, production, stockpiling, or use of biological weapons as well as outbreaks of newly emergent and epidemic disease". Biosecurity requires the cooperation of scientists, technicians, policy makers, security engineers, and law enforcement officials.

**Bioweapons:**

Biological warfare is the deliberate spreading of disease amongst humans, animals, and plants. Biological weapons (BW) introduce a bacteria or virus into an environment for hostile purposes that are not prepared to defend it from the intruder. As a result, this agent can become very effective at killing plants, livestock, pets, and humans. There are a huge variety of genetically or traditionally modified bacteria's and viruses to withstand antibiotics, that could be used as biological weapons, but some of the most common types today are bacteria, rickettsiae, viruses, toxins, and fungi. When compared to the cost of a nuclear weapons program, biological

weapons are extremely cheap. It is estimated that 1 gram of toxin could kill 10 million people. A purified form of botulinum toxin is approximately 3 million times more potent than Sarin, a chemical nerve agent. As a comparison, a SCUD missile filled with botulinum toxin could affect an area of 3700 sq.km, an area 16 times greater than could be affected with Sarin. It is important to note that while it is relatively cheap to produce the biological weapons agents in large quantities, sophisticated weapons are slightly more difficult to develop and produce. For example, when a missile is flying it gets very hot, biological agents are killed. Therefore, the missile has to be fitted with a cooling system. In addition, storing biological weapons agents requires much effort, due to the quick decay of many of these sorts of agents. However, as far as weapons of mass destruction are concerned, biological weapons are relatively cheap to develop and produce. In one analysis, the comparative cost of civilian casualties is "\$2,000 per square kilometer with conventional weapons, \$800 with nuclear weapons, \$600 with nerve-gas weapons, and \$1 with biological weapons." Not surprisingly, biological weapons have long since become known as the poor man's atom bomb. Any nation with a reasonably advanced pharmaceutical and medical industry has the capability of mass producing biological weapons. This fact also leads to problems with determining what countries have programs. Anything from a piece of fruit to a ballistic missile could be used to deliver a biological weapon to a target. Along with this is the fact that with certain organisms, only a few particles would be needed to start an infection that could potentially cause an epidemic. Conventional weapons explode once and are finished. With a few particles of Hanta virus many thousands of people could become carriers that infect thousands more people.

A seed culture of anthrax bacteria could be grown to mass quantities in around 96 hours. The level of technology needed to do this kind of work is also much lower when compared to Nuclear weapons. Most of the techniques used can be found in textbooks and journals available worldwide. The information is not considered "hot" like certain kinds of nuclear information. The techniques are taught in undergraduate courses in Colleges and Universities worldwide. The first recorded use of biological agents is the Romans using dead animals to foul the enemies water supply. This had the dual effects of decreasing enemy numbers and lowering morale. 1346-1347 - Mongols catapult corpses contaminated with plague over the walls into Kaffa (in Crimea), forcing besieged Genoans to flee. Some historians believe that this event was the cause of the epidemic of plague that swept across medieval Europe killing 25 million. 1710 - Russian troops allegedly use plague-infected corpses against Swedes. 1767 - During the French and Indian Wars, the British give blankets used to wrap British smallpox victims to hostile Indian tribes. 1916-1918 - German agents use anthrax and the equine disease glanders to infect livestock and feed for export to Allied forces. Incidents include the infection of Romanian sheep with anthrax and glanders for export to Russia, Argentinian mules with anthrax for export to Allied troops, and American horses and feed with glanders for export to France. 1937 - Japan begins its offensive biological weapons program. Unit 731, the BW research and development unit, is located in Harbin, Manchuria. Over the course of the program, at least 10,000 prisoners are killed in Japanese experiments. 1939 - Nomonhan Incident - Japanese poison Soviet water supply with intestinal typhoid bacteria at former Mongolian border. First use of biological weapons by Japanese. 1937 - Japan begins its offensive biological weapons program. Unit 731, the BW research and development unit, is located in Harbin, Manchuria. Over the course of the program, at least 10,000 prisoners are killed in Japanese experiments. 1940 - The Japanese drop rice and wheat mixed with plague-carrying fleas over China and Manchuria. 1942 - U.S. begins its offensive biological weapons program and chooses Camp Detrick, Frederick, Maryland as its research and development site. 1945 - Only known tactical use of BW by Germany. A large reservoir in Bohemia is poisoned with sewage. 1951 - In a test of BW dispersal methods, biological simulants are sprayed over San Francisco. 1966 - The United States conducts a test of vulnerability to covert BW attack by releasing a harmless biological simulant into the New York City subway system. 1969 - President Nixon announces unilateral dismantlement of the U.S. offensive BW program. 1970 - President Nixon extends the dismantlement efforts to toxins, closing a loophole which might have allowed for their production. 1978 - In a case of Soviet state-sponsored assassination, Bulgarian exile Georgi Markov, living in London, is stabbed with an umbrella that injects him with a tiny pellet containing ricin (a highly toxic, natural protein). 1979 - Outbreak of pulmonary anthrax in Sverdlovsk, Soviet Union. 1992 - Russian president Boris Yeltsin acknowledges that the outbreak was caused by an accidental release of anthrax spores from a Soviet military microbiological facility. 1985-1991 - Iraq develops an offensive biological weapons capability including anthrax, botulinum toxin, and aflatoxin.

Biological defense may be divided into the following categories: prevention, protection, detection, treatment, and decontamination. *Prevention* may take several forms. In the case of biological warfare, international disarmament and inspection regimes may deter production and dissemination of biological warfare agents. Intelligence assets may indicate potential threats and allow for preventative action to be undertaken. *Protection* against biological warfare agents is limited. Protective suits, clothing, gas masks and filters may provide limited protection for short periods of time. However, the persistence of biological agents such as anthrax makes such protections mainly useful for military personnel and first responders. Anthrax can remain

active and potentially lethal for at least 40 years. (source: Biological Warfare: A Historical Perspective) It should be noted that anthrax is an exception, as most other agents do not live that long. Protection (as detection and treatment) of Biological Warfare is the establishment and maintenance of a good health care system. In addition, vaccination is a form of protection, which may provide substantial protection against naturally occurring agents, although vaccines often provide limited or no protection against genetically engineered variants designed to defeat such vaccines. *Detection.* During the Gulf War, US and allied forces suffered from a lack of reliable biological agent detection systems. Subsequently, a number of detection systems have been developed. Often it takes from a few hours to a few days to detect exposure to a biological weapon. However, advances in biotechnology will help develop improved and quicker detectors. Current detectors include: SMART (Sensitive Membrane Antigen Rapid Test) JBPDS (Joint Biological Point Detection System) BIDS (Biological Integrated Detection System) IBAD (Interim Biological Agent Detector) (source: Biological Warfare and Detection Capabilities) Treatment options after infection depend on whether or not the infectious agent is identified. If not identified, massive doses of antibiotics may be given in hopes that something may work. Again, treatment of victims of biological warfare largely depends on the establishment and maintenance of a good health care system. *Decontamination.* Unlike chemical weapons, which disperse over time, biological agents may grow and multiply over time. Anthrax can remain active in the soil for at least 40 years and is highly resistant to eradication. (Source: Biological Warfare: A Historical Perspective) However, the anthrax contaminated Gruinard Island in the UK was decontaminated - decontamination is possible, using chemicals, heat or UV rays.

Using biological and chemical weapons was condemned by international declarations and treaties, notably by the 1907 Hague Convention (IV) respecting the laws and customs of war on land. Efforts to strengthen this prohibition resulted in the conclusion, in 1925, of the Geneva Protocol, which banned the use of asphyxiating, poisonous or other gases, usually referred to as chemical weapons, as well as the use of bacteriological methods of warfare. The latter are now understood to include not only bacteria, but also other biological agents, such as viruses or rickettsiae which were unknown at the time the Geneva Protocol was signed. However, the Geneva Protocol did not prohibit the development, production and stockpiling of chemical and biological weapons. Attempts to achieve a complete ban were made in the 1930s in the framework of the League of Nations, but with no success. The prohibition of chemical and biological weapons appeared on the agenda of the Eighteen-Nation Committee on Disarmament in Geneva in 1968. One year later, the United Nations published an influential report on the problems of chemical and biological warfare, and the question received special attention at the UN General Assembly. The UN report concluded that certain chemical and biological weapons cannot be confined in their effects in space and time and might have grave and irreversible consequences for humans and nature. This would apply to both the attacking and the attacked nations. Due to interest in the topic in the end of the 1960s, the Biological Weapons and Toxin Convention was signed in 1972 and entered into force in 1975. The Biological and Toxin Weapons Convention (BTWC) entered into force in March 1975 after 22 governments had ratified, and was the first multilateral disarmament treaty banning an entire category of weapons of mass destruction. The Convention, about four pages long, bans the development, production stockpiling, or acquisition of biological agents or toxins of any type or quantity that do not have protective, medical, or other peaceful purposes, or any weapons or means of delivery for such agents or toxins. Under the treaty, all such materiel is to be destroyed within nine months of the treaty's entry into force. The BTWC currently has 163 states parties and 110 signatories. Since the entry of the Convention, seven review conferences have taken place. On the Seventh Review Conference in December 2011, 103 states parties to the Convention participated in the conference.

### **Biohazard:**

Biohazard outbreaks from pathogens and infectious diseases occur every day in the U.S. and throughout the world from *Avian Influenza virus*, *HIV/AIDS*, *Hepatitis viruses*, *Norovirus (Norwalk virus)*, *Salmonella* bacteria, *Mycobacterium tuberculosis* bacteria, *Vibrio cholerae* bacteria (cholera), MRSA superbugs, Plasmodium parasites (malaria) and hundreds of other microorganisms. Bacteria, viruses and parasites are responsible for the bulk of the 18.4 million deaths worldwide from communicable diseases in 2004 estimated by the World Health Organization plus additional deaths from non-communicable diseases and cancers. Pathogens currently infects billions of people and trends indicate a rising number of pathogen deaths and infections from population growth in developing countries, urbanization, poor sanitation, broken water infrastructure, reduced food safety, globalization, international travel, extreme weather, and the rising costs of new drugs, vaccines and antibiotics. Many of these deaths are premature and preventable. The key to preventing major outbreaks is frequent and comprehensive testing for each suspected pathogen, as most occurrences of pathogens are not detected until

after people get sick or die. With advances in nanotechnology, biotechnology, information technology and wireless technology, new generations of low cost biosensors and early warning systems will provide a front line of defense against the transmission of deadly pathogens. It is easy to recognize the biggest threat to humankind. Just count the dead, the dying, environmental damage, and economic costs. The world record holder for human deaths is *Yersinia pestis*. This disease-causing bacterium killed as many as 75 to 100 million people during the Black Plague, or roughly 20% of the world's 450 million population in the 14th century.

Also at the top of the list is the human, animal, and environmental catastrophes. With advances in nanotechnology, biotechnology, information technology and wireless technology, new generations of low cost biosensors and early warning systems will provide a front line of defense against the transmission of pathogens. Individual bacteria, viruses and protozoa parasites will be rapidly detected at transmission sources, then contained and prevented from spreading. This will stop the mass transmission of illness and death along with the massive economic consequence associated with major outbreaks. One strain, the Influenza A H1N1 virus or Spanish Flu killed as many as 50 million people in 1918 [1]. Unlike the Black Plague which took many years for its deadly transmission to take place, most of the Spanish flu deaths took place in only one year. In 2009, a new strain of the Influenza A H1N1 virus or Swine Flu resulted in dozens of deaths and fears of a possible worldwide pandemic.

Another Influenza virus strain is the Avian Influenza H5N1 virus or Bird Flu that at present mainly affects the bird population. Recent outbreaks caused the urgent culling of 3.5 million poultry in Saudi Arabia in November 2007 and 2.9 million poultry in India in January 2008 due to the fear of the strain mutating into a form more easily transmitted to people. The Bird Flu killed 103 out of 126 infected people in Indonesia by the end of February 2008, an 82% mortality rate so far. In anticipation of a possible Influenza virus pandemic, the UK government announced an emergency plan to permit as many as 700,000 dead bodies to be rapidly processed using mass graves, inflatable mortuaries, 24-hour cremations and express funerals. In 2008 the World Bank predicted that a Flu pandemic could kill 71 million people worldwide and cause a major global recession costing more than \$3 trillion.

Another virus, the Human Immunodeficiency Virus or HIV currently infects 33.2 million people around the world. HIV causes Acquired Immune Deficiency Syndrome or AIDS by damaging immune systems which protects people against diseases by killing pathogens and tumor cells. AIDS killed 2.1 million people in 2007 which is triple the 700,000 AIDS deaths in 1993 only 14 years earlier. The annual AIDS death rate is believed to have peaked. Over two thirds of AIDS sufferers live in Africa where eight countries have over 15% of its adult population infected with AIDS. According to the WorldWatch Institute, the gross domestic product of 33 African countries with a significant HIV/AIDS population declined by an average of 1.1 percent per year between 1992 and 2002. The combined loss in GDP from these countries is projected to reach \$144 billion by 2020. More people are infected with the *Hepatitis C virus* than with HIV. China alone has 38 million Hepatitis C sufferers affecting over 3% of its entire population. China's high Hepatitis C infection rates are believed to be linked to illegal blood and plasma donation practices during the 1980s and early 1990s, and failure to screen transfusion recipients [9]. About 85% of those infected with Hepatitis C Virus become chronically infected with the virus which replicates and can slowly attack the liver over a period of decades. This results in advanced liver scarring or cirrhosis in 10 to 20% percent of cases. Liver cancer develops in 1 to 5% of cases.

China was also the home to the Severe Acute Respiratory Syndrome or SARS epidemic in 2002 caused by the SARS coronavirus. China's inaction in containing the virus and delay in informing its citizens and the World Health Organization of the outbreak have been cited as significant factors that caused the wide transmission of SARS. China's national tourist bureau estimated China's loss from the SARS outbreak to be \$8.8 billion in tourism revenue from foreign sources and an additional \$24.5 billion from domestic sources. The World Health Organization claims that loss of tourism revenue is a primary factor for countries to not report epidemics. Another respiratory infection is tuberculosis (TB) caused by the *Mycobacterium tuberculosis* bacteria. The World Health Organization estimated that in 2006 1.5 million people died from TB plus another 200,000 died from HIV associated with TB. A TB infected person typically infects 10 to 15 new people each year through coughing, sneezing, talking or spitting. One-third of the world's population is believed to be infected with the TB bacillus with nine million new cases occurring each year. While TB can become non-infectious and cured if properly treated, about one quarter of the new cases are multi-drug resistant. These drug resistant strains are highly concentrated in south-western Russia and nearby countries in the former Soviet Union. Closer to home, the Methicillin-resistant *Staphylococcus aureus* or MRSA bacteria kills nearly 19,000 Americans every year which is more than the annual number of AIDS deaths in the US.

MRSA affects about 2 million Americans and costs \$20 billion a year due to its high incidence in health-care facilities. Health care facilities have a high immuno-compromised population with weakened immune systems, cancer and surgical patients, organ transplant recipients, HIV patients, elderly, malnourished, pregnant, new born and sick kids, who are least able to fight off invading pathogens. When MRSA adds a severe illness to a patient's original medical condition, the death rate increases by 4 times, and hospital stays are extended, making other patients wait longer for their treatments. MRSA infections are increasingly appearing in places where people are in close contact such as locker rooms, military facilities, and prisons. The Infectious Diseases Society of America (IDSA) has listed MRSA as one of 6 extremely dangerous superbugs which are not readily killed by antibiotics [16]. IDSA's five other superbugs are *Acinetobacter baumannii* which is a growing cause of hospital-acquired pneumonia with mortality rates range of 20 to 50%; *Aspergillus* fungus with a 50-60% death rate; Vancomycin-resistant *Enterococcus faecium* (VRE) a major cause of bloodstream infections, infections of the heart, meningitis, and intra-abdominal infections; *Pseudomonas aeruginosa* (*P. aeruginosa*) a hospital-acquired pneumonia following surgery and urinary tract infections with a particular threat to children with cystic fibrosis; and *Escherichia coli* (*E. coli*) and *Klebsiella spp.* which are the major causes of urinary tract, gastrointestinal tract, and wound infections. In addition to these superbugs which are mostly bacteria, antibiotics have no effect on viruses or viral infections.

Some of the most common foodborne biohazards are *Salmonella* bacteria which are commonly found in poultry, eggs, unprocessed milk and meat; *Campylobacter* bacteria which infect people from undercooked chicken; *Listeria* bacteria which are found in soft French style cheeses, pates, uncooked hot dogs and sliced deli meats; and *Toxoplasma gondii*, a parasitic protozoa transmitted from under cooked meats and contact with cats, and is particularly dangerous to pregnant woman and their unborn children. *Norovirus* (*Norwalk virus*) is primarily spread from infected people such as kitchen workers contaminating restaurant food. The CDC lists 34 cruise ships in 2006 having Norovirus or other pathogens outbreaks affecting 5% or more of their passengers. Food can be infected by biohazards at anytime in the processing cycle. Fresh fruits, vegetables and seafood can be contaminated by pathogens if they are washed or irrigated with water contaminated with animal manure or human sewage. In 2008 a *Salmonella* Saintpaul outbreak in possibly from imported Jalapeno peppers from Mexico linked to 1,442 cases, 286 hospitalizations, and 2 deaths in the US. In 2009 a *Salmonella typhimurium* outbreak caused by peanut butter resulted in 9 deaths and 691 illnesses in the US. Meat and poultry can be infected with biohazards when the animals are being raised, slaughtered, processed into food products, mixed with infected ingredients, or improperly handled in stores, transport, or in meal preparation. In 2008, 20 people died from a *Listeria* outbreak in Canada which was traced to a Maple Leaf Foods meat-packing plant [18c]. In the kitchen, microbes can be transferred from one food to another food by using the same contaminated knife or cutting board. Lightly infected food left unrefrigerated overnight can become highly infectious in the morning.

Biohazards found in food have led to major recalls with enormous economic consequences. In the early 1990's a pathogenic prion protein from infected sheep was fed to cattle and caused a BSE (bovine spongiform encephalopathy) or Mad Cow Disease epidemic in the UK affecting as many as 200,000 cattle. Evidence suggested that when people eat diseased tissue from BSE cattle they can become infected with variant Creutzfeldt-Jakob disease (vCJD), the human form of mad cow disease. In 2003, the first Mad Cow Disease case was detected in the US from a cow imported from Canada. The U.S. beef industry claimed losses in 2004 of up to \$4.7 billion while a 26 month ban on Canadian beef entering the US cost Canadian producers around \$5.7 billion. Even with the potential risks, the current low incident of Mad Cow Disease in the US has allowed testing to be scaled back to only 0.1% of the 37 million cows slaughtered each year. Related events include the culling of 6 million sheep, cattle and pigs along with £5.6 billion in economic losses and government payouts from *Picornavirus* which caused a Foot and Mouth Disease Outbreak in the UK in 2001; a recall of 21.7 million pounds of frozen ground beef patties infected with *E. coli* O157:H7 from Topps Meat Company of New Jersey in September 2007; and a recall of 143 million pounds of beef from cows that could not walk and believed to pose a higher contamination risk from *E. coli*, mad cow disease and salmonella from Westland/Hallmark Meat Co in California in February 2008. Animals on farms, in the wild and domestic pets are also potential sources of pathogens. One source of infection is the fecal oral route of infected animal feces finding their way into people's mouths by touching an infected surface containing animals' feces. Pet owners kissing their pets or touching their mouths after playing with their pets can also be at risk. Other infectious routes include scratches, bites, breathing droplets containing feces, or bites from insects or fleas present on the animals.

According to the World Health Organization, 1.1 billion people lack access to safe water and 2.6 billion people lack access to proper Diarrheal diseases from drinking contaminated water kill 1.8 million people each year, mostly children under 5 in developing countries. The biggest source of diarrheal diseases is *Vibrio cholerae* bacteria which causes Cholera, a rapidly fatal illness that could kill people in as little as three hours if

treatment is not provided. In 2009 a cholera outbreak in Zimbabwe water killed 4,037 and infected over 91,000. Another bacterium, *Salmonella typhi* causes typhoid fever which affects 21 million people every year and kills 200,000. When infected water is used to irrigate crops, feed animals, or is dumped near fish and shellfish, pathogens can contaminate the food chain. Intestinal helminth infections from parasites such as *Ascaris lumbricoides* often leads to severe consequences such as cognitive impairment, massive dysentery, or anaemia and affects 133 million people with 9,400 deaths every year. Other pathogens enter the body on contact. The *Schistosoma* parasite is contracted when swimming and infects 160 million people with schistosomiasis, causing tens of thousands of deaths every year mainly in sub-Saharan Africa. When the *Chlamydia trachomatis* bacteria comes in contact through peoples' eyes through washing or damp linen, it causes trachoma which threatens blindness in 146 million people including 6 million who are already visually impaired. Pathogen-induced diseases can also be closely associated with the availability of water, particularly when the pathogens are transmitted by insects whose larva develops in water bodies. Plasmodium parasites cause malaria which infects 300 to 500 million people and kills over one million each year. Irrigation systems and reservoirs in hot climate countries increase mosquito breeding sites and accelerate the transmission of malaria. Other pathogens transmitted by mosquito include *Flavivirus* (Dengue Fever) and *West Nile virus* (neuroinvasive illness and West Nile fever). West Nile virus from disease carrying mosquitoes have been found in abandoned pools at foreclosed homes in California resulting from the US sub-prime mortgage crisis.

People living in industrialized countries have a much lower risk of contracting a water-borne pathogen. One principal reason is that drinking water is usually treated with chlorine or other disinfectants that kill bacteria such as *Vibrio cholerae* (cholera), and *Salmonella typhi* (typhoid fever). However, chlorination can give a false sense of security as protozoan parasites such as *Cryptosporidia* and *Giardia lamblia*, and viruses like hepatitis A and E, rotavirus, Norovirus, poliovirus and echovirus can be present in drinking water even when water is chlorinated. People can become extremely sick by swallowing a few protozoa since they rapidly reproduce once inside a host organism. *Cryptosporidium* caused a cryptosporidiosis outbreak in Milwaukee in 1993 that resulted in over 400,000 cases of serious illness and 100 deaths, principally among AIDS patients. Chlorination systems can become ineffective when overwhelmed by severe weather, heavy rains and floods. In November 2007, doctors in Pascagoula, Mississippi began petitioning local authorities to relocate a wastewater treatment plant after Hurricane Katrina's storm surge diverted raw sewage from the plant into nearby homes, businesses and industrial facilities, and causing potential contamination from salmonella, shigella, campylobacter, vibrio, hepatitis and flesh-eating diseases. In 2000, heavy rains brought livestock manure laden with *E.coli* O157:H7 and *Campylobacter jejuni* bacteria into Walkerton, Ontario's water supply. Half of the town's 5,000 residents were sickened and 7 died. Following the incident, it was found that 25 miles of the town's pipeline was filled with biofilm that became a breeding ground for *E.coli* and other pathogens to obtain nutrients and multiply. *E.coli* contained in biofilms are extremely resistant to chlorine, and can be released into the drinking water when there is a significant pressure change in the water distribution system due to an industrial plant turning on a production process or a fire hydrant being opened. Pathogens can also enter the water supply after the water is treated. Cities with aging or broken water mains, new developments that have left dead ends in the old water network, and pipelines connected to wells can allow pathogens to access the water supply. Pathogen sources can include storm run offs, industrial and agricultural by-products, leaking septic tanks, untreated waste from infected animals and people, and cemeteries. The EPA estimates that the expense to repair and replace the US water and wastewater infrastructure could cost up to \$1 trillion over the first 20 years of the twenty-first century. Many communities and individuals get their drinking water from underground wells or surface water which have no treatment at all. As well, some people especially children drink water from potential sources of pathogens such as hotwater tanks, swimming pools, waterparks, and ice bins in hotels.

The following trends indicate that the biohazard problem has not yet reached its peaked.

1. The world's population is the highest in history and still increasing. United Nations' statistics reveal that the world's population had increased by 5 billion people during the twentieth century from 1 billion to 6 billion people [33]. As the population increases so does the number of sick and vulnerable people who are least able to fight off pathogens.
2. Developing countries currently make up 80% of world's population. With the world's fastest growing population in Africa and slow or negative growth in industrialized nations, more people will be living with improper sanitation, unsanitized water, inadequate food, and a lack of basic medicines. This will further increase biohazard morbidity and mortality.
3. Population in urban areas is rising at the rate of 1 million people per week. When people live in close proximity, pathogens can more quickly spread as was experienced during plagues and epidemics. Increased city populations put added stress on water mains with a greater water demand for drinking and industrial water, and a greater output of sewage water from human and industrial waste. An increased

demand on urban hospitals puts more people at risk of infections and disease. A greater use of antibiotics and drugs to control pathogens is also creating new families of multiple drug-resistant microbes.

4. Urbanization also requires land and forests to be cleared to make way for more housing. Microorganisms living in the forests are forced to enter populated areas. A greater demand for food and biofuels that are produced from crops also increases the demand for water, as well as greater output of fertilizer and animal feces into the water supply.
5. Mass production of food leads to lower food safety and high risk practices. These include grinding up dead animal parts to feed live animals and introduce unnatural organisms to the food supply as in the case of Mad Cow disease. When food is imported from vicinities with lower safety standards little can be done to prevent animals from being infected with biohazards when sewage water is used to increase their weight. Organic foods which are not produced with herbicides or pesticides that can kill dangerous microorganisms also increase the risk of pathogens to people.
6. Extreme weather appears increasingly more frequently. This can overwhelm a water network and bring pathogens past safeguards. Hot climate diseases such as cholera, malaria and yellow fever are increasingly appearing in milder regions where there is a higher population.
7. More people in the world increase the potential for sexually transmitted diseases (STD) and unprotected sex with multiple partners. While HIV/AIDS is the most deadly sexually transmitted disease and most common in Africa, it is not the only STD. In March 2008, the Centers for Disease Control and Prevention found that 26% of American girls between 14 and 19 have at least one sexually transmitted disease.
8. Globalization including international trade and travel is accelerating the transmission of pathogens. This is especially the case for trade between industrialized nations such as North America and Europe and developing nations such as China and India pathogens where contact is made between previously unexposed people and food products. The World Health Organization estimated 2.1 billion airline passengers travel each year. Airline passengers are at risk of pathogen exposure. For example, airplanes typically fill galley water from local countries sources which can bring pathogens into airplane water and ice. In May 2007 an Air France passenger exposed other passengers with extensively multidrug-resistant tuberculosis. There are virtually no procedures preventing pathogens to be transmitted from travelers, illegal immigrants or people displaced from war or natural disasters. Increased trade also means more transportation of biohazards to testing labs and research centers with a greater chance of the pathogen being improperly handled and people being exposed.

Billions of people throughout the world are at increasing risk of contracting hundreds of different pathogens from the water, food, air, surfaces, people, animals and insects. Not only do pathogens accumulate in human bodies, unlike chemical toxins pathogens are living organisms and once inside a person pathogens reproduce and increase their potency as they grow in numbers to infect and potentially kill its hosts. Over the years advances in medical research and technologies have produced disinfectants, antibiotics and vaccines which have greatly reduced the spread of pathogens mostly in industrialized countries. However, with countless investments only one infectious disease, smallpox from the *Variola virus* has been completely eradicated. According to the World Watch Institute old illnesses such as tuberculosis, malaria, and cholera have spread geographically and more than thirty previously unrecognized diseases such as Ebola, HIV, Hantavirus, and SARS have emerged as new threats to human well-being. Microorganisms have survived on the earth for 4 billion years by adapting to the most severe environments. This is seen today as drug resistant pathogens which have no treatment or cure. Even if new drugs or vaccines are developed for a particular pathogen, exorbitant prices can limit their use to only a small percentage of the sufferers who need it. As well, a particular drug or vaccine might only be useful for a single pathogen and ineffective on the next outbreak. In every case of human and economic catastrophe from biohazards and infectious disease, pathogens had entered into a geographic area and were rapidly transmitted to a greater area. Early detection and containment is the simplest and most effective way to prevent human, animal, and environmental catastrophes. With advances in nanotechnology, biotechnology, information technology and wireless technology, new generations of low cost biosensors and early warning systems will provide a front line of defense against the transmission of pathogens. Individual bacteria, viruses and protozoa parasites will be rapidly detected at transmission sources, then contained and prevented from spreading. This will stop the mass transmission of illness and death along with the massive economic consequence associated with major outbreaks.

### **Application to use Biohazardous waste:**

Application to use Biohazardous waste, also called infectious waste or biomedical waste, is any waste containing infectious materials or potentially infectious substances such as blood. Of special concern are sharp wastes such as needles, blades, glass pipettes, and other wastes that can cause injury during handling. Biohazardous waste includes the materials like human blood and blood products, human Body Fluids, microbiological wastes, pathological waste, animal waste and sharps waste

Laboratories that generate biohazardous waste are responsible for:

1. Ensuring that the waste is either correctly treated and disposed of within the lab, or is properly packaged and transported to the appropriate treatment facility within the Center;
2. Packaging the waste as directed to prevent exposure or injury (needlesticks, cuts) to anyone handling the waste; and
3. Labeling the waste with the generator's name and the room number of the lab where the waste was generated.

Although biohazard waste bags are often conveniently placed throughout the lab, it is important to remember that these bags are for biohazard and contaminated wastes only, and are not to be used for regular trash. Disposal of non-biohazard waste in a biohazard waste container adds significant costs to waste management. The following are examples of items that do not need to be disposed as biohazard waste gloves used to handle containers of blood or body fluids; paper towels or bench paper on which containers of blood or body fluids may have been placed but did not spill; and any other material used to handle blood indirectly but that did not come into direct contact with the blood. Biohazardous liquids and liquids that contain human blood should be disinfected in the lab and flushed down the drain. To disinfect small amounts within the lab add a disinfectant. Cover all objects in the liquid with the solution. Make sure there are no bubbles in the solution or on any submerged surfaces. Let the solution stand for at least 30 minutes. If using any other disinfectant for required concentration and contact time. Pour the solution down the drain with cold water. Biohazardous wastes that cannot be treated in the lab must be prepared and transported by lab personnel for treatment and disposal. Such waste includes large amounts of protein or clotted blood. Containers of protein, stock solutions, clotted blood, etc., are steam-sterilized in the infectious waste autoclave located in the E-Level of the Thomas Building. Each bag of biohazardous waste must be labelled with the lab building and room number in which the waste was generated, and the date the waste was packaged. Using a permanent marker, write the information directly on the waste bag. Dry, solid biohazardous waste must be placed in an autoclave bag. Bags should be closed or covered when not in use or at the end of the day. Use only autoclave bags these bear the biohazard symbol and are available in various sizes. Use autoclave bags for biohazardous waste only. Do not fill bag more than halfway to allow for a five-inch grip. Tie the bag tightly before transporting. Biohazardous waste to be autoclaved must be transported by lab personnel to an autoclave within 14 days of first generating the waste. When available, use the designated freight elevator for your building. Gloves are not allowed in elevators, so the use of a cart is recommended for transporting biohazard waste. The infectious waste autoclave is located in the E-level of the Thomas Building. Deliver bags of biohazard waste to DE-417. All bags must be deposited in red, covered holding containers. Lab personnel are required to log in the waste at the autoclave room in the logbook provided. Any waste that is not properly packaged or labelled will be returned to the designated lab. Plastic pipettes are used in many laboratories. When contaminated, they may be safely disposed of in either an autoclave bag or a sharps container. If not contaminated, intact plastic pipettes should be disposed of in a laboratory glass box for disposal in regular garbage. To dispose of contaminated plastic pipettes in a bag, the pipettes must be intact. Use only the clear autoclave biohazard bags, and be sure to double-bag. When placed in bags randomly with other debris, pipettes have a tendency to puncture the bags. Please place pipettes into autoclave bags in a manner which reduces the likelihood of a punctured bag. For example, stack the pipettes in a small bag, and then place this bag into a larger autoclave bag with other debris. Although an intact, used plastic pipette is not considered a sharp, it may be disposed of in a sharps container if contaminated with blood or other potentially infectious material. Please note that a broken plastic pipette is always considered a sharp, and therefore must be disposed of in a sharps container.

**Laboratory safety protocol:**

Before starting any work in the lab, personnel should be familiar with the procedures and equipment being used. Lab personnel should be aware of the chemical hazards before working with them. Personnel who are unfamiliar with the hazardous material or a new procedure should consult their supervisor. Lab coats, gloves and safety glasses should be worn as appropriate in all laboratories. Do not wear shorts, sandals, or open-toed shoes in lab. Minors or personal pets are not permitted in laboratories. Do not mouth pipette. Secure any dangling jewellery, restrain loose clothing, and tie back long hair that might get caught in equipment before starting work. Food and drink should not be consumed in the lab. Do not store food and drinks in laboratory refrigerators. Avoid working alone in the lab. If you must work alone, make someone (such as a supervisor) aware of your location. Wash your hands frequently throughout the day and before leaving the lab. Do not wear lab coats, gloves, or other personal protective clothing outside of lab areas. This clothing may have become contaminated and you could spread the contamination. Cell phones and use of music headphones should be avoided while working in the lab. They can be distracting and thereby increase the potential for an accident to occur. They can also become contaminated if handled while working with hazardous materials. Work areas must be kept clean and free of unnecessary chemicals. Clean the work area throughout the day and before leaving the lab for the day. If necessary, clean equipment after use to avoid the possibility of exposing the next person who uses it. Keep all aisles and walkways in the lab clear to provide a safe walking surface and an unobstructed exit. Do not block doors. Do not block access to emergency equipment (i.e. fire extinguishers, eyewashes, etc.), emergency shut-offs, and utility controls (i.e. electrical panels).

Supplies for cleaning up minor spills should be readily available. In case of release, promptly clean up spills using appropriate personal protective equipment (PPE). An inert absorbent such as kitty litter or vermiculite or a 50/50 mixture of the two or a commercial absorbent. A plastic (non-sparking) scoop, plastic bags for the spilled material. Chemical resistant gloves, goggles, sodium bicarbonate to neutralize acids. Develop and encourage safe habits. Avoid unnecessary exposure to chemicals by any route. Do not smell or taste chemicals. Vent any apparatus which may discharge toxic chemicals (e.g., vacuum pumps, distillation columns) into local exhaust devices such as fume hoods. Inspect gloves and test glove boxes before use. Do not allow release of toxic substances in cold rooms or warm rooms, since these have contained, re-circulated air. Inspect all glassware before use. Discard any broken, cracked, or chipped glassware. Tape or shield glass vacuum vessels to prevent flying glass in the case of an implosion. Also, tape or shield glass vacuum desiccators. Transport all glass chemical containers in rubber or polyethylene bottle carriers when leaving one lab area to enter another. Use a cart if transporting more than two bottles. Fire-polish all cut glass tubing and rods before use.

Firmly clamp apparatus and set up away from the edge of the lab bench. Only use equipment that is free from cracks, chips, or other defects. If possible, place a pan under a reaction vessel or other container to contain liquid if the glassware breaks. Do not allow burners or any other ignition sources nearby when working with flammable liquids. Lubricate glass stopcocks. Properly support and secure condensers and water hoses with clamps and wires. Be sure to direct the water hoses so that any drips that come off the hoses do not splash down onto any electrical wires. Position apparatus that is attached to a ring stand with the center of gravity over the base and not to one side. Assemble the apparatus so that burners or baths can be removed quickly. Use an appropriate vapor trap and confine the setup to a fume hood if there is a possibility of hazardous vapors. Put the setup in a fume hood whenever conducting a reaction that could result in an implosion or explosion. Keep the sash pulled down. If it is not possible to use a fume hood, use a standing shield that is stabilized and secured.

Securely anchor tabletop centrifuges and place in a location where the vibration will not cause lab equipment to fall off the bench top. Keep the centrifuge lid closed while operating and do not leave the centrifuge until you are certain it is running safely without vibration. If the centrifuge starts vibrating, stop and check the load balances. Regularly clean rotors and buckets with a non-corrosive cleaning solution. Use sealed safety cups while centrifuging hazardous materials. Wear ultraviolet absorbing protective safety glasses while working with ultraviolet light. Protect your skin from potential burns due to ultraviolet light. Shield any project in which ultraviolet light is used to prevent escape of the direct beam or scattered radiation. Always wear goggles that protect against the specific wavelength of the laser. Never look directly at the beam. Do not allow any reflective materials in or along the path of the beam. Post warning signs in all laser areas. If required, use a flashing light at the lab entrance to indicate when a laser is in use.

Do not use solvents which might damage the pump. Always close the valve between the vacuum vessel and the pump before shutting off the pump to avoid sucking vacuum oil into the system. Place a pan under pumps to catch oil drips. Check oil levels and change oil when necessary. Replace and properly dispose of vacuum pump oil that is contaminated with condensate. Used pump oil must be disposed as hazardous waste. With oil rotary pumps many vapors condense in the pump oil. Solvents in the oil degrade its performance (and eventually ruin the pump), create a chemical hazard when the oil is changed, and are emitted in an oil mist vented from the system. Other vapors pass directly into the exhaust stream. To avoid these problems like trap evaporated materials with a cold trap before they reach the pump. Depending on the material that is to be trapped, this can be a filtration flask either at room temperature or placed in an ice bath. For more volatile solvents more sophisticated options exist (e.g. dry ice trap). Vent the pump exhaust properly.

Examine all electrical cords periodically for signs of wear and damage. If damaged electrical cords are discovered, unplug the equipment and have it repaired. Properly ground all electrical equipment. If sparks are noticed while plugging or unplugging equipment or if the cord feels hot, do not use the equipment until it can be serviced by an electrician. Do not run electrical cords along the floor where they will be a tripping hazard and be subject to wear. If a cord must be run along the floor, protect it with a cord cover. Do not run electrical cords above the ceiling. The cord must be visible at all times to ensure it is in good condition. Do not plug too many items into a single outlet. Cords that enable you to plug more than one item in at a time should not be used. Multi-plug strips can be used if they are protected with a circuit breaker. Do not overuse or daisy-chain in a series. Do not use extension cords for permanent wiring. If you must use extension cords throughout the lab, then it is time to have additional outlets installed.

### **Classification of pathogens by risk groups:**

Classification of organisms according to risk group has traditionally been used to categorize the relative hazards of infective organisms. The factors used to determine which risk group an organism falls into is based upon the particular characteristics of the organism, such as pathogenicity, infectious dose, mode of transmission, host range, availability of effective preventive measures and availability of effective treatment. These classifications presume ordinary circumstances in the research laboratory or growth in small volumes for diagnostic and experimental purposes. Four levels of risk have been defined

*Risk Group 1 (low individual and community risk):* Any biological agent that is unlikely to cause disease in healthy workers or animals.

*Risk Group 2 (moderate individual risk, low community risk):* Any pathogen that can cause human disease but, under normal circumstances, is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures rarely cause infection leading to serious disease; effective treatment and preventive measures are available, and the risk of spread is limited.

*Risk Group 3 (high individual risk, low community risk):* Any pathogen that usually causes serious human disease or can result in serious economic consequences but does not ordinarily spread by casual contact from one individual to another, or that causes diseases treatable by antimicrobial or antiparasitic agents.

*Risk Group 4 (high individual risk, high community risk):* Any pathogen that usually produces very serious human disease, often untreatable, and may be readily transmitted from one individual to another, or from animal to human or vice-versa, directly or indirectly, or by casual contact.

### **Containment:**

Classification of organisms according to risk group is not meant to establish the actual handling of biological hazards in the laboratory setting. For example, the risk group system does not take into account the procedures that are to be employed during the manipulation of a particular organism. Containment levels are selected to

provide the end-user with a description of the minimum containment required for handling the organism safely in a laboratory setting. The containment system includes the engineering, operational, technical and physical requirements for manipulating a particular pathogen. These containment levels are applicable to facilities such as diagnostic, research, clinical, teaching and production facilities that are working at a laboratory scale. Four containment levels are described as follows:

*Containment Level 1 (CL1):* This applies to the basic laboratory that handles agents requiring containment level 1. CL1 requires no special design features beyond those suitable for a well-designed and functional laboratory. Biological safety cabinets (BSCs) are not required. Work may be done on an open bench top, and containment is achieved through the use of practices normally employed in a basic microbiology laboratory.

*Containment Level 2 (CL2):* This applies to the laboratory that handles agents requiring containment level 2. The primary exposure hazards associated with organisms requiring CL2 are through the ingestion, inoculation and mucous membrane route. Agents requiring CL2 facilities are not generally transmitted by airborne routes, but care must be taken to avoid the generation of aerosols (aerosols can settle on bench tops and become an ingestion hazard through contamination of the hands or splashes). Primary containment devices such as BSCs and centrifuges with sealed rotors or safety cups are to be used as well as appropriate personal protective equipment (i.e., gloves, laboratory coats, protective eyewear). As well, environmental contamination must be minimized by the use of handwashing sinks and decontamination facilities.

*Containment Level 3 (CL3):* This applies to the laboratory that handles agents requiring containment level 3. These agents may be transmitted by the airborne route, often have a low infectious dose to produce effects and can cause serious or life-threatening disease. CL3 emphasizes additional primary and secondary barriers to minimize the release of infectious organisms into the immediate laboratory and the environment. Additional features to prevent transmission of CL3 organisms are appropriate respiratory protection, HEPA filtration of exhausted laboratory air and strictly controlled laboratory access.

*Containment Level 4 (CL4):* This is the maximum containment available and is suitable for facilities manipulating agents requiring containment level 4. These agents have the potential for aerosol transmission, often have a low infectious dose and produce very serious and often fatal disease; there is generally no treatment or vaccine available. This level of containment represents an isolated unit, functionally and, when necessary, structurally independent of other areas. CL4 emphasizes maximum containment of the infectious agent by complete sealing of the facility perimeter with confirmation by pressure decay testing; isolation of the researcher from the pathogen by his or her containment in a positive pressure suit or containment of the pathogen in a Class III BSC line; and decontamination of air and other effluents produced in the facility.

### **Safe handling of biological spills:**

A biological spill shall be followed by prompt action to contain and clean up the spill. When a spill occurs, warn everyone in the area and call for assistance as needed. The degree of risk involved in the spill depends on the volume of material spilled, the potential concentration of organisms in the material spilled, the hazard of the organisms involved, the route of infection of the organisms, and the diseases caused by the organisms. Spills of biological agents can contaminate areas and lead to infection of laboratory workers. Prevention of exposure is the primary goal in spill containment and cleanup, exactly as in chemical spills. In evaluating the risks of spill response, generation of aerosols or droplets is a major consideration. If an accident generates droplets or aerosols in the laboratory room atmosphere, especially if the agent involved requires containment at Biosafety Level 2 or higher, the room shall be evacuated immediately. Doors shall be closed and clothing decontaminated. Call ORS to supervise the cleanup. In general, a 30-minute wait is sufficient for the droplets to settle and aerosols to be reduced by air changes. Longer waiting periods may be imposed depending on the situation. Laboratory personnel and/or ORS must exercise judgment as to the need for outside emergency help in evacuation.

If a spill of a biological agent requiring containment at Biosafety Level 2 or higher occurs in a public area, evacuation of the area shall be immediate. The principal investigator shall be responsible for designating the extent of evacuation until ORS or emergency personnel arrive. Prevention of exposure to hazardous aerosols is of primary importance. Anyone cleaning a spill shall wear personal protective equipment (for example, laboratory coat, shoe covers, gloves, and possible respiratory protection) to prevent exposure to organisms. An air-purifying negative-pressure respirator with P-100 filter cartridges is generally adequate protection against inhalation of most biological agents. However, there may be exceptions. Contact ORS for advice in choosing the correct respiratory protection and for information regarding the requirements that must be met to wear a respirator. The following procedure is recommended for decontaminating spills of agents used at BSL-2:

1. Wear gloves and a laboratory coat or gown. Heavyweight, puncture-resistant utility gloves, such as those used for housecleaning and dishwashing, are recommended.
2. Do not handle sharps with the hands. Clean up broken glass or other sharp objects with sheets of cardboard or other rigid, disposable material. If a broom and dustpan are used, they must be decontaminated later.
3. Avoid generating aerosols by sweeping.
4. Absorb the spill. Most disinfectants are less effective in the presence of high concentrations of protein, so absorb the bulk of the liquid before applying disinfectants. Use disposable absorbent material such as paper towels. After absorption of the liquid, dispose of all contaminated materials as waste.
5. Clean the spill site of all visible spilled material using an aqueous detergent solution (e.g., any household detergent). Absorb the bulk of the liquid to prevent dilution of the disinfectant.
6. Disinfect the spill site using an appropriate disinfectant, such as a household bleach solution. Flood the spill site or wipe it down with disposable towels soaked in the disinfectant.
7. Absorb the disinfectant or allow it to dry.
8. Rinse the spill site with water.
9. Dispose of all contaminated materials properly. Place them in a biohazard bag or other leakproof, labeled biohazard container for sterilization.

A spill that is confined within a biological safety cabinet generally presents little or no hazard to personnel in the area. However, chemical disinfection procedures are to be initiated at once while the cabinet continues to operate. The disinfectant shall be one that is active against the organisms of potential hazard. Flammable liquids, such as ethanol or isopropanol, shall not be used, even if effective, because of the fire hazard of generating dangerous vapor concentrations within the cabinet that could be ignited by an electrical spark or other source. Spray or wipe the walls, work surfaces, and equipment with the chosen disinfectant. Allow the disinfectant to remain on the surface for the appropriate contact time. Minimize the generation of aerosols and use sufficient disinfectant to ensure that drain pans and catch basins below the work surface contain disinfectant. The front exhaust shall also be wiped and the disinfectant drained into a container.

- Maintain cabinet ventilation.
- Warn others in the laboratory.
- Notify the principal investigator.
- Wear protective gloves, a lab coat or gown, and eye protection during the procedure.
- Spray or wipe walls, work surfaces, and equipment with appropriate disinfectant. A disinfectant with detergent has the advantage of detergent activity that will help clean the surfaces by removing both dirt and microorganisms.
- Use sufficient disinfectant to ensure that drain pans and catch basins below the work surface contain the disinfectant. Lift the front exhaust grill and tray and wipe all surfaces. Wipe the catch basin and drain the disinfectant into a container.
- Observe the recommended contact time for the disinfectant.
- Dispose of in ORS biowaste programs.

This procedure will not disinfect the filters, fans, air ducts, and other interior parts of the cabinet. For a spill in the open laboratory outside a biological safety cabinet, the spill response depends on the size of the spill and

hazard of the material. A minimally hazardous material spilled without generating appreciable aerosols can be cleaned with a paper towel soaked in a chemical disinfectant. A spill of a larger volume of hazardous material with aerosol generation requires evacuating the room, waiting for aerosol reduction, donning personal protective gear (including appropriate respiratory protection), selecting a disinfectant effective against the organisms involved, and cleaning as described above. Following cleanup, response personnel shall wash or shower with a disinfectant soap. For a small spill of biological material in the open laboratory, take the following action:

- Warn others in the laboratory.
- Notify the principal investigator.
- Wear gloves and protective clothing.
- Decontaminate with an appropriate.
- Dispose of as described above.
- If clothing is known to be contaminated, carefully remove it, folding the contaminated area inward.
- Place the clothing into an autoclavable bag.
- Wash arms, face, and hands.

A biological spill in a centrifuge has the potential for producing large volumes of aerosols. On becoming aware that a spill may have occurred within a centrifuge or other piece of equipment, turn off the equipment, warn others in the area, notify the principal investigator, allow aerosols to settle, and decontaminate following the principles described above.

- Turn off the centrifuge and allow time for the aerosols to settle.
- Warn others in the laboratory.
- Notify the principal investigator.
- Wear gloves and protective clothing.
- Decontaminate with an appropriate disinfectant. Place contaminated equipment in a leakproof bag and move it to a biological safety cabinet, if possible, for decontamination.
- If a biological material is spilled on a person, emergency response is based on the hazard of the biological agent spilled, the amount of material spilled, and whether significant aerosols were generated. If aerosol formation is believed to have been associated with the spill, a contaminated person shall leave the contaminated area immediately. If possible, (s)he should go to another laboratory area so that hallways and other public areas do not become contaminated.
- If a biological material is spilled on a person, emergency response is based on the hazard of the biological agent spilled, the amount of material spilled, and whether significant aerosols were generated. If aerosol formation is believed to have been associated with the spill, a contaminated person shall leave the contaminated area immediately. If possible, (s)he should go to another laboratory area so that hallways and other public areas do not become contaminated.

### **Sterilization and disinfection:**

Sterilizer is an agent intended to destroy all microorganisms and their spores on inanimate surfaces. Disinfectant is an agent intended to destroy or irreversibly inactivate specific viruses, bacteria, or pathogenic fungi, but not necessarily their spores, on inanimate surfaces. Most disinfectants are not effective sterilizers. Hospital Disinfectant: An agent shown to be effective against specific organisms such as *Staphylococcus aureus*, *Salmonella choleraesuis*, and *Pseudomonas aeruginosa*. It may also be effective against other organisms and some viruses. The labels of all commercially available hospital disinfectants contain a claim (which must be documented) of effectiveness for specific agents. Antiseptic: A chemical germicide formulated for use on skin or tissue. Antiseptics should not be used as disinfectants. Decontamination: A procedure that eliminates or reduces microbial contamination to a safe level with respect to the transmission of infection. Sterilization and disinfection procedures are often used for decontamination. The OSHA Bloodborne Pathogens Standard requires that all equipment and environmental and working surfaces shall be cleaned and decontaminated after contact with blood or other potentially infectious materials. The standard also requires decontamination of contaminated work surfaces after completion of procedures, immediately or as soon as

feasible after any overt contamination of surfaces or any spill of potentially infectious material, and at the end of the work shift if the work surface has become contaminated. All reusable equipment shall be decontaminated immediately or as soon as feasible upon visible contamination. It should be emphasized that, for any infectious material, adequate precleaning of surfaces is important for any disinfection or sterilization procedure. Ten minutes of exposure to a disinfectant may not be adequate to disinfect objects that have narrow channels or other areas that can harbor microorganisms.

Alcohols, for example, are effective for killing hepatitis B virus (HBV) but are not recommended for this purpose because of their rapid evaporation and the consequent difficulty of maintaining proper contact times. Chlorine compounds are probably the most widely used disinfectants in the laboratory. You can easily prepare an inexpensive, broad-spectrum disinfectant by diluting common household bleach. Bleach is a 5.25% sodium hypochlorite solution-this is equal to approximately 50,000 ppm of free available chlorine. This level of chlorine can be harmful to skin and eyes. Lower concentrations are effective in disinfection and are less hazardous for the worker. The concentration to be used is based on your assessment of the severity of the contamination or spill of infectious materials. For small spills of infectious agents or for contamination on hard, smooth surfaces, a 1:100 dilution of commercial bleach is adequate. This is equivalent to 500 ppm of free chlorine. In the case of large or concentrated spills of infectious agents, a higher level of chlorine is needed to be effective in destroying the microorganisms. Use a 1:10 dilution (5,000 ppm of free chlorine) and flood the contaminated area with the solution. Alternatively, you can mix the disinfectant with the spilled material. This higher concentration is more suitable for porous surfaces that may harbor organisms in tiny cracks or pits. Make the solution fresh each day. Be aware that chlorine compounds may corrode metals, especially aluminum. While a 10% household bleach solution is a commonly used decontaminant concentration, it is probably stronger than necessary for ordinary uses. It can be extremely irritating to personnel. Therefore, the use of higher concentrations of bleach in chemical fume hoods, and the autoclaving of materials that have been treated with bleach, should be reserved for significant contamination.

Formaldehyde is an OSHA-regulated chemical that is a suspect carcinogen, so its use as a disinfectant is not recommended. Iodophors that are registered with the EPA may be effective hard-surface decontaminants when used per manufacturer's instructions but iodophors formulated as antiseptics are not suitable for use as disinfectants. Peracetic (peroxyacetic) acid and hydrogen peroxide mixtures minimize the negative effects of corrosiveness sometimes seen with chlorine compounds and high concentrations of peracetic acid alone. A limited number of trade-name products containing <0.1% peracetic acid and <1.0% hydrogen peroxide and registered with the EPA as sterilants/disinfectants are available. The benefit of these products is their rapid action and broad-spectrum of germicidal activity, in addition to the reduced corrosiveness. Peracetic acid is generally a strong irritant. The low percentage in these products reduces this danger. Nonetheless, these products are intended only for highly concentrated spills of biological materials. Quaternary ammonium compounds are low-level disinfectants and are not recommended for spills of human blood, blood products, or other potentially infectious materials.

### **Biohazards associated with animal handling:**

Exercise care and thoughtfulness when using animals in research. Numerous risks may be present when animals are used in studies of microorganisms, as well as studies of hazardous chemicals. Use containment and personal protective equipment (PPE) that protects against both the biological and chemical hazards. Precautions commonly include use a lab coat, gloves and eye protection when handling animals and their bedding; respiratory protection may be recommended when specific conditions present a concern. There are some inherent risks in working with animals (e.g., allergenicity, bites, and scratches). Laboratory and wild-trapped animals may harbor microorganisms that can produce human diseases following bites, scratches, or exposure to excreted microorganisms. Rhesus macaques present a significant potential for hazards, requiring that stringent procedures be followed to guard against Herpes B virus (Cercopithecine herpesvirus 1). Even in the absence of known hazards, animal care providers should use precautions to avoid exposure to animal allergens. In the process of inoculating animals, an investigator can be exposed to infectious material by accidental self-inoculation or inhalation of infectious aerosols. During surgical procedures, necropsies, and processing of tissues, aerosols can be produced inadvertently, or the operator can inflict self-injury with contaminated instruments. Since animal excreta can also be a source of infectious microorganisms, investigators should take precautions to minimize aerosols and dust when changing bedding and cleaning cages. Containment equipment such as a fume hood or biosafety cabinet is sometimes appropriate for doing cage changes. Bedding from animals infected with pathogens and those potentially infected must be decontaminated prior to disposal, typically by autoclaving. Transfer of human cells, primate cells or opportunistic microbes; whether newly isolated or well established, into immunocompromised animals could result in propagation of pathogens that

would be suppressed in the normal host. BSL2 containment must be applied to mitigate against such risks and also to prevent spread of animal pathogens within a research colony. Some research animals are treated with hazardous chemicals. Handling of the hazardous chemicals, administration of the chemicals to animals, and handling of these animals, animal tissues (necropsy), and their wastes must be done with appropriate containment and PPE. Preparation of stock solutions of hazardous chemicals (even small amounts of volatile hazardous chemicals), preparation of animal feed containing hazardous chemicals, and cage changes of animals with hazardous chemicals in their wastes are all steps best done in the fume hood. Bedding contaminated chemical or radioactive hazardous substances must be decontaminated prior to disposal; the Chemical Safety and Radiation Safety Offices should be consulted for this determination.

### **Safe handling of laboratory equipment:**

Although attention is usually concentrated on chemical hazards in laboratories, consideration must be given to the safe use of laboratory equipment. Equipment in the laboratory must be set up and operated properly to ensure that accidents are minimized. Cuts and burns from handling glassware are among the most common sources of laboratory accidents. Breaking glassware may cause a chemical spill and possible injury. Chemicals exploding in glassware can send fragments of glass flying into the laboratory. Vacuum systems may implode, sending flying glass and chemicals across the room. Flammable vapors contacting sparking electrical equipment may cause an explosion. Laboratory workers may be electrocuted if they handle electrical equipment improperly. The following safety procedures should reduce the potential for accidents in laboratories. Inexperienced users should receive training in the proper handling of glassware, especially with systems that present unusual risks such as excess pressure or vacuums. Careful handling and storage of glassware is necessary to prevent damage to the glassware and injury to the worker. Damaged glassware should be properly discarded. Care must be used while inserting glass tubing through a stopper or when connecting flexible tubing to the glass. The glass tubing should be polished, or rounded and lubricated with glycerine or stopcock grease. Hands must be protected with cloth or leather gloves. Hands should be held close together to reduce pressure on the tubing, and out of the direct line of the glass should it break. Vacuum glass apparatus should be handled with extreme caution. Dewar flasks and other glass vacuum vessels should be taped or shielded to protect against flying glass in case of an implosion.

Most distillation units operate with water cooled condensers. Water pressure can change however, and cause unexpected problems. Inadequate water supply can allow distillate vapours to escape. Too high a flow can cause the tubing connectors to burst, flooding the laboratory. All flexible hoses should be free of cracks, slits, or kinks and kept away from hot plates and flames. All those connections should be firm and clamped or wired for prolonged use. Flow rates should be approximately one litre per minute. For unattended operations, the water pressure should be regulated automatically. Heating mantles must be used to heat distillation flasks. A variable voltage transformer should be used. The temperature of the mantle must be monitored carefully. If left unattended the mantle must be connected to a thermal cut-off device that turns the heater off if too high a temperature is reached. These units are usually intended to operate automatically and are left unattended for long periods. This unit must be equipped with a thermal cut off, independent of the temperature controlling devices. This feature is needed to prevent overheating that could cause a fire. When a still is set up, or ceases to operate, the Safety Office should be notified.

In a vacuum system the pressure on the outside of the containment vessel is greater than on the inside. A break in the container will cause an implosion, resulting in flying glass, splattered chemicals, and a possible fire. Even equipment under moderate pressure, such as those achieved in water aspirators, can be potentially hazardous. Another hazard associated with vacuum equipment is rapid pressure change that can draw hazardous liquids and gases into the building vacuum system or equipment. Depending on the hazard, safety goggles, impact resistant glasses, or face shields must be worn when working with vacuum equipment. Glass flasks should be taped with friction tape or placed in a metal container large enough to hold the flask. If this is not possible, a safety shield should be placed between the flask and the operator. The vessel should be inspected for cracks or scratches before use. Only round bottomed or thick walled flat bottomed flasks specifically designed for vacuum work should be used. Ordinary glass ware, especially flat bottomed flasks, is not intended for vacuum work and may burst. The reaction flask should be taped and placed in a wire cage. The distillation should be performed behind an explosion shield. Operators should wear a face shield. A safety trap should be used to protect equipment (such as a manometer) and the vacuum source from contamination. Pressure should be equalized slowly after the experiment is over and the flask has cooled to room temperature. trap or check valve should be placed between the aspirator and the container under vacuum to prevent water from being drawn back from the aspirator into the container. A safety trap should be placed between the apparatus and the pump to prevent solvents and corrosives from getting into the pump oil or the atmosphere of the laboratory. Exhaust from pumps should be vented to a hood.

The improper use of electrical equipment is a common source of accidents in laboratories. Electrical shocks, fires, and explosions are some of the potential hazards found in the laboratory. Effects of contact with electrical circuits range from a mild tingling sensation to painful shock and burns to cardiac arrest. Because electrical shorts often get worse, any equipment that produces a mild shock should be reported immediately and removed from service. Proper design of equipment, maintenance, and training of personnel should reduce these hazards. To reduce shock hazards, all electrical equipment must be properly grounded. Electrical outlets in the laboratory will be tested periodically for proper grounding. Equipment that does not have a three-prong plug should be re-wired unless it is double insulated. Electrical equipment should not be handled with wet hands or while standing on a wet floor. Wet equipment should never be turned on. Any electrical equipment that emits noises and odors should be turned off and unplugged. Safety devices or interlocks on electrical equipment should not be bypassed. Arcing electrical equipment may cause an explosion in laboratories where volatile flammable solvents are used. Equipment with non-sparking induction motors and enclosed electrical contact must be used with volatile flammable solvents. This applies to the motors used in vacuum pumps, mechanical shakers, heating devices, magnetic stirrers and rotary evaporators. Kitchen appliances such as mixers and blenders are not equipped with induction motors and should not be used in labs if flammable materials are present. Electrical fixtures may need to be explosion-proof if flammable vapours or gases reach high concentrations. Flammable liquids must be stored in explosion-safe or explosion-proof refrigerators or freezers.

Heating devices are the most common type of electrical device found in the laboratory. Although much safer than Bunsen burners, these devices pose electrical and fire hazards if used improperly. Variable transformers control the temperature on many laboratory heating devices. Because some sparking may occur when the control knob is turned, transformers should be located where they will not be exposed to flammable liquids or vapours. Connections from the variable transformer to the heating device should not be done with alligator clips because of the potential shock and spark hazard. Heating devices left unattended overnight should be equipped with a device that turns the power off if a preset temperature is exceeded. The heating element in any laboratory heating device should be enclosed in an insulated case that prevents contact with the worker and protects against sparks. Laboratory hot plates are normally used when solutions must be heated above 100 C. Hot plates should be designed specifically for laboratory use. Household type units should never be used in the laboratory. Hot plates with exposed heating elements or spark producing switches should not be used to heat flammable liquids. Care should be exercised when heating solvents on hot plates with enclosed elements to ensure that the liquid does not boil over into the electrical heating equipment.

### **Reporting of accidents:**

All laboratory incidents shall be reported to Officer for Research Safety (ORF), including minor spills, fires, or injuries. Laboratory incidents shall be investigated. ORS requires that an Incident Report Form be completed by the person(s) involved in the incident. The person's supervisor is expected to sign the completed form. The supervisor shall be responsible for ensuring that corrective action to prevent repeat incidents is undertaken. ORS may also prepare an investigation report, depending on the staff's involvement in the cleanup of spilled materials or as follow-up for the incident. Investigations are made and reports written not only to satisfy certain laws but also to learn the cause of the problem and what changes in procedures, equipment, or training should be made to avoid other accidents. Fires or injuries not requiring outside assistance shall be reported to the Office of Risk Management. The Office of Risk Management documents all fires and shall report all accidental employee injuries to the University's Workers' Compensation carrier and lost-time injuries to the Illinois Industrial Commission. The injuries shall also be entered in the OSHA Injury Log. In case of a fire, injury, or other accident requiring outside assistance, the Office of Risk Management shall write an investigation report.

An incident is defined as any unplanned and unwanted event that occurred during the performance of work activities and that resulted in or could have led to injury or material damage to property. Incident repercussions range from minor. An Incident Report is appropriate for "near misses," incidents not resulting in personal harm or property damage, but which might have, under slightly different circumstances. The Incident Report requires responses from the person involved any witnesses to the incident, and from the Principal Investigator/Supervisor. Attach additional pages if necessary to complete the report. Reports that are not signed by the PI/supervisor will be returned for completion. The committees require input from the supervisor. See completed Example following the instructions. Commonly, there are multiple causes in any given incident-all of which should be identified. Provide a complete and detailed response to each question, making a serious attempt to identify all "root cause(s)." The contributing factors were probably evident, but overlooked or unrecognized previously. These factors become more distinctly identifiable in light of the specifics of the incident A well-planned work process will include multiple layers of safeguards. Once causes are identified at all levels, consider safeguards and procedures that might be changed to prevent future incidents. This report is not

intended to assign blame; it should be used as a tool to foster recommendations for procedural improvement. A well-prepared report will identify all work systems that need to be redesigned to compensate for foreseeable human errors. These reports will also be used to improve safety policies.

### **Waste disposal:**

Landfill as a form of waste management is now an on-going issue amongst many authorities and is now widely regarded by many environmental bodies as more of a problematic solution than a viable one. With consumer products evolving and becoming more sophisticated so too does the waste streams which can contain toxic substances. Over time, these toxins leach into our soil and groundwater, and become environmental hazards for years. Leachate is the liquid formed when waste breaks down in the landfill and water filters through that waste. This liquid is highly toxic and can pollute the land, ground water and water ways. When organic material such as food scraps and green waste is put in landfill, it is generally compacted down and covered. This removes the oxygen and causes it to break down in an anaerobic process. Eventually this releases methane, a greenhouse gas that is 21 times more potent than carbon dioxide. The implications for global warming and climate change are enormous. Methane is also a flammable gas that can become dangerous if allowed to build up in concentration. Incineration is now not only a financially more feasible solution but also a preferred environmental solution. As landfill is no becoming slowly obsolete and the ever increasing landfill levies on the raise globally highly advanced incinerator technologies are now becoming not only a more environmentally friendly option but also a financially viable one too. Advantages include incineration is a practical method of disposal that saves a lot of money on transport of waste to approved landfill sites which can be great distance from the waste location. This also has an indirect benefit on the environmental by decreasing the carbon footprint that such transport methods leave behind. The sheer reduction in the space required to dispose of the 5-10% of waste that incineration produces relieves pressure on land, which in urban areas can constitute a big saving. Landfills have never been a pretty site and also give rise to a lot of pests and insects. An incinerating plant will look like any other industrial structure and can be easily maintained and controlled. Gases and leachates that are produced in landfills by waste are totally eliminated and the waste that is produced in the incineration is totally free of any environmental risk.

### **Laboratory biosafety level criteria:**

The essential elements of the four biosafety levels for activities involving infectious microorganisms and laboratory animals are summarized in Table 2 of this section and discussed in Section 2. The levels are designated in ascending order, by degree of protection provided to personnel, the environment, and the community. Standard microbiological practices are common to all laboratories. Special microbiological practices enhance worker safety, environmental protection, and address the risk of handling agents requiring increasing levels of containment. Biosafety Level 1 is suitable for work involving well-characterized agents not known to consistently cause disease in immunocompetent adult humans, and present minimal potential hazard to laboratory personnel and the environment. BSL-1 laboratories are not necessarily separated from the general traffic patterns in the building. Work is typically conducted on open bench tops using standard microbiological practices. Special containment equipment or facility design is not required, but may be used as determined by appropriate risk assessment. Laboratory personnel must have specific training in the procedures conducted in the laboratory and must be supervised by a scientist with training in microbiology or a related science.

Biosafety Level 2 builds upon BSL-1. BSL-2 is suitable for work involving agents that pose moderate hazards to personnel and the environment. It differs from BSL-1 in that: 1) laboratory personnel have specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures; 2) access to the laboratory is restricted when work is being conducted; and 3) all procedures in which infectious aerosols or splashes may be created are conducted in BSCs or other physical containment equipment. Biosafety Level 3 is applicable to clinical, diagnostic, teaching, research, or production facilities where work is performed with indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure. Laboratory personnel must receive specific training in handling pathogenic and potentially lethal agents, and must be supervised by scientists competent in handling infectious agents and associated procedures. All procedures involving the manipulation of infectious materials must be conducted within BSCs or other physical containment devices. A BSL-3 laboratory has special engineering and design features.

Biosafety Level 4 is required for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that is frequently fatal, for which there are no vaccines or treatments, or a related agent with unknown risk of transmission. Agents with a close or identical antigenic relationship to agents requiring BSL-4 containment must be handled at this level until sufficient data are obtained either to confirm continued work at this level, or re-designate the level. Laboratory staff must have

specific and thorough training in handling extremely hazardous infectious agents. Laboratory staff must understand the primary and secondary containment functions of standard and special practices, containment equipment, and laboratory design characteristics. All laboratory staff and supervisors must be competent in handling agents and procedures requiring BSL-4 containment. The laboratory supervisor in accordance with institutional policies controls access to the laboratory. There are two models for BSL-4 laboratories: 1. A Cabinet Laboratory—Manipulation of agents must be performed in a Class III BSC; and 2. A Suit Laboratory—Personnel must wear a positive pressure supplied air protective suit. BSL-4 cabinet and suit laboratories have special engineering and design features to prevent microorganisms from being disseminated into the environment.

#### **Lab biosafety level 1 criteria:**

This level is suitable for work involving well-characterized agents not known to consistently cause disease in healthy adult humans, and of minimal potential hazard to laboratory personnel and the environment. Research with these agents may be performed on standard open laboratory benches without the use of special containment equipment and it is not necessary for Biosafety Level 1 labs to be isolated from the general building. It includes several kinds of bacteria and viruses including canine hepatitis, non-pathogenic *Escherichia coli*, as well as some cell cultures and non-infectious bacteria. At this level, precautions against the biohazardous materials in question are minimal and most likely involve gloves and some sort of facial protection. The laboratory is not necessarily separated from the general traffic patterns in the building. Work is generally conducted on open bench tops using standard microbiological practices. Usually, contaminated materials are left in open (but separately indicated) waste receptacles. Decontamination procedures for this level are similar in most respects to modern precautions against everyday microorganisms (i.e., washing one's hands with anti-bacterial soap, washing all exposed surfaces of the lab with disinfectants, etc.). In a lab environment all materials used for cell and/or bacteria cultures are decontaminated via autoclave. Laboratory personnel have specific training in the procedures conducted in the laboratory and are supervised by a scientist with general training in microbiology or a related science.

#### **Lab biosafety level 2 criteria:**

This level is similar to Biosafety Level 1 and is suitable for work involving agents of moderate potential hazard to personnel and the environment. It includes various bacteria and viruses that cause only mild disease to humans, or are difficult to contract via aerosol in a lab setting, such as *C. difficile*, most Chlamydiae, hepatitis A, B, and C, human immunodeficiency virus (HIV), orthopoxviruses (other than smallpox), influenza A, Lyme disease, *Salmonella*, mumps, measles, scrapie, MRSA, and VRSA. BSL-2 differs from BSL-1 in that laboratory personnel have specific training in handling pathogenic agents and are directed by scientists with advanced training; access to the laboratory is limited when work is being conducted; extreme precautions are taken with contaminated sharp items; and certain procedures in which infectious aerosols or splashes may be created are conducted in biological safety cabinets or other physical containment equipment.

#### **Lab biosafety level 3 criteria:**

This level is applicable to clinical, diagnostic, teaching, research, or production facilities in which work is done with indigenous or exotic agents which may cause serious or potentially lethal disease after inhalation.<sup>[8]</sup> It includes various bacteria, parasites and viruses that can cause severe to fatal disease in humans but for which treatments exist, such as *Yersinia pestis*, *Francisella tularensis*, *Leishmania donovani*, *Mycobacterium tuberculosis*, *Chlamydia psittaci*, Venezuelan equine encephalitis virus, Eastern equine encephalitis virus, SARS coronavirus, *Coxiella burnetii*, Rift Valley fever virus, *Rickettsia rickettsii*, several species of *Brucella*, rabies virus, chikungunya, yellow fever virus, and West Nile virus. Laboratory personnel have specific training in handling pathogenic and potentially lethal agents, and are supervised by competent scientists who are experienced in working with these agents. This is considered a neutral or warm zone.

All procedures involving the manipulation of infectious materials are conducted within biological safety cabinets, specially designed hoods, or other physical containment devices, or by personnel wearing appropriate personal protective clothing and equipment. The laboratory has special engineering and design features. It is recognized, however, that some existing facilities may not have all the facility features recommended for Biosafety Level 3 (i.e., double-door access zone and sealed penetrations). In this circumstance, an acceptable level of safety for the conduct of routine procedures, (e.g., diagnostic procedures involving the propagation of an agent for identification, typing, susceptibility testing, etc.), may be achieved in a biosafety level 2 facility, providing the filtered exhaust air from the laboratory room is discharged to the outdoors, the ventilation to the laboratory is balanced to provide directional airflow into the room, access to the laboratory is restricted when work is in progress, and the recommended Standard Microbiological Practices, Special Practices, and Safety Equipment for Biosafety Level 3 are rigorously followed.

#### **Lab biosafety level 4 criteria:**

This level is required for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections, agents which cause severe to fatal disease in humans for which vaccines or other treatments are *not* available, such as Bolivian and Argentine hemorrhagic fevers, Marburg virus, Ebola virus, Lassa virus, Crimean-Congo hemorrhagic fever, and various other hemorrhagic diseases. This level is also used for work with agents such as smallpox that are considered contagious enough to require the additional safety measures, regardless of vaccination availability. When dealing with biological hazards at this level the use of a positive pressure personnel suit, with a segregated air supply is mandatory. The entrance and exit of a level four biolab will contain multiple showers, a vacuum room, an ultraviolet light room, and other safety precautions designed to destroy all traces of the biohazard. Multiple airlocks are employed and are electronically secured to prevent both doors from opening at the same time. All air and water service going to and coming from a biosafety level 4 lab will undergo similar decontamination procedures to eliminate the possibility of an accidental release. Agents with a close or identical antigenic relationship to biosafety level 4 agents are handled at this level until sufficient data are obtained either to confirm continued work at this level, or to work with them at a lower level.

Members of the laboratory staff have specific and thorough training in handling extremely hazardous infectious agents and they understand the primary and secondary containment functions of the standard and special practices, the containment equipment, and the laboratory design characteristics. They are supervised by qualified scientists who are trained and experienced in working with these agents. Access to the laboratory is strictly controlled by the laboratory director. The facility is either in a separate building or in a controlled area within a building, which is completely isolated from all other areas of the building. A specific facility operations manual is prepared or adopted. Building protocols for preventing contamination often use negatively pressurized facilities, which, even if compromised, would severely inhibit an outbreak of aerosol pathogens. Within work areas of the facility, all activities are confined to Class III biological safety cabinets, or Class II biological safety cabinets used with one-piece positive pressure personnel suits ventilated by a life support system.

#### **Essential biosafety measures for TB labs:**

All TB laboratories, regardless of the procedures being undertaken, should enact a set of essential biosafety measures to minimize risks. These measures affect codes of practice, equipment, laboratory design and facilities, health surveillance, training and waste handling. Depending on the specific tests conducted by the laboratory and the results of a procedural risk assessment, additions and modifications to the measures described below may be made to accommodate different levels of risk. A code of practice describes the laboratory practices and procedures essential for implementing good microbiological technique. The laboratory manager should use the code of practice to develop written descriptions of procedures that should be followed to perform

work safely. This safety or operations manual should also identify known and potential hazards, and specify practices and procedures to minimize the risks associated with such hazards. Specialized laboratory equipment should always be accompanied by, but can never replace, appropriate procedures and good microbiological technique. The international biohazard warning symbol and sign must be displayed on the laboratory door. Only authorized persons should be allowed to enter the laboratory's working areas. Children should not be authorized or allowed to enter the laboratory's working areas. It is the responsibility of the laboratory manager to ensure that a biosafety management system is developed and adopted, as well as a safety or operations manual and a set of standard operating procedures. The manager should ensure that a staff is trained and their technical competence evaluated for performing different procedures. Personnel should be advised of special hazards and be required to read the safety (or operations) manual as well as follow standard practices and procedures. The manager should make sure that all personnel have read the appropriate manuals and have signed a statement declaring that they have understood them. A copy of the most recent safety or operations manual, with its date of issue, should be available in the laboratory. Systems for heating, ventilation, air and containment (directional airflow) must have a permanent maintenance plan to ensure they always function properly.

Protective laboratory clothing must be worn at all times while staff is working in the laboratory. Protective clothing must not be worn outside the laboratory area (for example, in canteens, coffee rooms, offices, libraries, staff rooms and toilets). Laboratory coats and gowns must be stored separately from personal clothing. Clean gowns and used gowns must be stored in different areas of the laboratory. Laboratory coats and gowns should be changed at least weekly, but laundering should not occur at home. Laboratory gowns should have long sleeves and elasticized cuffs (at least 30 mm long); they should fasten at the back. Different sizes of gowns should be available for staff. Gowns must be worn when working in a laboratory where there is a high risk of TB infection. Laboratory coats usually have long sleeves and fasten in the front. Different sizes of laboratory coats should be available for staff. Gloves must be worn for all procedures that involve direct contact, or may involve accidental contact, with sputum, blood, body fluids and other potentially infectious materials. After use, gloves should be removed aseptically and hands washed. Personnel must wash their hands after any overt contamination, after completing work during which infectious materials were handled, and always before they leave the laboratory's working areas. Personnel should thoroughly lather their hands with soap, using friction, for at least 15 seconds; rinse them in clean water; and dry them using a clean paper towel. Automated or hands-free taps are preferable. However, where these are not available, a paper towel should be used to turn off the tap to avoid recontaminating clean hands. Eating, drinking, smoking, applying cosmetics and handling contact lenses are prohibited in the laboratory. Storing food or drink anywhere in the laboratory's working areas is prohibited. Open-toed footwear must not be worn in the laboratory. Mobile telephones should not be used in the laboratory.

All procedures must be performed in such a way as to minimize or prevent the formation of aerosols and droplets. Mouth pipetting must be strictly prohibited. No materials should be placed in the mouth. All labels used in the laboratory must be self-adhesive. The use of needles and syringes should be limited, and they should never be used as a substitute for pipetting. Written documentation that may be removed from the laboratory must be protected from contamination. All contaminated materials, specimens and cultures must be decontaminated appropriately before disposal or cleaning for reuse. All accidents, spills and potential exposures to infectious materials must be reported to the laboratory manager. Records of such incidents and corrective actions taken need to be maintained for future prevention. Standard operating procedure for handling accidents and spills must be developed and be available in the laboratory. Practical training must be provided at least annually to ensure the procedure is adopted and becomes an automatic response. Packing and transportation of samples must follow applicable national or international regulations. Standard operating procedures must be developed and staff trained to be competent in their use. Manuals explaining the procedures must be readily available in different parts of the laboratory. Procedures should be reviewed annually. Standard operating procedures should include details of risk assessments, and the mitigation and control measures identified and implemented.

The laboratory should be divided into "functionally clean" and "potentially contaminated" areas, with the clean areas reserved for administrative and preparatory work. Access to the clean areas and the contaminated areas must be controlled and enforced by the laboratory's manager. The laboratory should be kept neat, clean and free of materials and equipment not used for performing routine work. Equipment and materials that are not being used or that do not work should be removed from work areas. Work surfaces must be decontaminated after any

spill of potentially infectious material and at the end of each work session. Equipment should be selected to take certain general principles into account – that is equipment should be designed to prevent or limit contact between the operator and the infectious material; constructed of materials that are impermeable to liquids and resistant to corrosion; fabricated to be smooth and without sharp edges and unguarded moving parts; designed, constructed and installed to facilitate simple operation, and provide for easy maintenance, cleaning, decontamination and certification testing; glassware and other breakable materials should be avoided, whenever possible. The proper design and construction of laboratory facilities contributes to the protection of all laboratory workers and provides a barrier that protects the community from TB aerosols that may be created with the laboratory. Specific features of the laboratory, including separated laboratory areas and a ventilation system, are secondary containment measures. The secondary barriers that are recommended for a laboratory depend on the procedures conducted and their associated risk of transmission. Human error and poor technique can compromise the best safeguards put in place to protect laboratory workers. Well informed, competent and safety-conscious staff are essential for preventing laboratory-acquired infections, incidents and accidents. All staff should have safety training; this should include reviewing the code of practice and the practices and procedures incorporated into the safety manual. The laboratory manager should ensure that staff are trained, and that their technical competence in performing different procedures is evaluated. Training should always include information on safe practices to be followed to avoid or minimize risks of inhalation, ingestion and inoculation. Training should also include information on how to properly decontaminate and dispose of infectious material. Waste-management procedures must comply with all pertinent local or national requirements and regulations. Waste is anything that is to be discarded. The overriding principle in minimizing risks from waste is that all infectious materials should be decontaminated, incinerated, prepared to be buried or autoclaved. Discard bags should be used to segregate waste. Most glassware, instruments and laboratory clothing will be reused or recycled.

#### **Low risk TB labs:**

Minimum requirements needed to limit or reduce risks of infection in laboratories by carrying out specific procedures that are considered to have a low risk of spreading TB. Additional measures may be deemed necessary following a site-specific risk assessment. Low-risk laboratories that follow the minimum biosafety requirements described in this chapter can safely perform certain procedures with sputum specimens, given that the viscous nature of sputum is not prone to generating aerosols when good microbiological techniques are followed. Low risk laboratories can manipulate sputum specimens for direct sputum-smear microscopy; and manipulate sputum specimens for the Xpert MTB/RIF<sup>®</sup> assay. While opening sputum containers and making a direct sputum smear may produce aerosols, the risk of transmission from such procedures is negligible in comparison with aerosols produced by a single unprotected cough. There is little epidemiological evidence that preparing a direct smear is associated with a measurable excess risk of acquiring TB infection. The low-risk TB laboratory may also face the following challenges, all of which increase risks such as bench spaces may be used improperly; specimen containers may leak; specimens manipulated carelessly may lead to subsequent aerosolization; specimens may be shaken vigorously; and ventilation or illumination may be poor.

To address specific potential risks, the following biosafety requirements should be established in a low-risk TB laboratory. Use of bench spaces: The bench used to process specimens for direct sputum-smear microscopy or the Xpert MTB/RIF assay should be separate from areas used to receive specimens and from administrative areas used for paperwork and telephones. Ventilation: Smears performed directly on sputum samples, and processing specimens for the Xpert MTB/RIF assay, may both be carried out on an open bench in an adequately ventilated area when appropriate microbiological techniques are used. Adequate ventilation for TB laboratories is typically described as directional airflow with 6–12 air exchanges per hour. For low-risk procedures, natural ventilation should be sufficient providing that air flows away from the technician and across the work area along with potentially infectious materials, then away from occupied areas of the room and outside the laboratory; this flow should provide protection from aerosols that might be generated in the work area. In order to have directional control of contaminants in the air, air should move at least 0.5 m/s. Ventilation can be ensured by opening windows if the local climate allows. When the climate prevents windows from being opened, consideration should be given to using mechanical ventilation systems that provide an inward flow of air without recirculation in the room. Air conditioners should be placed only after the direction of airflow has been considered. It is important to ensure that air in the laboratory flows away from the technicians.

Ventilated work stations are an optional solution for aerosol containment for direct sputum-smear microscopy or the Xpert MTB/RIF assay in environments where natural or mechanical ventilation is not practical. Guidance and specifications for ventilated work stations are available. Standards for adequate ventilation in laboratories have not been defined internationally. The Expert Group recommended as adequate ventilation for TB laboratories a pragmatic definition of directional airflow to include 6–12 air exchanges per hour. The Expert Group noted that there is no evidence to suggest that a greater number of air exchanges per hour would reduce the risk of a laboratory-acquired infection, and recognized that the costs of ventilation systems with higher capacity are considerable.

### **Moderate risk TB labs:**

The minimum requirements needed to limit or reduce risks of infection in laboratories carrying out specific procedures that are considered to have a moderate risk of spreading TB. Additional measures may be deemed necessary following a site-specific risk assessment. Moderate-risk laboratories that follow the minimum biosafety requirements described in this chapter can safely perform certain procedures that entail a moderate risk of specimen aerosolization with a relatively low concentration of infectious particles. Moderate-risk laboratories can process specimens for inoculation on primary solid-culture media; and perform direct DST (for example, direct line-probe assays, Microscopic observation drug susceptibility [MODS], Nitrate reductase assay [NRA] on processed sputum). In addition to the general risks that are addressed by the biosafety measures. The TB laboratory classified as moderate risk also faces the following challenges, all of which increase risks such as staff may work in areas with poor ventilation; they may work with poor illumination; BSCs may be poorly maintained and not certified; BSCs may not be properly ducted; the work environment may be dusty, and high-efficiency particulate air (HEPA) filters in BSCs may become blocked; careless manipulation of specimens may lead to aerosolization; precautions for using the vortex may not be followed properly (for example, it may be used outside the BSC); specimen containers may break or leak during centrifuging; problems may be associated with opening centrifuge buckets outside the BSC; adequate warnings of biohazards may be lacking, and information on who should be contacted during an emergency may be inadequate; and cooling or heating systems may not work properly. In addition to the BSC (the primary barrier), the secondary barrier (provided by the laboratory itself) is achieved by maintaining a unidirectional airflow into the laboratory, and by ensuring there are a minimum of 6–12 ACHs.

### **High risk TB labs:**

The term TB-containment laboratory refers to a facility that has the minimum design features necessary to safely manipulate TB cultures. This type of facility may or may not meet all of the requirements of a Biosafety Level 3 laboratory as described in WHO's Laboratory biosafety manual.<sup>2</sup> All laboratory facilities must comply with local and national regulations. The recommendations in this manual are the minimum requirements needed to limit or reduce risks of infection in laboratories carrying out specific procedures that are considered to have a high risk of spreading TB. Additional measures may be deemed necessary following a site-specific risk assessment. High-risk laboratories (also known as TB-containment laboratories) that follow the minimum biosafety requirements. They are designed to work with high volumes and concentrations of *M. tuberculosis* organisms and to engage in procedures that pose an increased risk of aerosol spread. High-risk TB laboratories can manipulate cultures to identify *M. tuberculosis*; and manipulate cultures or suspensions of tubercle bacilli for all indirect DST methods and molecular assays. Laboratories classified as high-risk (or containment) also face the following challenges, all of which increase risks to the staff open positive culture vials; staff must prepare smears from positive cultures; DNA extraction must be performed on a positive culture; manipulation of cultures for identification and indirect DST; broken culture containers must be disposed of; and cultures or areas where spills occurred must be decontaminated. Similar to the moderate-risk laboratory, there are two levels of containment in a high-risk laboratory: the BSC (primary containment) and the laboratory itself (secondary containment). In TB laboratories classified as high risk, all procedures for handling viable *M. tuberculosis* cultures and aqueous suspensions of TB bacilli for identification, indirect DST and molecular assays must be conducted within a BSC in a TB-containment laboratory.

## **Safety equipments:**

### **Personal protective equipments:**

The appropriate use of personnel protective equipment (PPE) is critical in reducing exposure to potentially infectious materials. PPE use must be put into its proper context, however. PPE is to be considered the 'last line of defense' when risk assessment does not indicate that engineering controls and work practices can be relied upon for adequate protection. These situations frequently exist, necessitating the use of PPE. Gloves must be worn whenever handling infectious materials. Users of latex gloves are at risk for developing allergies to latex or the chemicals used in manufacturing these gloves. Nitrile or vinyl gloves should be used instead of latex. Those who prefer latex should use only powder-free gloves that are designated "low protein" by the manufacturer. Glove manufacturers should be able to document their products' resistance to permeation. Corrosives and organic solvents may penetrate gloves or diminish their protective ability; it may be necessary to stock more than one type of glove for the full range of a laboratory's activities. When using any glove check for visible tears and other defects. Remove rings and other jewelry if they may rip gloves. Protective ability diminishes as gloves are worn due to stretching and abrasion; change gloves regularly or as soon as possible if they are overtly contaminated. Wash hands immediately after removing gloves. Remove gloves when leaving the laboratory; even if they are "clean", their presence in an elevator or other common area justifiably causes misgivings among other building occupants - they do not want to turn the same door knob.

Eye injuries are among the most preventable types of laboratory accidents. Glasses routinely worn for vision correction do not provide the appropriate level of protection for work with hazardous materials. Safety glasses with side shields provide the minimum level of protection for handling any hazardous material. Goggles, which unlike safety glasses fit tightly all around the eyes are required for activities with a small splash hazard or work with organisms transmissible through mucous membrane exposure. Goggles are used with a face shield when an elevated risk of large quantity splashes exists or when working with highly toxic, corrosive, or infectious materials. Face shields must also be used for protection against UV radiation and when handling liquid nitrogen. Lab coats must not be worn outside of the laboratory if they were used during work with infectious materials. Wear coats that are resistant to liquid penetration for activities with splash potential or use a plasticized apron. For high risk activities, use a rear-fastening lab coat. Provision, laundering, and replacement of lab coats is the responsibility of the Principal Investigator, or Department; employees must not launder contaminated lab coats at their home. Masks will help prevent ingestion and protect the mucous membranes of the nose and mouth. They do not provide sufficient protection against infection from organisms transmitted by inhalation, e.g., *M. tuberculosis*. Respirators are used when there is the risk of airborne exposure to organisms transmitted by inhalation and containment devices are unavailable or unable to provide sufficient protection. Respirators use must be preceded by medical clearance, training, and fit testing.

### **Plans for emergency:**

Institution is committed to the safety and well-being of its staff, students and guests. Upholding this commitment requires planning and practice. This plan exists to satisfy those needs and to outline the steps to be taken to prepare for and respond to an emergency affecting the department or the College. The goals in responding to an emergency situation include:

- The safety of all staff, students, and guests.
- The physical and emotional well-being of staff, students, and guests.
- The timely stabilization of an emergency situation.
- The protection of facility, property, and the belongings of staff, students, and guests.

This plan applies to all employees and any person occupying the physical plant includes students, employees, and guests. The scope of this plan is intended to encompass all hazards. This plan may be consulted when responding to any and all emergencies. When encountering a situation which has not been expressly addressed in this plan, use good judgment and the guiding principles. The emergency plan is the responsibility of Head of the Department to update this plan at least once annually. Revisions will be made as needed throughout the year. Any suggestions, comments, or questions should be directed to Individual's Name or Position. Leadership authority during an emergency should be listed before. During an emergency, Institution will use the following means and methods of communication. Inquiries from the media during or after an emergency will be addressed

by the institution. The Office of Public Affairs will be consulted in releasing any information to the media. At any time the media can simply be referred to the Office of Public Affairs. Test, Training, and Exercises are required.

*Possible means and methods:*

*Landline Telephones*

*Cell Phones (possible outages during emergency)*

*Texting (more reliable during an emergency)*

*Two-way Radios*

*Email*

***Take time to develop specific communications procedures defining who will be responsible for communications and what information will be communicated.***

### **Transport of infectious material:**

These guidelines are applicable to the transport of infectious substances and diagnostic specimens both nationally and internationally. They provide information for identifying and classifying the material to be transported and for its safe packaging and transport. The guidelines stress the importance of developing a working relationship between the groups involved – the sender, the carrier and the receiver – in order to provide for the safe and expeditious transport of this material. Postal, airline and other transport industry personnel hold concerns about the possibility of their becoming infected as the result of exposure to infectious microorganisms that may escape from broken, leaking or improperly packaged material. The packaging of infectious materials for transport must therefore address these concerns and be designed to minimise the potential for damage during transport. In addition, the packaging will serve to ensure the integrity of the materials and timely processing of specimens. There are no recorded cases of illness attributable to the release of specimens during transport, although there are reported incidents of damage to the outer packaging of properly packaged materials. The shipment of unmarked and unidentified infectious materials, improperly packaged, obviously increases the overall potential for exposure to all persons. The international regulations for the transport of infectious materials by any mode of transport are based upon the Recommendations of the United Nations Committee of Experts on the Transport of Dangerous Goods (UN). The Universal Postal Union (UPU) reflects these recommendations in its regulations, particularly for packaging. The International Civil Aviation Organization (ICAO) and the International Air Transport Association (IATA) have also incorporated the UN Recommendations in their respective regulations, as have other international transport organizations. The World Health Organization serves in an advisory capacity to these bodies.

### **Biosafety and recombinant DNA technology:**

When creating or handling recombinant organisms, it is essential to perform a detailed risk assessment, which must take into account the nature of the donor, the recipient organism and the environment. In many cases the risk assessment will show that the recombinant organism can be handled at the same BSL as the wild-type recipient. In some instances, however, higher BSLs will be required. This is the case, for example, when ill-defined DNA sequences from a donor organism are transferred, which could potentially increase the virulence of the recipient organism. This situation is typically encountered in random (“shot-gun”) cloning experiments in which genomic DNA libraries are established. Risk assessment is particularly important when creating GMOs expressing proteins with pharmacological activity, such as toxins. It is obvious that such organisms must be handled with caution. Some pharmacologically active proteins are only toxic when expressed at high levels. In this case, the risk assessment becomes very demanding and requires an estimation of the expected expression levels of the protein by a particular recombinant organism and the levels at which a given protein becomes toxic in an organism accidentally exposed to it. The NIH, which established guidelines for work with GMOs, helps scientists classify their work at the appropriate BSL. Risk assessment is thus a dynamic process and has to take

into account new developments and the progress of science. It is the responsibility of the scientists involved in genetic engineering to keep up to date on these developments and to respect the guidelines established by the NIH.

### **Hazardous chemicals:**

Hazardous chemicals stay in the environment for long periods of time, and do not biodegrade or break down easily. Because hazardous chemicals are slow to break down, they can remain in the soil, water or ice for many years after they have been banned. DDT, one of the most notorious toxic pesticides, is still found in the environment today, even though it was banned in many nations in the 70s and 80s. Hazardous chemicals can build up in the bodies of organisms over time, and they can be spread via the food chain. For example, a factory may discharge perfluorinated compounds (PFCs), an extremely persistent pollutant, into the river. The PFCs may then be absorbed by small fish and other aquatic organisms. As they are eaten by bigger animals, the PFCs are passed on as well, moving up to the next level of the food chain. As the PFCs travel up the food chain, they become more concentrated – thus, the largest quantity of chemicals are usually found in top-level predators such as polar bears or people. Numerous studies have found PFCs throughout the food chain, from aquatic invertebrates, fish and amphibians to large mammals such as whales and polar bears. Polar bears especially face many health threats from hazardous chemicals, not just PFCs.

Hazardous chemicals have a range of toxic effects to animals and people. Depending on the type of chemical, they can cause cancer, damage the nervous system, disrupt the reproductive system or alter the function of hormones, just to name a few negative effects. A special group of hazardous chemicals is called endocrine disrupting chemicals (EDCs). Also known as hormone disruptors, they are particularly harmful due to their ability to disrupt the proper function of the body's hormones. Hormones act as the body's chemical messengers, passing along critical information. The system of hormones is called the endocrine system, and it is crucial to the body's healthy functioning. Exposure to EDCs is the most dangerous for developing fetuses. The chemicals can impact – sometimes severely – the development of the brain, nervous system and reproductive system. EDC exposure in adults has also been linked to various cancers, decreased sperm count, thyroid disease, lowered fertility and more. EDCs encompass many different kinds of hazardous chemicals, such as drugs, pesticides, industrial pollutants and persistent organic pollutants. Some examples include DDT, phthalates (plasticizers), alkylphenols, bisphenol A and some types of brominated fire retardants.

### **Fire Hazard:**

Cooking is the number one cause of home fires. Keep appliances clean, and wipe surfaces after spills. Clean stove surfaces and ovens regularly. Wear tight-fitting sleeves, or roll them up when cooking. Keep flammable objects, including pot holders, dish towels and curtains, at least three feet away from the stove. Wood and coal stoves, fireplaces, chimneys, and all other solid-fuelled heating equipment needs to be inspected annually by a professional and cleaned accordingly. Assure microwaves have enough room to breathe, that all the vents are cleared of obstructions. If there is a microwave fire, keep the door closed and unplug the microwave. Make sure to have the microwave oven serviced before you use it again. If there is an oven fire, keep the door closed and turn off the heat. If the fire doesn't go out immediately, call the fire department. A grease fire occurs when oil or greasy foods are heated and ignite. The simplest way to fight a grease fire is to carefully slide a lid over the pan. Turn off the burner, don't move the pan, and keep the lid on until the pan cools completely. Baking Soda may also be used to suffocate the fire. Never put water on a grease fire. Water causes the grease to splatter and the fire to spread. Also, never attempt to take a grease fire outdoors. It will be too hot to carry and you will drop it, causing a major house fire. Heating equipment is the leading cause of home fires during the winter months of December, January and February, and is the second-leading cause of home fires year-round. When buying heaters, look for devices with automatic shut off features. Be sure any gas-fuelled heating device is installed with proper attention to ventilation, and never put unvented gas space heaters in bedrooms or bathrooms. Liquefied Petroleum (LP) gas heaters with self-contained fuel supplies are prohibited for home use by NFPA codes. Never leave space heaters on when you leave the room.

Space heaters should be kept at least three feet away from anything that can burn. Don't use extension cords with space heaters. The high amount of current they require could melt the cord and start a fire. When lighting a gas space heater, strike your match first, then turn on the gas. Never use a gas range as a substitute for a furnace or space heater. Wiring, outlets, switches, circuit breakers and other electrical devices are the third

leading cause of home fires and the second leading cause of fire deaths. Replace or repair loose or frayed cords on all electrical devices. If outlets or switches feel warm, shut off the circuit and have them checked by an electrician. Try to avoid extension cords. If you feel an extension cord is necessary, make sure that it is not frayed or worn. Do not run it under carpet or around doorways. Never overload a socket. The use of "octopus" outlets or "power bar", outlet extensions that accommodate several plugs, is strongly discouraged. Try to limit one high-wattage appliance into each individual outlet at a time. If a circuit breaker trips or a fuse blows frequently, cut down on the number of appliances on that line. In many older homes, the capacity of the wiring system has not kept pace with today's modern appliances and can overload electrical systems. Some overload signals include: dimming lights when an appliance goes on, fuses blowing frequently or shrinking TV picture. Assure there's plenty of air space around home entertainment units such as the TV and stereo to avoid overheating. Smoking is the leading cause of home fire deaths in the United States. Never smoke in bed. Always look under cushions and in trashcans for burning cigarettes before going to bed. Check carpeting where ashtrays have been used.

### **Electrical hazards:**

Replace or repair loose or frayed cords on all electrical devices. If outlets or switches feel warm, shut off the circuit and have them checked by an electrician. Try to avoid extension cords. If you feel an extension cord is necessary, make sure that it is not frayed or worn. Do not run it under carpet or around doorways. Never overload a socket. The use of "octopus" outlets or "power bar", outlet extensions that accommodate several plugs, is strongly discouraged. Try to limit one high-wattage appliance into each individual outlet at a time. If a circuit breaker trips or a fuse blows frequently, cut down on the number of appliances on that line. In many older homes, the capacity of the wiring system has not kept pace with today's modern appliances and can overload electrical systems. Some overload signals include: dimming lights when an appliance goes on, fuses blowing frequently or shrinking TV picture. Assure there's plenty of air space around home entertainment units such as the TV and stereo to avoid overheating.

### **Noise:**

Noise is a variety of sound. It means any unwanted sound. Sounds, particularly loud ones, that disturb people or make it difficult to hear wanted sounds, are noise. For example, conversations of other people may be called noise by people not involved in any of them; any unwanted sound such as domesticated dogs barking, neighbours playing loud music, portable mechanical saws, road traffic sounds, or a distant aircraft in quiet countryside, is called noise. Acoustic noise can be anything from quiet but annoying to loud and harmful. At one extreme users of public transport sometimes complain about the faint and tinny sounds emanating from the headphones or earbuds of somebody listening to a portable audio player; at the other the sound of very loud music, a jet engine at close quarters, etc. can cause irreversible hearing damage. At intermediate levels there are a range of deleterious health effects from noise. This "intolerable corruption of human space" can be called noise pollution.

Noise can be perceived either physiologically or psychologically. We perceive noise physiologically when we "hear" it. On the other hand, when we "listen" to a noise we are doing this psychologically. When we perceive a physiological noise we subconsciously feel the vibrations of the noise (sound) waves with our particles in our physical body whereas psychological noise refers to noise that is perceived when our conscious awareness shifts its attention to that noise rather than letting it filter through our subconscious where it goes unnoticed. Sound intensity follows an inverse square law with distance from the source; doubling the distance from a noise source reduces its intensity.

### **Ionizing radiation:**

Ionizing radiation, also called radioactivity, is electromagnetic radiation whose waves contain energy sufficient to overcome the binding energy of electrons in atoms or molecules, thus creating ions. The wavelength is shorter than that of ultraviolet (UV). Ionizing radiation can occur as a barrage of photons having a nature similar to that of visible light, but with far shorter wavelength and consequently higher frequency. This type of radiation includes X rays and gamma rays. More massive particles also comprise ionizing radiation if they travel at sufficient speed. These include high-speed electrons (beta particles), protons, neutrons, and helium nuclei (alpha particles). Ionizing radiation is dangerous because it damages the internal structures of living cells. This can cause cell death in high doses over a short period of time, and errors in the reproductive process (mutations) in lower doses over longer periods of time.

Examples of non-ionizing EM radiation include radio (RF) waves, extremely low frequency (ELF) fields, infrared (IR), visible light, and UV. These forms of EM energy are generally not dangerous, with some exceptions: high-energy radio microwaves and IR which can cause destructive heating of biological tissue; intense visible light which can cause blindness; and intense UV which can cause blindness and superficial skin burns in high doses over a short period of time, and skin cancer and cataracts of the eye at lower doses over long periods of time. There is debate as to whether long-term exposure to moderate-to-intense radio-frequency (RF) fields and ELF fields is harmful to human beings. The most common unit of ionizing radiation is the becquerel (Bq), equal to one disintegration or nuclear transformation per second. Reduced to base units in the International System of Units (SI),  $1 \text{ Bq} = 1/\text{s}$  or  $1 \text{ s}^{-1}$ . An alternative unit is the curie (Ci), equivalent to  $3.7 \times 10^{10}$  disintegrations per second or  $2.2 \times 10^{12}$  disintegrations per minute. To convert from curies to becquerels, multiply by  $3.7 \times 10^{10}$ . To convert from becquerels to curies, multiply by  $2.7 \times 10^{-11}$ .

To limit the harmful effects of ionizing radiation, the use of radioisotopes should be controlled and should comply with relevant national standards. Protection from radiation is managed on the basis of four principles: 1. Minimizing the time of radiation exposure 2. Maximizing the distance from the radiation source 3. Shielding the radiation source 4. Substituting the use of radionuclides with non-radiometric techniques. Protection activities include the following. 1. Time. The time of exposure experienced during manipulations of radioactive material can be reduced by: Practising new and unfamiliar techniques without using the radionuclide until the techniques are mastered — Working with radionuclides in a deliberate and timely manner without rushing — Ensuring that all radioactive sources are returned to storage immediately after use — Removing radioactive waste from the laboratory at frequent intervals — Spending as little time as possible in the radiation area or laboratory — Exercising effective time management and planning of laboratory manipulations involving radioactive material. The less time spent in a radiation field, the smaller the received personal dose, as described in the equation: Dose = Dose rate x time 2. Distance. The dose rate for most  $\gamma$ - and X-radiation varies as the inverse square of the distance from a point source: Dose rate = Constant x  $1/\text{Distance}$ . Doubling the distance from a radiation source will result in reducing the exposure by one-fourth over the same period of time. Various devices and mechanical aids are used to increase the distance between the operator and the radiation source, e.g. long-handled tongs, forceps, clamps and remote pipetting aids. Note that a small increase in distance can result in significant decrease in the dose rate. 3. Shielding. Radiation energy-absorbing or attenuating shields placed between the source and the operator or other occupants of the laboratory will help limit their exposure. The choice and thickness of any shielding material depends on the penetrating ability (type and energy) of the radiation. A barrier of acrylic, wood or lightweight metal, thickness 1.3–1.5 cm, provides shielding against high-energy  $\beta$  particles, whereas high-density lead is needed to shield against high energy  $\gamma$ - and X-radiation. 4. Substitution. Radionuclide-based materials should not be used when other techniques are available. If substitution is not possible, then the radionuclide with the least penetrating power or energy should be used. Safe practices for work with radionuclides.

Rules for working with radioactive substances should include considerations in four areas: 1. Radiation area 2. Work-bench area 3. Radioactive waste area 4. Records and emergency response. Some of the most important rules include the following: 1. Radiation area — Use radioactive substances only in dedicated areas. Allow the presence of essential staff only. Use personal protective equipment, including laboratory coats, safety spectacles and disposable gloves. Monitor personal radiation exposures. Laboratories where radionuclides are used should be designed to simplify containment, cleaning and decontamination. The radionuclide work area should be located in a small room adjoining the main laboratory, or in a dedicated area within the laboratory away from other activities. Signs displaying the international radiation hazard symbol should be posted at the entrance to the radiation area. 2. Work-bench area — Use spill trays lined with disposable absorbent materials. Limit radionuclide quantities. Shield radiation sources in the radiation, work bench and radioactive waste areas. Mark radiation containers with the radiation symbol, including radionuclide identity, activity and assay date. Use radiation meters to monitor working areas, protective clothing and hands after completion of work. Use appropriately shielded transport containers. 3. Radioactive waste area — Remove radioactive waste frequently from the working area. Maintain accurate records of use and disposal of radioactive materials. Screen dosimetry records for materials exceeding the dose limits. Establish and regularly exercise emergency response plans. In emergencies, assist injured persons first. Clean contaminated areas thoroughly. Request assistance from the safety office, if available. — Write and keep incident reports.

### **Biosafety officer:**

Wherever possible a biosafety officer should be appointed to ensure that biosafety policies and programmes are followed consistently throughout the laboratory. The biosafety officer executes these duties on behalf of the head of the institute or laboratory. In small units, the biosafety officer may be a microbiologist or a member of the technical staff, who may perform these duties on a defined part-time basis. Whatever the degree of

involvement in biosafety, the person designated should possess the professional competence necessary to suggest, review and approve specific activities that follow appropriate biocontainment and biosafety procedures. The biosafety officer should apply relevant national and international rules, regulations and guidelines, as well as assist the laboratory in developing standard operating procedures. The person appointed must have a technical background in microbiology, biochemistry and basic physical and biological sciences. Knowledge of laboratory and clinical practices and safety, including containment equipment, and engineering principles relevant to the design, operation and maintenance of facilities is highly desirable. The biosafety officer should also be able to communicate effectively with administrative, technical and support personnel.

The activities of the biosafety officer should include the following: 1. Biosafety, biosecurity and technical compliance consultations. 2. Periodic internal biosafety audits on technical methods, procedures and protocols, biological agents, materials and equipment. 3. Discussions of violation of biosafety protocols or procedures with the appropriate persons. 4. Verification that all staff has received appropriate biosafety training. 5. Provision of continuing education in biosafety. 6. Investigation of incidents involving the possible escape of potentially infectious or toxic material, and reporting of findings and recommendations to the laboratory director and biosafety committee. 7. Coordination with medical staff regarding possible laboratory-acquired infections. 8. Ensuring appropriate decontamination following spills or other incidents involving infectious material(s). 9. Ensuring proper waste management. 10. Ensuring appropriate decontamination of any apparatus prior to repair or servicing. 11. Maintaining awareness of community attitudes regarding health and environmental considerations. 12. Establishment of appropriate procedures for import/export of pathogenic material to/from the laboratory, according to national regulations. 13. Reviewing the biosafety aspects of all plans, protocols and operating procedures for research work involving infectious agents prior to the implementation of these activities. 14. Institution of a system to deal with emergencies.

#### **Biosafety Committee:**

A biosafety committee should be constituted to develop institutional biosafety policies and codes of practice. The biosafety committee should also review research protocols for work involving infectious agents, animal use, recombinant DNA and genetically modified materials. Other functions of the committee may include risk assessments, formulation of new safety policies and arbitration in disputes over safety matters. The membership of the biosafety committee should reflect the diverse occupational areas of the organization as well as its scientific expertise. The composition of a basic biosafety committee may include: 1. Biosafety officer(s) 2. Scientists 3. Medical personnel 4. Veterinarian(s) (if work with animals is conducted) 5. Representatives of technical staff 6. Representatives of laboratory management. The biosafety committee should seek advice from different departmental and specialist safety officers (e.g. with expertise in radiation protection, industrial safety, fire prevention, etc.) and may at times require assistance from independent experts in various associated fields, local authorities and national regulatory bodies. Community members may also be helpful if there is a particularly contentious or sensitive protocol under discussion.

#### **Safety for support staff:**

The safe and optimum operation of a laboratory is dependent to a great extent on the support staff, and it is essential that such personnel are given appropriate safety training. Engineering and building maintenance services. Skilled engineers and craftsmen who maintain and repair the structure, facilities and equipment, should have some knowledge of the nature of the work of the laboratory, and of safety regulations and procedures. Testing of equipment after servicing, e.g. testing the efficiency of biological safety cabinets after new filters have been fitted, may be carried out by or under supervision of the biosafety officer. Laboratories or institutions that do not have internal engineering and maintenance services should establish good relationships with local service providers to familiarize them with the equipment and work of the laboratory. Engineering and maintenance staff should only enter Biosafety Level 3 or Biosafety Level 4 laboratories with clearance and supervision by the biosafety officer and/or the laboratory supervisor. Cleaning (domestic) services Biosafety Level 3 and Biosafety Level 4 laboratories should be cleaned by the laboratory staff. Cleaning personnel should only enter Biosafety Level 3 or Biosafety Level 4 laboratories with clearance and supervision by the biosafety officer and/or the laboratory supervisor.

## **Training programs:**

A continuous, on-the-job safety training programme is essential to maintain safety awareness among laboratory and support staff. Laboratory supervisors, with the assistance of the biosafety officer and other resource persons, play the key role in staff training. The effectiveness of biosafety training, indeed all safety and health training, depends on management commitment, motivational factors, adequate initial job training, good communications, and ultimately the organization's goals and objectives. The following are critical elements for an effective biosafety training programme. 1. Needs assessment. This process includes defining the tasks involved, the order of importance (in terms of frequency, criticality, complexity) and details of the steps necessary to accomplish them. 2. Establishing training objectives. These are observable behaviours that the trainee is expected to demonstrate, on the job, after the training. Objectives may acknowledge the conditions under which certain activities or behaviours are performed and the required level of proficiency. 3. Specifying training content and media. Content is the knowledge or skill that the trainee must master to be able to meet the behavioural objectives. Those individuals who know the job and its demands best usually define the content of the biosafety training programme. Other approaches used may focus on the products of problemsolving exercises or the design of learning measures to correct mistakes people have made in using a skill. It is not clear that one teaching method (lectures, televised instruction, computer-aided instruction, interactive video, etc.) is superior to another. Much depends on specific training needs, the make-up of the trainee group, etc. 4. Accounting for individual learning differences. Effective training must take into account the characteristics or attributes of the trainees. Individuals and groups may differ in aptitude, literacy, culture, spoken language and pre-training skill levels. How the training programme is viewed by trainees in terms of improving their job performance or personal safety may dictate the approach used. Some individuals are more visual or "hands-on" learners; others learn well from written materials. Any special needs of employees must also be addressed, such as course adaptation for those with hearing impairments. In addition to taking account of these elements, it is recommended that the developers of any safety training programme become acquainted with the principles of adult learning. Specifying learning conditions.

The instructional event (e.g. training course, videotape, written materials, etc.) should not conflict with, inhibit or be unrelated to mastery of the skill or topic being taught. For example, if the intent of the instruction is to develop capabilities in problem-solving techniques, the instructional approach should stress thinking/reasoning approaches rather than rote memorization. The instruction provided should require productive behaviour and/or appropriate feedback (positive/accurate/credible). In addition, instructional events that provide opportunities for practice under conditions similar to that of the job will enhance the transfer of the skill to the actual job. 6. Training evaluation. This provides information that helps to determine whether the instruction has had the intended effect. Training evaluations generally take four forms: — measuring the trainees' reaction to the instruction provided — measuring the trainees' recollection and/or performance — assessing behavioural change on the job — measuring tangible results in terms of the organization's objectives or goals. The most complete evaluation of a training effort involves assessments for each of the four areas. The least efficient method of evaluation is to consider only the trainees' reactions to the instruction as this may bear little relationship to the extent of actual learning. It should not be used as the sole measurement of training effectiveness. 7. Training revision. Training evaluations rarely indicate that a training programme is a complete success or failure because multiple criteria are used to measure results. Usually the data indicate a better understanding, retention or application of some parts of the course material as compared with others. Variation or gaps in knowledge or the desired competencies resulting from the training effort may reflect the need to consider more training time, alternative instructional techniques or more capable instructors. WHO provides various tools for microbiological safety training.

## **Safety checklist:**

This checklist is intended to assist in assessments of microbiological laboratory safety and security status of biomedical laboratories.

### *Laboratory premises*

1. Have guidelines for commissioning and certification been considered for facility construction or post-construction evaluations?
2. Do the premises meet national and local building requirements, including those relating to natural disaster precautions if necessary?
3. Are the premises generally uncluttered and free from obstructions?
4. Are the premises clean?
5. Are there any structural defects in floors?
6. Are floors and stairs uniform and slip-resistant?
7. Is the working space adequate for safe operation?
8. Are the circulation spaces and corridors adequate for the movement

of people and large equipment? 9. Are the benches, furniture and fittings in good condition? 10. Are bench surfaces resistant to solvents and corrosive chemicals? 11. Is there a hand-washing sink in each laboratory room? 12. Are the premises constructed and maintained to prevent entry and harbourage of rodents and arthropods? 13. Are all exposed steam and hot water pipes insulated or guarded to protect personnel? 14. Is an independent power support unit provided in case of power breakdown? 15. Can access to laboratory areas be restricted to authorized personnel? 16. Has a risk assessment been performed to ensure that appropriate equipment and facilities are available to support the work being considered?

#### *Storage facilities*

1. Are storage facilities, shelves, etc. arranged so that stores are secure against sliding, collapse or falls? 2. Are storage facilities kept free from accumulations of rubbish, unwanted materials and objects that present hazards from tripping, fire, explosion and harbourage of pests? 3. Are freezers and storage areas lockable?

#### *Sanitation and staff facilities*

1. Are the premises maintained in a clean, orderly and sanitary condition? 2. Is drinking-water available? 3. Are clean and adequate toilet (WC) and washing facilities provided separately for male and female staff? 4. Are hot and cold water, soap and towels provided? 5. Are separate changing rooms provided for male and female staff? 6. Is there accommodation (e.g. lockers) for street clothing for individual members of the staff? 7. Is there a staff room for lunch, etc.? 8. Are noise levels acceptable? 9. Is there an adequate organization for the collection and disposal of general household rubbish?

#### *Heating and ventilation*

1. Is there a comfortable working temperature? 2. Are blinds fitted to windows that are exposed to full sunlight? 3. Is the ventilation adequate, e.g. at least six changes of air per hour, especially in rooms that have mechanical ventilation? 4. Are there HEPA filters in the ventilation system? 5. Does mechanical ventilation compromise airflows in and around biological safety cabinets and fume cupboards?

#### *Lighting*

1. Is the general illumination adequate (e.g. 300–400 lx)? 2. Is task (local) lighting provided at work benches? 3. Are all areas well-lit, with no dark or ill-lit corners in rooms and corridors? 4. Are fluorescent lights parallel to the benches? 5. Are fluorescent lights colour-balanced?

#### *Services*

1. Is each laboratory room provided with enough sinks, water, electricity and gas outlets for safe working? 2. Is there an adequate inspection and maintenance programme for fuses, lights, cables, pipes, etc.? 3. Are faults corrected within a reasonable time? 4. Are internal engineering and maintenance services available, with skilled engineers and craftsmen who also have some knowledge of the nature of the work of the laboratory? 5. Is the access of engineering and maintenance personnel to various laboratory areas controlled and documented? 6. If no internal engineering and maintenance services are available, have local engineers and builders been contacted and familiarized with the equipment and work of the laboratory? 7. Are cleaning services available? 8. Is the access of cleaning personnel to various laboratory areas controlled and documented? 9. Are information technology services available and secured?

#### *Laboratory biosecurity*

1. Has a qualitative risk assessment been performed to define risks that a security system should protect against? 2. Have acceptable risks and incidence response planning parameters been defined? 3. Is the whole building securely locked when unoccupied? 4. Are doors and windows break-proof? 5. Are rooms containing hazardous materials and expensive equipment locked when unoccupied? 6. Is access to such rooms, equipment and materials appropriately controlled and documented?

### *Fire prevention and fire protection*

1. Is there a fire alarm system? 2. Are the fire doors in good order? 3. Is the fire detection system in good working order and regularly tested? 4. Are fire alarm stations accessible? 5. Are all exits marked by proper, illuminated signs? 6. Is access to exits marked where the routes to them are not immediately visible? 7. Are all exits unobstructed by decorations, furniture and equipment, and unlocked when the building is occupied? 8. Is access to exits arranged so that it is not necessary to pass through a high-hazard area to escape? 9. Do all exits lead to an open space? 10. Are corridors, aisles and circulation areas clear and unobstructed for movement of staff and fire-fighting equipment? 11. Is all fire-fighting equipment and apparatus easily identified by an appropriate colour code? 12. Are portable fire extinguishers maintained fully charged and in working order, and kept in designated places at all times? 13. Are laboratory rooms with potential fire hazards equipped with appropriate extinguishers and/or fire blankets for emergency use? 14. If flammable liquids and gases are used in any room, is the mechanical ventilation sufficient to remove vapours before they reach a hazardous concentration? 15. Are personnel trained to respond to fire emergencies?

### *Flammable liquid storage*

1. Is the storage facility for bulk flammable liquids separated from the main building? 2. Is it clearly labelled as a fire-risk area? 3. Does it have a gravity or mechanical exhaust ventilation system that is separate from the main building system? 4. Are the switches for lighting sealed or placed outside the building? 5. Are the light fittings inside sealed to protect against ignition of vapours by sparking? 6. Are flammable liquids stored in proper, ventilated containers that are made of non-combustible materials? 7. Are the contents of all containers correctly described on the labels? 8. Are appropriate fire extinguishers and/or fire blankets placed outside but near to the flammable liquid store? 9. Are "No smoking" signs clearly displayed inside and outside the flammable liquid store? 10. Are only minimum amounts of flammable substances stored in laboratory rooms? 11. Are they stored in properly constructed flammable storage cabinets? 12. Are these cabinets adequately labelled with "Flammable liquid – Fire hazard" signs? 13. Are personnel trained to properly use and transport flammable liquids?

### *Compressed and liquefied gases*

1. Is each portable gas container legibly marked with its contents and correctly colour coded? 2. Are compressed-gas cylinders and their high-pressure and reduction valves regularly inspected? 3. Are reduction valves regularly maintained? 4. Is a pressure-relief device connected when a cylinder is in use? 5. Are protection caps in place when cylinders are not in use or are being transported? 6. Are all compressed gas cylinders secured so that they cannot fall, especially in the event of natural disaster? 7. Are cylinders and liquid petroleum gas tanks kept away from sources of heat? 8. Are personnel trained to properly use and transport compressed and liquefied gases?

### **Electrical hazards**

1. Are all new electrical installations and all replacements, modifications or repairs made and maintained in accordance with a national electrical safety code? 2. Does the interior wiring have an earthed/grounded conductor (i.e. a three-wire system)? 3. Are circuit-breakers and earth-fault interrupters fitted to all laboratory circuits? 4. Do all electrical appliances have testing laboratory approval? 5. Are the flexible connecting cables of all equipment as short as practicable, in good condition, and not frayed, damaged or spliced? 6. Is each electric socket outlet used for only one appliance (no adapters to be used)?

### *Personal protection*

1. Is protective clothing of approved design and fabric provided for all staff for normal work, e.g. gowns, coveralls, aprons, gloves? 2. Is additional protective clothing provided for work with hazardous chemicals and radioactive and carcinogenic substances, e.g. rubber aprons and gloves for chemicals and for dealing with spillages; heat-resistant gloves for unloading autoclaves and ovens?

3. Are safety glasses, goggles and shields (visors) provided? 4. Are there eye-wash stations? 5. Are there emergency showers (drench facilities)? 6. Is radiation protection in accordance with national and international standards, including provision of dosimeters? 7. Are respirators available, regularly cleaned, disinfected, inspected and stored in a clean and sanitary condition? 8. Are appropriate filters provided for the correct types of respirators, e.g. HEPA filters for microorganisms, appropriate filters for gases or particulates? 9. Are respirators fit-tested?

#### *Health and safety of staff*

1. Is there an occupational health service? 2. Are first-aid boxes provided at strategic locations? 3. Are qualified first-aiders available? 4. Are such first-aiders trained to deal with emergencies peculiar to the laboratory, e.g. contact with corrosive chemicals, accidental ingestion of poisons and infectious materials? 5. Are non-laboratory workers, e.g. domestic and clerical staff, instructed on the potential hazards of the laboratory and the material it handles? 6. Are notices prominently posted giving clear information about the location of first-aiders, telephone numbers of emergency services, etc.? 7. Are women of childbearing age warned of the consequences of work with certain microorganisms, carcinogens, mutagens and teratogens? 8. Are women of childbearing age told that if they are, or suspect that they are, pregnant they should inform the appropriate member of the medical/scientific staff so that alternative working arrangements may be made for them if necessary? 9. Is there an immunization programme relevant to the work of the laboratory? 10. Are skin tests and/or radiological facilities available for staff who work with tuberculous materials or other materials requiring such measures? 11. Are proper records maintained of illnesses and accidents? 12. Are warning and accident prevention signs used to minimize work hazards? 13. Are personnel trained to follow appropriate biosafety practices? 14. Are laboratory staff encouraged to report potential exposures?

#### *Laboratory equipment*

1. Is all equipment certified safe for use? 2. Are procedures available for decontaminating equipment prior to maintenance? 3. Are biological safety cabinets and fume cupboards regularly tested and serviced? 4. Are autoclaves and other pressure vessels regularly inspected? 5. Are centrifuge buckets and rotors regularly inspected? 6. Are HEPA filters regularly changed? 7. Are pipettes used instead of hypodermic needles? 8. Is cracked and chipped glassware always discarded and not reused? 9. Are there safe receptacles for broken glass? 10. Are plastics used instead of glass where feasible? 11. Are sharps disposal containers available and being used?

#### *Infectious materials*

1. Are specimens received in a safe condition? 2. Are records kept of incoming materials? 3. Are specimens unpacked in biological safety cabinets with care and attention to possible breakage and leakage? 4. Are gloves and other protective clothing worn for unpacking specimens? 5. Are personnel trained to ship infectious substances according to current national and/or international regulations? 6. Are work benches kept clean and tidy? 7. Are discarded infectious materials removed daily or more often and disposed of safely? 8. Are all members of the staff aware of procedures for dealing with breakage and spillage of cultures and infectious materials? 9. Is the performance of sterilizers checked by the appropriate chemical, physical and biological indicators? 10. Is there a procedure for decontaminating centrifuges regularly? 11. Are sealed buckets provided for centrifuges? 12. Are appropriate disinfectants being used? Are they used correctly? 13. Is there special training for staff who work in containment laboratories – Biosafety Level 3 and maximum containment laboratories – Biosafety Level 4?

#### *Chemicals and radioactive substances*

1. Are incompatible chemicals effectively separated when stored or handled? 2. Are all chemicals correctly labelled with names and warnings? 3. Are chemical hazard warning charts prominently displayed? 4. Are spill kits provided? 5. Are staff trained to deal with spills? 6. Are flammable substances correctly and safely stored in minimal amounts in approved cabinets? • 131 • 7. Are bottle carriers provided? 8. Is a radiation protection officer or appropriate reference manual

available for consultation? 9. Are staff appropriately trained to safely work with radioactive materials? 10. Are proper records of stocks and use of radioactive substances maintained? 11. Are radioactivity screens provided? 12. Are personal radiation exposures monitored?

### **First Aid:**

First aid is the skilled application of accepted principles of medical treatment at the time and place of an accident. It is the approved method of treating a casualty until he or she is placed in the care of a doctor for definitive treatment of the injury. The minimum first-aid equipment consists of a first-aid box, protective clothing and safety equipment for the person rendering the first aid, and eye irrigation equipment. The first-aid box The first-aid box should be constructed from materials that will keep the contents dust- and damp-free. It should be kept in a prominent position and be easily recognized. By international convention, the first-aid box is identified by a white cross on a green background. The first-aid box should contain: 1. Instruction sheet giving general guidance 2. Individually-wrapped sterile adhesive dressings in a variety of sizes 3. Sterile eye-pads with attachment bandages 4. Triangular bandages 5. Sterile wound coverings 6. Safety pins 7. A selection of sterile but unmedicated wound dressings 8. An authoritative first-aid manual, e.g. one issued by the International Red Cross. Protective equipment for the person rendering first aid includes: 1. Mouthpiece for mouth-to-mouth resuscitation 2. Gloves and other barrier protections against blood exposures, 3. Clean-up kit for blood spills. Eye irrigation equipment should also be readily available and staff trained in its correct use.

### **Immunization of the staff:**

The risks of working with particular agents should be fully discussed with individual researchers. The local availability, licensing state and utility of possible vaccines and/ or therapeutic drugs (e.g. antibiotic treatments) in case of exposure should be evaluated before work with such agents is started. Some workers may have acquired immunity from prior vaccination or infection. If a particular vaccine or toxoid is locally licensed and available, it should be offered after a risk assessment of possible exposure and a clinical health assessment of the individual have been carried out. Facilities for specific clinical case management following accidental infections should also be available.

### **WHO biosafety collaborating centres:**

Information on the availability of training courses, aids and materials may be obtained by writing to any of the following:

Biosafety programme, Department of Communicable Disease Surveillance and Response, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (<http://www.who.int/csr/>).

WHO Collaborating Centre for Biological Safety, Swedish Institute for Infectious Disease Control, Nobels Väg 18, S-171 82 Solna, Sweden (<http://www.smittskyddsinstitutet.se/English/english.htm>).

WHO Collaborating Centre on Biosafety Technology and Consultative Services, Office of Laboratory Security, Health Canada, 100 Colonnade Road, Loc.: 6201A, Ottawa, Ontario, Canada K1A 0K9 (<http://www.hc-sc.gc.ca/pphb-dgsp/ols-bsl>).

WHO Collaborating Centre for Applied Biosafety Programmes and Training, Office of Health and Safety, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop F05, Atlanta, GA 30333, USA (<http://www.cdc.gov/>).

WHO Collaborating Centre for Applied Biosafety Programmes and Research, Division of Occupational Health and Safety, Office of Research Services, National Institutes of Health, Department of Health and Human Services, 13/3K04 13 South Drive MSC 5760, Bethesda, MD 20892-5760, USA (<http://www.nih.gov/>).

WHO Collaborating Centre for Biosafety, Victorian Infectious Diseases Reference Laboratory, 10 Wreckyn St, Nth Melbourne, Victoria 3051, Australia. Postal address: Locked Bag 815, PO Carlton Sth, Victoria 3053, Australia (<http://www.vidrl.org.au/>).

### **US biosecurity legislations:**

Biosecurity bill 2014 was passed by the government and become biosecurity act 2015. Agricultural biosecurity department worked with 400 organizations that is 630 pages long. This biosecurity act support biosecurity system in any age regardless of the advances in technology. Scientific advances and advices help to make right

decisions. Modern and responsive legislative framework helps in improving underpinning processes. Robust biosecurity system that benefits everyone prevents the entry and establishment of invasive species, exotic pests, and stop to harm natural environment, agriculture, health and economy.

### **US biosecurity regulations:**

The new biosecurity legislation is a large body of work; success is critical to large number of clients/stakeholders. They understand the implementation and regulations. For the regulation of GM crops, it is divided into three regulatory agencies; Environment protection agency (EPA), Food and drug administration (FDA), US department of agriculture (USDA) EPA includes insecticide/pesticide/ fungicide/rodenticide. GM crop carrying a gene of Bt toxins are environmentally friendly. They also work for food safety analysis/non-allergic FDA is concerned with the safety of GM crops eaten by humans and animals. This requires pre-market approval. Sometimes GM crops equivalent to non-GM crops but difficulty arises when there is expression of foreign proteins. Functions are to solve the problems like of toxicity, allergy, and introduction of pharmaceutical products.

### **US biosecurity guidance:**

AFIA stands for America Feed Industry Association. It provides bioweapons guidelines. It also provides recommendations to feed and ingredient manufacturers. It develops biosecurity plan-control spread of animal diseases. Location, business, and facility are the criteria help to develop a biosecurity plan based on potential hazards and risk of occurrence within processes. It develops procedures- plan implementation-effective as situation changes. Responsibility of the director is to reduce biorisk by the establishment and implementation of the procedures as well as the establishment of biorisk management committee. Responsibility of vulnerable biological materials is to require administrative oversight, control, accountability and protective measure value of population. VBM includes toxins, non-pathogenic strains, foods/vaccines, GMOs, cell-components and extraterrestrial samples.

### **Canada Biosecurity legislations and guidance:**

The Canadian Food Inspection Agency develops national biosecurity standards, protocols and strategies in collaboration with producer organizations, provincial/territorial governments, and academia. The National Avian On-Farm Biosecurity Standard forms the basis of a comprehensive voluntary program designed to provide applicable guidance for owners or managers in all the poultry sectors in Canada. It has been developed as a tool for all people and businesses handling and keeping poultry, including large-scale supply-managed producers, backyard flock owners and other domestic bird keepers. This On-Farm Biosecurity Standard is supplemented by a General Producer Guide that provides guidance to producers on how the Target Outcomes may be achieved. The Standard and associated Producer Guide are designed to support the development of farm-specific biosecurity protocols for sectors that do not already participate in a provincial association or On-Farm Food Safety (OFFS) program (such as the non-regulated commercial and non-commercial sectors). They have also been designed to be complementary with, and enhance, existing On-Farm Programs. The OFFS programs developed by industry formally address many of the elements of biosecurity and will be the primary avenue for implementation where OFFS programs exist. This program is based on clear, scientifically justified principles. It details a range of measures intended to prevent disease-causing agents from entering or leaving a premises housing poultry. Product on the Canadian market originates from both domestic and imported suppliers. Regardless of the source, the same standards should, ideally, apply to the production of all products being sold in Canada.

Diseases such as infectious bovine rhinotracheitis (IBR), bovine viral diarrhoea (BVD), mycobacterium avium paratuberculosis (Johne's disease) and neonatal calf diarrhoea (scours) are all too familiar to producers throughout the industry and, in many cases, are endemic throughout most of North America. Although these diseases may be eradicated from a particular herd, there is an ongoing risk of re-occurrence that can be managed through biosecurity.

These diseases, along with others, come at a cost to producers, whether measured in terms of dollars and cents, lowered productivity, or animals lost. It is estimated that respiratory disease accounts for 16% of calf loss. Other estimates suggest that the diarrhoea in neonatal calves results in 5% of all calf losses – a figure that increases to 25% when older calves are included. When multiplying these losses and their related costs across

the more than 80,000 operations that raise beef cattle in Canada, it is clear that reducing the impacts of such diseases may result in significant savings to the industry as a whole. The same principles that enable producers to better manage the risks of endemic disease within their operations may have a cumulative effect if applied across the industry, and thus facilitate the reduction of diseases that are considered endemic. Applied across the industry, these principles will also reduce the risk of an emerging disease or a foreign animal disease (FAD), namely, foot-and-mouth disease (FMD). An outbreak, particularly one such as FMD, could have devastating impacts on individual operations and on the industry as a whole. It is estimated that the economic impacts of an FMD outbreak in Canada could be reduced from \$48 billion to \$23 billion, and possibly to \$6.6 billion, by the presence of moderately effective, or even highly effective, policies that address zoning, identification and traceability, and biosecurity. Although the severity and impact of endemic, emerging, and FAD outbreaks may differ, they are all caused by diseases which themselves are caused by organisms. Managing the outbreak, therefore, requires management of the organism. Just as these principles can control and reduce the impacts of endemic diseases, so, too, can they control and reduce the impacts of a FAD or an emerging disease.

#### **Japan biosecurity legislation and guidance:**

Japan ministry of health, labor and welfare has two pillars of biosecurity. It deals with the surveillance of infection and infectious agents, regulations of pathogen handling, screening of foods, human, and vectors at the point of entry. Japan ministry of agriculture, forest and fisheries deals with health issues of animals and plants. There are also bioweapon-prohibition laws.

#### **Other countries biosecurity legislation and guidance:**

New Zealand work with other organizations for hazardous substance and new organism act as it was not developed till 1993. Biosecurity legislation and guidance were developed in 1996 that deals with environment safety and human health. Queensland biosecurity act 2014 facilitates responding -impact of biosecurity consideration, safety and quality of animal field, agriculture inputs and the entire requirement at national level. India has alien species. It deals with sanitary and phytosanitary measures, GMOs so bioethical considerations in research.

#### **Design biosecurity plan:**

Biosecurity plan is a written plan-prevent the introduction and spread of disease to farm. Daily operation procedures and disinfecting procedures are the part of the plan. Principal investigator has the responsibility to plan procedures and implement it. Workers must follow the plan. Training FOR THE lab workers, responsible official and of the campus security staff is required. Management services are also needed. Biosecurity officer must be contacted if biological agent is theft or lost, contact agencies if there is threat or spill. Other aspects such as risk assessment, physical protection, personnel protection, pathogen accountability and emergency response should be considered.

#### **Objectives of lab biosecurity:**

The term "biosecurity" has multiple definitions. In the animal industry, the term biosecurity relates to the protection of an animal colony from microbial contamination. In some countries, the term biosecurity is used in place of the term biosafety. For the purposes of this section the term "biosecurity" will refer to the protection of microbial agents from loss, theft, diversion or intentional misuse. This is consistent with current WHO and American Biological Safety Association (ABSA) usage of this term.<sup>2,3</sup> Security is not a new concept in biological research and medical laboratories. Several of the security measures are embedded in the biosafety levels that serve as the foundation for good laboratory practices throughout the biological laboratory community. Most biomedical and microbiological laboratories do not have select agents or toxins, yet maintain control over and account for research materials, protect relevant sensitive information, and work in facilities with access controls commensurate with the potential public health and economic impact of the biological agents in their collections. These measures are in place in most laboratories that apply good laboratory management practices and have appropriate biosafety programs. The objective of biosecurity is to prevent loss, theft or misuse of microorganisms, biological materials, and research-related information. This is accomplished by limiting access to facilities, research materials and information. While the objectives are different, biosafety and biosecurity measures are usually complementary.

#### **Lab biosecurity and risk of bioterrorism:**

Material control is a widely used measure for arms control. It prevents the proliferation of weapons of mass destruction by many nations; and also prevents terrorists from acquiring substances that could be used to do great harm. This is especially critical for preventing the proliferation of nuclear weapons which require plutonium or enriched uranium. Access to these critical elements for nuclear weapons is restricted through an international nuclear nonproliferation accord, export controls, and an internationally enforced system of inspections. Although there are important differences between nuclear and biological weapons, an effective biosecurity regime must include measures that limit access to dangerous pathogens that could be used as biological weapons. But, given the fact that pathogens that could be used as biological weapons are widely distributed in nature and that many laboratories around the world, including many Asian nations, possess potential bioterror agents, the challenge of preventing bioterrorism and biowarfare is considerably greater than preventing nuclear proliferation. Even though it would not eliminate the threat that terrorists could acquire bioterror agents directly from nature, it is critical that laboratories and microbial culture collections (Biological Resource Centers— BRCs) institute appropriate security and safety procedures to prevent the accidental and/or intentional spread of infectious disease. This requires systems of national oversight and compliance within the scientific community to standards of practice necessary to ensure biosafety and biosecurity. The WHO (2004)) says: “National standards should be developed that recognize and address the ongoing responsibility of countries and institutions to protect specimens, pathogens and toxins from misuse.”

### **Lab biosecurity and international obligations:**

Realization of the threat of bioterrorism and biocrime has prompted many international and national initiatives on laboratory biosafety and biosecurity beyond regulations. International agreements, including the Biological and Toxins Weapons Convention (BWC) and United Nations Security Council Resolution 1540 (UNSCR 1540), compel countries to strengthen their implementation of biosecurity. Since the 2003 Experts Group Meeting of the BWC, much attention has been devoted by the international community to raising awareness about the importance of laboratory biosecurity for bioscience laboratories. On 28 April 2004, the United Nations Security Council unanimously passed UNSCR 1540, which established, for the first time, binding obligations on all UN member states under Chapter VII of the UN Charter, to take and enforce effective measures against the proliferation of weapons of mass destruction, their means of delivery, and related materials. One way that countries can demonstrate their compliance with UNSCR 1540 is through the implementation of laboratory biosecurity measures that secure biological weapons source materials in bioscience facilities. In fact, UNSCR 1540 specifically calls on countries to secure biological materials in production, use, storage, and transport, and implement physical protection measures, border controls, other law enforcement efforts, and end-user controls.

The passage of the World Health Assembly Resolution 58.29 in 2005 is another landmark measure that recognizes the importance of laboratory biosafety and biosecurity. This resolution specifically urged member states of the WHO to implement an integrated approach to laboratory biosafety, including containment of microbiological agents and toxins. Member states were advised to review protocols for ensuring the safe handling of harmful biological agents. States were also instructed to establish biosafety practices in accordance with WHO guidance. Mobilization of national and financial resources sufficient to accomplish these goals, as well as the requisite international support and cooperation, were also recognized as important components. The WHO has also developed a number of benchmark documents, including the third edition of the *Laboratory Biosafety Manual* in 2004. This document serves as a global resource that offers practical guidance on biosafety for all types of laboratories and biosafety levels; the third edition includes a chapter that introduced, for the first time, laboratory biosecurity. Other influential WHO documents include *Biorisk management: Laboratory Biosecurity Guidance*, which promotes the protection and control of laboratory biological materials to prevent intentional misuse, and the *Guidance on Regulations for the Transport of Infectious Substances*.

In 2007, the Organization for Economic Cooperation and Development (OECD) published the *OECD Best Practice Guidelines for Biological Resource Centers*. This comprehensive report describes a rationale for establishing a global network for biological resource centers (BRCs), and contains four sets of best practice guidelines, including the *Best Practice Guidelines on Biosecurity for BRCs*. Other organizations, such as the World Organization for Animal Health, have also recently published guidelines that endorse good biosafety and biosecurity practices in laboratory environments. Three of the most important include *The Terrestrial Animal Health Code (2007)*, *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (2004)*, and *Quality Standard and Guidelines for Veterinary Laboratories: infectious diseases (2008)*. All of these publications are available online, and have been translated into multiple languages. These international initiatives are designed to strengthen the implementation of biosafety and biosecurity at the laboratory level. In particular, UNSCR 1540 should compel more countries to enact national legislation that addresses biosecurity. And the guidance from

WHO and other international organizations should help establish a new international norm, setting the expectation that laboratories will implement needed changes to ensure that pathogens and toxins are handled safely and securely.

### **Pakistan biosecurity legislation and guidance:**

The Government of Pakistan (GoP) has a system of administration and control of imports which has been adapted to accommodate enhanced communication and transport systems and the liberalising trade environment. The Government of Pakistan is committed to compliance with the WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) and has a program of legislation revision and enhancement of entry access/regulation, infrastructure and capacity building underway. This report examines the status of the current regulatory system in Pakistan and selected neighbouring countries, assesses strengths and weaknesses and makes recommendations for improvement and future action. In promoting Pakistan exports, imports will also grow through: opening up trade under bilateral Free Trade Agreements, enhanced dialogue with other countries, strengthening Pakistan's trade office presence abroad, and investment in infrastructure and capacity building in Pakistan. These key initiatives affect both capacity requirements and the complexity of challenges and reinforce the urgency for strengthening import regulation. Relevant legislative authority that governs SPS controls over imports to Pakistan.

Pakistan does not have clearly defined Federal laws to regulate SPS control over imports. Most current laws are available from the internet, and an excellent body of additional information is very accessible in electronic form. In terms of the overall system, Pakistan is broadly compliant with the requirements of SPS, but some laws are old and in need of revision/broadening. The revised laws should be more comprehensive, flexible and effective: Pakistan does not have laws to regulate genetically modified organism (GMO) crops; however, bio-safety guidelines have been developed. Pakistan does not have provisions for monitoring or regulating maximum residue limits (MRLs) in imported or domestic produce. Roles and responsibilities of key Federal and Provincial Government Departments Federal Agencies are responsible for most elements of import control. Legislation for Food Safety, however, is under the responsibility of the Provincial Governments. Responsibilities are reasonably well defined, but implementation in practice can be limited by lack of resources and infrastructure, particularly at land borders. There is no system in place for contaminant testing of imports and, for some commodities; 'condition of import' specifications may not provide adequate SPS protection. Other principal stakeholders include industry bodies, non-government organisations and the private sector. There are industry bodies to represent most key groups. Consultation processes are variable and more attention is needed in this area. Import controls in neighbouring countries: Afghanistan, and Iran Import Controls and legal frameworks in Pakistan are broadly similar level to those of Iran and the two countries have consulted and agreed on specific import/export protocols (e.g. citrus and mangoes to Iran). Development of the legal frameworks, infrastructure and capacity for import controls by Afghanistan is much more basic, and produce entry from and through Afghanistan represent considerable biosecurity risk to Pakistan. FAO agencies are providing some generic guidelines for biosecurity risk management of imports to Afghanistan. Pakistan could potentially provide mutually beneficial assistance in legal frameworks and capacity building. Relevant international conventions and agreements Pakistan is a member/signatory to most key relevant agreements and an active contributor to some organisations. Capacity and resources limit full participation and progress in compliance with some agreements. Pakistan has not yet ratified the Cartagena Protocol on Biosafety. Strengths and weaknesses of the Pakistan's current system for SPS control over imports Strengths in SPS controls include: Key elements of an effective legal framework and commitment to international obligations. Pakistan has a commendable commitment to WTO and to upgrading legal and institutional frameworks. Pakistan is a signatory to most key relevant international and regional conventions and agreements. Current (and proposed) laws and ordinances cover many of the critical elements of import control and reflect key commitments to international conventions and agreements. Systems for entry approval (Import permit/Release Order) and regulation are in place and administered. GoP maintains dialogue with all land border countries and key trading partners on matters relating to border security, biosecurity and import control. Regular trading partners are familiar with and generally satisfied with the components of the system and the time/costs involved in delivering imports. Biosecurity: basic risk and compliance assessment (Quarantine certification) requirements are generally being met. Global and regional security concerns have heightened GoP, international trading partner and donor agency attention to the improvement of port of entry - 3 - access and security, and priorities for immediate attention have been established. GoP recognises the need for investment in training and capacity building. Existing institutional frameworks, international agency support systems and the education sector provide a sound base for strengthening training and capacity building. GoP

has a commitment to enhancing stakeholder access to information. Basic information on the system, relevant laws, import regulations and charges and clearance procedures are reasonably accessible. A web-based one-stop portal is needed. Internet connectivity and access to www is growing and mobile phone connectivity is high. Weaknesses in SPS controls include overarching weaknesses, administrative systems and operational effectiveness, mechanisms for motivating and rewarding staff, coordination between different regulatory agencies. Inadequate integration of the program of reform for laws (import/export), action plans for compliance to international obligations are needed. Some key elements of legislation (e.g. food laws) are provincial laws. Implementation strategies are needed to progress from 'law' to enforce regulatory/inspection requirements. The pace of review, progression from review to revision, and passing of new laws can be slow. Stakeholder consultation particularly at an early stage needs strengthening. Currently it can be inadequate. Pakistan lacks the resources and capacity to fully implement all international obligations or to actively participate in international benchmark setting negotiations. Systems for entry approval (Import permit/ RO) and regulation have deficiencies. With a long land border, with inhospitable terrain in some regions, and many traditional crossing points, it is difficult to control all import entry. Cross border smuggling is also a serious problem. Several road entry points operate limited hours. Biosecurity: risk and compliance assessment needs critical attention. An old and weak regulatory framework leaves gaps that represent biosecurity risks. Inadequate infrastructural capacity and competence hampers effectiveness and full compliance with SPS. Staffing levels are inadequate and coverage of plant quarantine and seed certification not available at several entry points. The system is possibly too complex and slow to respond to emergent threats. Access to data on import risks by commodity and risk alerts is inadequate. Capacity and coverage of risk assessment and emergency action plans is inadequate. Staffing levels at entry points does not match relative inspection/clearance requirements for some entry points. Training and capacity building is not co-ordinated and does not reach operational staff. Basic training and access to refresher courses for plant quarantine, standards and food safety and seed certification are inadequate. Planning and curriculum development are needed to strengthen technical and tertiary training in all aspects of SPS/WTO. Capacity building amongst the farming and trading sectors is also needed. Information is not accessible enough for stakeholders. It is difficult for Pakistan importers and overseas exporters to obtain complete information on import requirements and processes. Quarantine and seed certification staff does not have adequate access to information needed to do their jobs effectively.

### **Risk Assessment:**

As part of managing the health and safety of your business, you must control the risks in your workplace. To do this you need to think about what might cause harm to people and decide whether you are taking reasonable steps to prevent that harm. This is known as risk assessment and it is something you are required by law to carry out. If you have fewer than five employees you don't have to write anything down. A risk assessment is not about creating huge amounts of paperwork, but rather about identifying sensible measures to control the risks in your workplace. You are probably already taking steps to protect your employees, but your risk assessment will help you decide whether you have covered all you need to. Think about how accidents and ill health could happen and concentrate on real risks – those that are most likely and which will cause the most harm. For some risks, other regulations require particular control measures. Your assessment can help you identify where you need to look at certain risks and these particular control measures in more detail. These control measures do not have to be assessed separately but can be considered as part of, or an extension of, your overall risk assessment. One of the most important aspects of your risk assessment is accurately identifying the potential hazards in your workplace. A good starting point is to walk around your workplace and think about any hazards. In other words, what is it about the activities, processes or substances used that could injure your employees or harm their health? There are some hazards with a recognised risk of harm, for example working at height, working with chemicals, machinery, and asbestos. Depending on the type of work you do, there may be other risks that are relevant to your business.

Then think how employees (or others who may be present, such as contractors or visitors) might be harmed. Ask your employees what they think the hazards are, as they may notice things that are not obvious to you and may have some good ideas on how to control the risks. For each hazard you need to be clear about who might be harmed – it will help you identify the best way of controlling the risk. That doesn't mean listing everyone by name, but rather identifying groups of people. Some workers may have particular requirements, eg new and young workers, migrant workers, new or expectant mothers, people with disabilities, temporary workers, contractors, homeworkers and lone workers. Think about people who might not be in the workplace all the time, such as visitors, contractors and maintenance workers. Take members of the public into account if they could be harmed by your work activities. If you share a workplace with another business, consider how your work affects

others and how their work affects you and your workers. Talk to each other and make sure controls are in place. Ask your workers if there is anyone you may have missed.

Having identified the hazards, you then have to decide how likely it is that harm will occur, ie the level of risk and what to do about it. Risk is a part of everyday life and you are not expected to eliminate all risks. What you must do is make sure you know about the main risks and the things you need to do to manage them responsibly. Generally, you need to do everything 'reasonably practicable' to protect people from harm. This means balancing the level of risk against the measures needed to control the real risk in terms of money, time or trouble. However, you do not need to take action if it would be grossly disproportionate to the level of risk. Your risk assessment should only include what you could reasonably be expected to know – you are not expected to anticipate unforeseeable risks. Look at what you're already doing and the control measures you already have in place. Ask yourself: Can I get rid of the hazard altogether? If not, how can I control the risks so that harm is unlikely? Some practical steps you could take include: trying a less risky option; preventing access to the hazards; organising your work to reduce exposure to the hazard; issuing protective equipment; providing welfare facilities such as first aid and washing facilities; involving and consulting with workers. Improving health and safety need not cost a lot. For instance, placing a mirror on a blind corner to help prevent vehicle accidents is a low-cost precaution, considering the risks. Failure to take simple precautions can cost you a lot more if an accident does happen. Involve your workers, so you can be sure that what you propose to do will work in practice and won't introduce any new hazards. If you control a number of similar workplaces containing similar activities, you can produce a model risk assessment reflecting the common hazards and risks associated with these activities. You may also come across model assessments developed by trade associations, employers' bodies or other organisations concerned with a particular activity. You may decide to apply these model assessments at each workplace, but you can only do so if you: satisfy yourself that the model assessment is appropriate to your type of work; adapt the model to the detail of your own work situations, including any extension necessary to cover hazards and risks not referred to in the model.

Make a record of your significant findings – the hazards, how people might be harmed by them and what you have in place to control the risks. Any record produced should be simple and focused on controls. If you have fewer than five employees you don't have to write anything down. But it is useful to do this so you can review it at a later date, for example if something changes. If you have five or more employees you are required by law to write it down. Any paperwork you produce should help you to communicate and manage the risks in your business. For most people this does not need to be a big exercise – just note the main points down about the significant risks and what you concluded. An easy way to record your findings is to use our risk assessment template. When writing down your results keep it simple, for example 'fume from welding – local exhaust ventilation used and regularly checked'. A risk assessment must be suitable and sufficient, ie it should show that: a proper check was made; you asked who might be affected; you dealt with all the obvious significant hazards, taking into account the number of people who could be involved; the precautions are reasonable, and the remaining risk is low; you involved your employees or their representatives in the process. Where the nature of your work changes fairly frequently or the workplace changes and develops (eg a construction site), or where your workers move from site to site, your risk assessment may have to concentrate more on a broad range of risks that can be anticipated. They show you what a completed risk assessment might look like for your type of workplace. You can use these as a guide when doing your own. The site also has online risk assessment tools, to help employers complete and print off their own records. If your risk assessment identifies a number of hazards, you need to put them in order of importance and address the most serious risks first. Identify long-term solutions for the risks with the biggest consequences, as well as those risks most likely to cause accidents or ill health. You should also establish whether there are improvements that can be implemented quickly, even temporarily, until more reliable controls can be put in place. Remember, the greater the hazard the more robust and reliable the measures to control the risk of an injury occurring will need to be. Few workplaces stay the same. Sooner or later, you will bring in new equipment, substances and procedures that could lead to new hazards. So it makes sense to review what you are doing on an ongoing basis, look at your risk assessment again and ask yourself: Have there been any significant changes? Are there improvements you still need to make? Have your workers spotted a problem? Have you learnt anything from accidents or near misses? Make sure your risk assessment stays up to date.

### **Overview of biosecurity risk assessment methodology:**

Risk is defined by likelihood and consequences. For biosecurity, likelihood is defined as the likelihood of theft of a biological agent from a facility by a notional adversary, the likelihood of successful malicious release which leads to exposure/infection and the severity of the consequence of a successful malicious release with the agent. The assessment process is broken into components: Evaluate the biological agents that exist at the facility. Define specific or notional adversaries which pose a threat to the agents. Evaluate the facility processes and

procedures. Evaluate the in place biorisk mitigation measures. Within each component are several criteria and sub-criteria that are scored independently. These scores are weighted and then rolled up to provide the overall consequence and likelihood score. This method is based on a Multi Criteria Decision Analysis (MCDA) scheme, quantifying the various aspects of biorisk using qualitative definitions. The final results show the relative risk of agents at the given facility, and give program management a mechanism to determine risks that are unacceptable. This scheme can aid management in allocating resources to mitigate facility biorisks; or to assess current biorisk program management effectiveness. This model is not intended to provide a formal quantitative assessment of absolute risk but, rather provide a structured method for the comparison of the relative risks posed by laboratory practices and by biological agents. There are numerous approaches to structured risk assessment and decision analysis; multi-criteria decision analysis (MCDA) is one of these methods. MCDA has been identified as a scientifically sound method for decision analysis and has been extensively validated for use in risk analysis. "Research on quantitative decision making has proceeded from the study of decision theory founded on single criterion decision making towards decision support for more realistic decision making situations with multiple, often conflicting, criteria, and more than one decision-maker. In particular, MCDA stands out as a promising category within decision support methods."<sup>1</sup> Linkov<sup>2</sup> and others have advocated the use of a multi-criteria decision analysis as part of a traditional risk assessment in situations where there is a limited set of empirical data and a high level of uncertainty. MCDA is a robust discipline and is useful in illustrating and justifying decisions. MCDA has been accepted by the risk community as a process for conducting structured risk assessments, focusing on areas with limited detailed knowledge, and where information may vary with time. In addition to the structure, MCDA also offers a transparent method for conducting the risk assessment as it can help in quantifying and communicating the risks and support decision-makers choices on risk management. MCDA provides a mechanism to combine multiple information sources including those based upon expert judgment to assess risks. <sup>3</sup> The basic structure of MCDA models is to define the relevant criteria which define the problem(s) to be addressed, attach numerical measurements and relative importance to the criteria, and to combine the numerical values to arrive at a relative ranking.<sup>4</sup> In MCDA there are several mathematical models which define how the numerical measurements and relative importance rankings are determined. Likewise, combining of measurements varies from model to model. The method used in this analysis is based upon a weighted sum algorithm which is one of the most common approaches. This method combines all the criteria and weights into a single score (A) by summing all the weighted numerical values ( $a_{ij}w_j$ ). When using MCDA for risk analysis, the resulting score of the weighted sum is a component in the creation of the relative risk ranking. In this methodology, the weighted sum is used to define the likelihood and the consequences independently. These two values are combined to create the relative risk characterization.

The BioRAM model, being a risk assessment model, calculates both the likelihood of successful malicious use of a biological agent and the consequences of this use. The BioRAM model includes criteria which evaluate an agent's biological properties as they influence the likelihood of successful use. These include the potential routes of transmission, communicability, and natural stability. These criteria are evaluated using an absolute scale, with zero being the absence of ability for successful use and four being the worst case. Consequences are modelled based on the impact of disease to a human host (for human and zoonotic agents, the consequence model for animal diseases is slightly different) and the ability to mitigate the consequences of a malicious release. Additionally, socioeconomic impacts are also captured. As with the likelihood, these criteria are scored on an absolute scale with zero being the absence of consequence and four defining the worst credible consequence. In reviewing the use of BioRAM as a support tool for the US Select Agent Program, 49 agents from the CDC (and overlap) list were evaluated by use of open source<sup>5</sup> literature review. The results of evaluation highlighted several agents as having both notably higher likelihood and consequence (or overall risk) relative to the other agents. These results correlated very closely with the FESAP recommended Tier 1 agents. Specifically this group included, smallpox(*Variola major*) virus, *Burkholderia mallei*, *Bacillus anthracis*, *Burkholderia pseudomallei*, *Alastrim* (*Variola minor*) virus, *Yersinia pestis*. Additionally, the reconstituted 1918 Spanish Flu virus, which is not included in the FESAP Tier 1 agent list, fell in to this high risk area. Both of the recommended Tier 1 hemorrhagic fever viruses (*Marburg* and *Ebola*) were on the border. These agents could have significant consequences, but the potential for successful malicious use was lower than the other agents in the top tier in this model. The main drivers for their lower likelihood, as compared to the other agents, include their lack of environmental stability and the limited ability for transmission. This evaluation also highlighted several agents as being relatively a lower risk than the other agents on the CDC US Select Agent list.

The agents which were modelled and fell into the overall lower risk characterization include: *Cercopithecine herpesvirus 1 (Herpes B virus)*, *Coccidioides posadasii/ Coccidioides immitis*, *Eastern Equine Encephalitis virus*, Central European Tick-borne encephalitis, Venezuelan Equine *Encephalitis virus*, Bovine Spongiform Encephalitis, *Clostridium perfringens* epsilon toxin, shiga toxin and the shiga-like ribosome inactivating proteins, and the T-2 toxin, several of the haemorrhagic fever viruses, other encephalitis viruses, toxins, the rickettsia, and monkeypox. It should be noted that the majority of these agents were clustered toward the center

of the model, which when confidence intervals are added these agents would be characterized as a moderate risk and comparable to the other agents. *Smallpox virus (Variola Major Virus)* *Burkholderia mallei* *Bacillus anthracis* *Burkholderia pseudomallei* *Alastrim (Variola Minor Virus)* Reconstruction of the 1918 flu Yersinia pestis Marburg virus Ebola Virus included on the US Select Agent list. However, there are several very distinct lower risk agents; these include the T-2 toxin, Bovine Spongiform Encephalitis, the *tick-borne encephalitis viruses*, *Menangle virus*, and the *Herpes B virus*. The nature of the BioRAM model demonstrates utility in evaluation of bioscience laboratories to characterize the biosecurity risk. This model can be used in reviewing laboratories to determine compliance to the US Select Agent Regulation. Careful consideration to how each criterion is scored should be considered by the evaluator to ensure a laboratory is not vastly outside of compliance in one area. Additionally, the regulations do not include any considerations for the biological properties of the agent's (an agent is either on or off the list) the agent's properties which influence the likelihood of successful misuse or the consequences of the misuse must be evaluated separately from the laboratory. The agent portion of the model supports the tiring of the US Select Agent and demonstrates complementary results to the FESAP recommendations.

### **Evaluate the pathogens and toxins:**

We used eleven criteria for the evaluation of human and zoonotic pathogens. It is very hard to find in available literature all the data for the most important criterion, criterion number 1 - agents or toxins known to have been developed, produced, stockpiled or used as weapons. Therefore, we have made our best estimate for this. The key for producing large-scale respiratory infections is to generate an aerosol of suspended microscopic droplets, each droplet containing one to thousands of bacterial or virus particles. A high level of dissemination or large-scale contamination or coverage of a large area with aerosol for respiratory exposure plays the main role in evaluation of particular agent or toxin. The existence of immunization and appropriate treatment against a particular agent is inversely proportional to the likelihood that the agent will be used. There are no effective prophylaxes or therapies for the majority of listed agents and toxins, if they are used as biological and toxin warfare agents. A full vaccination series for most diseases takes at least three months and in some cases up to one year. Hence, it is difficult to imagine how a mass-vaccination would be effective against more than one disease.

The evaluation of agents and toxins according to existing criteria assumes all criteria have equal status. It may be that the criteria should be weighted. The criteria we used for evaluating these biological agents and toxins are based on the characteristic outbreaks of infectious diseases in "natural" forms. Genetically engineered and modified bacteria and viruses present a difficult problem. New criteria reflecting new characteristics of bacterial and viral strains enhanced for infectivity, transmissibility, virulence and antibiotic resistance should be inserted. Lethality alone is not an appropriate criterion on which to base a toxin's potential as an agent. Therefore, we included those toxins that act primarily as incapacitating agents, because these toxins have high potencies and represent a significant trend for the future. For example, Staphylococcal enterotoxin B (SEB), a so-called super-antigen, is one of the most potent agents for incapacitating because it can cause illness at extremely low doses (although lethal doses are relatively high). Trichothecene-Mycotoxins, Batrachotoxins and Brevetoxins can be included in this list. If we included only those lethal toxins, we would be underestimating the number and potential of toxins as agents. It is very hard to make a final decision on criteria, and, hence, on the final list of agents and toxins for the future needs of Protocol to the BTWC based on the current criteria.

The lists and criteria for agents and toxins should be well studied. The lists are not exhaustive; they do not exclude those unlisted microbial or other biological agents or toxins, which potentially can be used as weapons or vectors (such as pests, arthropods and helminthes). The lists of human, animal and plant pathogens do not include live-attenuated strains, which have been registered in official culture collections or are internationally recognized as such. Progress in modern genetics presents newer possibilities that have not been included, such as microorganisms carrying nucleic acid sequences coding for pathogenic properties of listed agents and toxins and nucleic acid sequences coding for toxins. Any State Parties of the BTWC may propose modifications to the lists. The Executive Council of the OPBTW shall review such proposed modifications to the list of agents and toxins. Any changes to the list shall be made in accordance with Articles III. and XIV. of the Protocol. In reviewing the lists of agents and toxins the Executive Council shall consider current criteria, as well as:

- Scientific and technological developments that may affect the potential of individual agents and toxins for use as weapons.
- Effects of potential inclusion or exclusion of an agent or toxin in the list on scientific and technical research and development.

**Evaluate the potential adversaries:**

According to Alkin and Christie, an adversary approach is one which reflects a valuing orientation. This approach developed in response to the dominant objectifying approaches in policy evaluation and is based on the notions that: 1) no evaluator can be truly objective, and, 2) no evaluation can be value-free. To this end, the approach makes use of teams of evaluators who present two opposing views (these teams are commonly referred to as adversaries and advocates). These two sides then agree on issues to address, collect data or evidence which forms a common database, and present their arguments. A neutral party is assigned to referee the hearing, and is expected to arrive at a fair verdict after consideration of all the evidence presented. There are many different models for adversary evaluations, including judicial, congressional hearing and debate models.

**Evaluate scenarios:**

Scenarios of specific adversaries attempting to steal and misuse specific pathogens or toxins. Can screen assets that do not present sufficient risk? Are they non-pathogenic and LMUR? Can screen adversaries for certain scenarios because they have no interest in biological agents or have insufficient means.

**Characterize the risk:**

Grouping of different risks according to their estimated cost or likely impact, likelihood of occurrence, counter measures required, etc. Credit risk. It is classified according to the likelihood of the collection of accounts receivable.

1. Corporate: Component of risk assessment in which risks are ranked according to the extent and severity of their potential economic, environmental, financial, social, or other consequences.

2. Food industry: According to FAO/WHO, it is the integration of hazard identification and exposure assessment into the estimation of risk, and is similar to the definition of risk assessment. Other organizations suggest inclusion of determination of causative factors, contributing to the risk from a particular food product, to facilitate the action(s) required to effectively reduce the risk.

**Risk reduction:**

Over the past 30 years, there has been a major shift in how emergencies and crises are managed. More emphasis used to be placed on humanitarian response and relief activities – national or international – with little attention given to strategies and actions in place prior to disasters that can mitigate the effects of these events on communities and preserve lives and assets. It is becoming increasingly clear that while humanitarian efforts remain important and need continued attention, community-based risk reduction and emergency preparedness programmes are critical for reducing the effects of emergencies, disasters and other crises, and thus essential for the attainment and protection of sustainable development. Emergency preparedness has traditionally focused on stockpiling relief goods and providing urgent services to meet the public's basic needs. In most countries political commitment and financial and human resources are concentrated overwhelmingly on these short-term emergency contingencies. While building up capacities for humanitarian response continues to be a priority for all countries, it is now widely believed (perhaps influenced by the severity and frequency of disasters and conflicts in the past decade) that more should be done to reduce the social, economic and human consequences of these emergencies. This translates into a need for placing much greater attention on the implementation of proactive strategies and a call for a more comprehensive approach to building national capacities in emergency preparedness and response as well as in risk reduction, focusing on those communities most at risk. Preparedness is essential in securing the right to life with dignity. States bear the primary responsibility for protecting their populations and ensuring a dignified life but the modern approach to preparedness extends well beyond those traditionally involved in relief efforts, such as civil protection forces, emergency offices and humanitarian organizations. Communities need to work closely with local authorities, public organizations and the relevant section of the private sector, in order to strengthen their own capacities to prepare for and manage the consequences of various risks. The health impact of emergencies and crises can be substantially reduced if both national and local authorities and communities in high-risk areas are well prepared and are able to reduce the level of their vulnerabilities and the health implications of their risks. International initiatives by the humanitarian community are geared increasingly towards supporting this objective. The challenge is to put in place systematic capacities such as legislation, plans, coordination mechanisms and procedures, institutional

capacities and budgets, skilled personnel, information, and public awareness and participation that can measurably reduce future risks and losses.

### **Components of biosecurity:**

Biosecurity is a strategic and integrated approach. It encompasses the policies / regulatory framework, analyzing and managing risk. Factors influencing biosecurity are globalization, new agricultural products and technologies, increase trade in food, travelling across borders, advances in communication, greater public attention to biodiversity, shift from country independence to interdependence, less technical and operational resources and some countries are dependent on food import. Components of biosecurity are physical security, personnel security, material control and accountability, transfer security and information security.

### **Physical security:**

Physical security describes security measures that are designed to deny unauthorized access to facilities, equipment and resources, and to protect personnel and property from damage or harm (such as espionage, theft, or terrorist attacks). Physical security involves the use of multiple layers of interdependent systems which include CCTV surveillance, security guards, protective barriers, locks, access control protocols, and many other techniques.

### **Physical security elements:**

Physical barriers such as fences, walls, and vehicle barriers act as the outermost layer of security. They serve to prevent, or at least delay, attacks, and also act as a psychological deterrent by defining the perimeter of the facility and making intrusions seem more difficult. Tall fencing, topped with barbed wire, razor wire or metal spikes are often emplaced on the perimeter of a property, generally with some type of signage that warns people not to attempt to enter. However, in some facilities imposing perimeter walls/fencing will not be possible (e.g. an urban office building that is directly adjacent to public sidewalks) or it may be aesthetically unacceptable (e.g. surrounding a shopping center with tall fences topped with razor wire); in this case, the outer security perimeter will be defined as the walls/windows/doors of the structure itself. Another major form of deterrence that can be incorporated into the design of facilities is natural surveillance, whereby architects seek to build spaces that are more open and visible to security personnel and authorized users, so that intruders/attackers are unable to perform unauthorized activity without being seen. An example would be decreasing the amount of dense, tall vegetation in the landscaping so that attackers cannot conceal themselves within it, or placing critical resources in areas where intruders would have to cross over a wide, open space to reach them.

Security lighting is another effective form of deterrence. Intruders are less likely to enter well-lit areas for fear of being seen. Doors, gates, and other entrances, in particular, should be well lit to allow close observation of people entering and exiting. When lighting the grounds of a facility, widely-distributed low-intensity lighting is generally superior to small patches of high-intensity lighting, because the latter can have a tendency to create blind spots for security personnel and CCTV cameras. It is important to place lighting in a manner that makes it difficult to tamper with (e.g. suspending lights from tall poles), and to ensure that there is a backup power supply so that security lights will not go out if the electricity is cut off. Alarms are only useful if there is a prompt response when they are triggered. In the reconnaissance phase prior to an actual attack, some intruders will test the response time of security personnel to a deliberately tripped alarm system. By measuring the length of time it takes for a security team to arrive (if they arrive at all), the attacker can determine if an attack could succeed before authorities arrive to neutralize the threat. Loud audible alarms can also act as a psychological deterrent, by notifying intruders that their presence has been detected. In some jurisdictions, law enforcement will not respond to alarms from intrusion detection systems unless the activation has been verified by an eyewitness or video.

### **Integration with lab biosecurity:**

Integration with lab biosecurity focus on awareness to change the current culture, clarify terminology, helps in the development of training strategies, secure commitment to stakeholders and increase capacity. Lab biosecurity supports lab biosafety; they work as coordinated and complementary system. Biosafety cannot provide sufficient biosecurity so biosecurity policies have to be developed. Conflicts between biosafety-biosecurity has to be resolved. Good lab biosecurity systems enforce and strengthen biosafety systems. Security measures should be considered as routine part.

### **Personal security:**

Personnel security is a system of policies and procedures which seek to manage the risk of staff (permanent, temporary or contract staff) exploiting, or intending to exploit, their legitimate access to an organisation's assets or premises for unauthorised purposes. Although many organisations regard personnel security as an issue resolved during the recruitment process, it is a discipline that needs to be maintained throughout a member of staff's time in employment. This includes robust pre-employment screening, effective line management, employee welfare, clear lines of communication, and a strong security culture. It should also include a formal process for managing staff leaving the business. When applied consistently, personnel security measures not only reduce operational vulnerabilities, they can also help build a hugely beneficial security culture at every level of an organisation. Robust personnel security helps organisations to employ reliable people; minimise the chances of staff becoming unreliable once they have been employed; and detect suspicious behaviour and resolve security concerns once they emerge.

### **Personal security elements:**

What your employees do and say online, or how they use digital devices, can make them and your organisation vulnerable to security threats if they are not careful. Some of the security vulnerabilities can be obvious, such as posting or sharing confidential organisational information that puts staff, processes or assets at risk. Others may be less so, such as search engines storing search history or smart phones tracking geolocation data which can be exploited by those with malicious intent. How your employees behave in the workplace can have a real impact on the security risks and vulnerabilities your organisation faces. Security breaches of any kind can result in loss of revenue, productivity or share price; they can damage an organisation's reputation; they might result in confidential data being leaked; or worse, they can result in physical harm to staff members or the public. When external visitors (e.g. non-cleared individuals including foreign liaison, commercial competitors and the media) are due to visit a sensitive work location, we recommend the creation of a security plan in order to mitigate the security risks. Most organisations have multi-tiered supply chains which are likely to be both upstream (supply) (i.e. between the organisation and the organisation's suppliers or suppliers' suppliers) and downstream (demand) (i.e. between the organisation and its market). Vulnerabilities in these supply chains can introduce vulnerabilities to the organisation itself and to its assets. Those vulnerabilities can expose the organisation and its assets to risk from national security threats, principally terrorism, hostile cyber-attacks by foreign states and large scale cyber-crime. As individuals and organisations improve their physical and electronic defences, those wishing to gain access to premises or acquire sensitive information may attempt to exploit people within the organisation who already have legitimate access.

Social engineering is the process whereby a third party can gain that information or access. Remote working, whether it is working from home, on the move or in clients' or satellite offices, is become ever more commonplace, growing to an estimated 20 per cent of the working population. A critical component of any security system is the security staff, specifically guard forces, such as those who undertake patrols, guard entrance points, and carry out security screening. Motivated, attentive and observant staff in these roles can form a highly-effective deterrent presence and final line of defence where other interventions (e.g. electronic security access) have failed. Conversely, demotivated staff that does not perform their role effectively can be a single point of failure within a security system. Developing a security culture within an organisation is about encouraging staff to respect common values and standards towards security whether they are inside or outside the workplace. Pre-employment screening is the foundation of good personnel security. It seeks to verify the credentials of those you are seeking to grant access to your sites and information, and to check that they meet preconditions of employment (e.g. that they are legally permitted to take up an offer of employment). Ongoing personnel security is the protection of an organisation's assets from unauthorised use by employees, and the identification and management of employees who may pose a security risk.

### **Material control and accountability:**

In the early years of the nuclear age all special nuclear material (SNM) was owned by the Federal government. It was a valuable commodity and the Atomic Energy Commission (AEC) had a financial duty to keep track of the material as it was lent to various scientists and organizations for their use. To accomplish this, procedures for tracking and accounting for the SNM, much as a bank account for money, were established. Unlike money, however, the amount of SNM cannot generally be counted but must be determined by weight and assay, as with precious metals such as gold and silver. The government no longer owns all SNM. The Department of Energy, a successor to the AEC, owns SNM and still has some on loan to other agencies and companies; however, the NRC, which inherited the regulatory functions of the AEC and is independent of DOE, owns no SNM. Yet the NRC still uses the procedures that began as financial and materials management tools, with modifications, for

verification that SNM intended for peaceful use has not been stolen or diverted to unauthorized users. In support of its policy of nonproliferation of nuclear weapons and the Non-Proliferation Treaty, the U.S. Government has voluntarily entered into an Agreement with the International Atomic Energy Agency (IAEA) to have a national system of accounting for source and special nuclear materials. This information system is called the Nuclear Materials Management and Safeguards System (NMMSS). NMMSS contains current and historical data on inventories and transactions involving source and special nuclear materials within the U.S. and on all exports and imports of that material. NMMSS is jointly funded by DOE and NRC and operated under a contract to DOE. Material control means the use of control and monitoring measures to prevent or detect loss when it occurs or soon afterward. Material accounting is defined as the use of statistical and accounting measures to maintain knowledge of the quantities of SNM present in each area of a facility. It includes the use of physical inventories and material balances to verify the presence of material or to detect the loss of material after it occurs, in particular, through theft by one or more insiders.

#### **Material control and accountability elements:**

An effective material control program element ensures that nuclear materials are properly protected and that they are not removed from their authorized location without approval or timely detection. The objectives of a nuclear material control system are to: detect, assess, and prevent unauthorized access to nuclear material. Detect, assess, and communicate alarms to response personnel in time to impede unauthorized use of nuclear material. Provide loss detection capability for nuclear material, and when not in its authorized location, be able to provide accurate information needed to assist in locating the material in a timely manner. The material containment and surveillance program in conjunction with other security program elements must have the capability to detect, assess, and respond to unauthorized activities and anomalous conditions/events. In coordination with security organizations, material control measures, assure that appropriate protection and controls are applied to nuclear materials, according to the quantity and attractiveness of the material.

#### **Transport security:**

Infectious substances and toxins are defined as dangerous goods. Transportation security include: training, security awareness training, specific training as appropriate, written security plan, based on assessment of transportation security risks, address personnel security, unauthorized access, en route security.

#### **Transport security elements:**

Transport security is the movement of biological materials from restricted areas that can occur within the country/even across borders. There are two elements of transport security; these are internal transport and external transport. Internal transport is the movement from / to restricted area within facility. It may involve personnel from labs for shipping, receiving, disposal areas. External transport is the movement of material from one facility to another. This involves commercial carriers able to move frozen materials. This need to be cost-effective. Infectious materials are included in category B such as cultures for this triple packaging system is required.

The triple packaging system continues to apply, including for local surface transport. Testing documents are not required, however. It may be possible to source packaging's locally rather than finding an authorized supplier, provided that the packaging manufacturer and the shipper can comply fully with the requirements of P650 (see Annex 4; Figure 9). As for P620, there is no comprehensive list of suppliers of packaging's that comply with Packing Instruction P650. However, an Internet search using a suitable international or national search engine usually provides appropriate information, as well as access to national regulations. Search phrases such as "UN packaging" and "UN infectious substance packaging" produce extensive results. Carriers and forwarding agents should also be able to supply details of local suppliers or local companies that can provide such information. To ensure correct preparation for transport, packaging manufacturers and subsequent distributors shall provide clear instructions to the consignor or persons preparing packages (e.g. patients) on how the packaging should be filled and closed. For surface transport there is no maximum quantity per package. For air transport: no primary receptacle shall exceed 1 l (for liquids) or the outer packaging mass limit (for solids) the volume shipped per package shall not exceed 4 l or 4 kg. These quantities exclude ice, dry ice or liquid nitrogen when used to keep specimens cold.

#### **Information security:**

Information Security Policy /ISP/ is a set of rules enacted by an organization to ensure that all users or networks of the IT structure within the organization's domain abide by the prescriptions regarding the security of data stored digitally within the boundaries the organization stretches its authority.

An ISP is governing the protection of information, which is one of the many assets a corporation needs to protect. The present writing will discuss some of the most important aspects a person should take into account when contemplates developing an ISP. Putting to work the logical arguments of rationalization, one could say that a policy can be as broad as the creators want it to be: Basically, everything from A to Z in terms of IT security, and even more. For that reason, the emphasis here is placed on a few key elements, but you should make a mental note of the liberty of thought organizations have when they forge their own guidelines.

### **Information security elements:**

Institutions create ISPs for a variety of reasons:

- To establish a general approach to information security
- To detect and forestall the compromise of information security such as misuse of data, networks, computer systems and applications.
- To protect the reputation of the company with respect to its ethical and legal responsibilities.
- To observe the rights of the customers; providing effective mechanisms for responding to complaints and queries concerning real or perceived non-compliances with the policy is one way to achieve this objective.

ISP should address all data, programs, systems, facilities, other tech infrastructure, users of technology and third parties in a given organization, without exception.

An organization that strive to compose a working ISP needs to have well-defined objectives concerning security and strategy on which management have reached an agreement. Any existing dissonances in this context may render the information security policy project dysfunctional. The most important thing that a security professional should remember is that his knowing the security management practices would allow him to incorporate them into the documents he is entrusted to draft, and that is a guarantee for completeness, quality and workability. Simplification of policy language is one thing that may smooth away the differences and guarantee consensus among management staff. Consequently, ambiguous expressions are to be avoided. Beware also of the correct meaning of terms or common words. For instance, “musts” express negotiability, whereas “shoulds” denote certain level of discretion. Ideally, the policy should be briefly formulated to the point. Redundancy of the policy’s wording (e.g., pointless repetition in writing) should be avoided as well as it would make documents long-winded and out of sync, with illegibility that encumbers evolution. In the end, tons of details may impede the complete compliance at the policy level. So how management views IT security seems to be one of the first steps when a person intends to enforce new rules in this department. Furthermore, a security professional should make sure that the ISP has an equal institutional gravity as other policies enacted within the corporation. In cases where an organization has sizeable structure, policies may differ and therefore be segregated in order to define the dealings in the intended subset of this organization.

Information security is deemed to safeguard three main objectives:

- Confidentiality – data and information assets must be confined to people authorized to access and not be disclosed to others;
- Integrity – keeping the data intact, complete and accurate, and IT systems operational;
- Availability – an objective indicating that information or system is at disposal of authorized users when needed.

### **Biosafety rules for a virology lab:**

The key elements for the establishment of a virology laboratory and diagnostic services are: (1) Physical infrastructure (2) Human resources (3) Equipment and supplies

Virus isolation and a number of methods for detection of viral antigens, nucleic acids, and antibodies (serology) are the core repertoire of techniques used in a diagnostic virology laboratory. Virus isolation using cell culture is always performed in designated virology laboratories although the other methods may be performed in diverse laboratory settings such as clinical microbiology, serology, blood bank, clinical chemistry, pathology or molecular biology. In future, the likelihood of viral diagnostic testing being conducted outside the traditional virology laboratory setting is likely to increase as rapid diagnostic techniques based on immunologic and nucleic acid detection methods gain greater acceptance. A diagnostic virology laboratory should ideally be located in a separate, multistoried building. If this is not possible, it must be separated from other areas and facilities that are open to unrestricted staff movement within the building. It is therefore ideal to have the virology laboratory situated at the end of a corridor in a building where other laboratories are located. This would restrict entry of visitors, prevent contamination and facilitate maintaining biosafety standard. A diagnostic virology laboratory should be adequately staffed. The minimum staff requirements for a diagnostic virology laboratory should include: A qualified virologist possessing a postgraduate qualification in virology with three to five years experience in diagnostic virology who will be the chief of the laboratory. This officer will have overall responsibility for activities of the laboratory and will supervise all the staff working at the centre. In addition, this officer will be directly responsible for reporting results of the various diagnostic assays performed in the laboratory. Two junior microbiologists possessing a Master's degree in Medical Microbiology with one to two years experience in diagnostic virology. These microbiologists will be responsible for the day-to-day functioning of the diagnostic laboratory such as supervision of technical staff who carry out the various diagnostic tests, stock management and procurement of lab supplies and diagnostic kits, quality control and quality assurance. Two laboratory technologists possessing a graduate degree in science with a diploma in Medical Laboratory Technology (one to be trained in cell culture and virus isolation methods and the other to be trained in serology). The technicians will be responsible for specimen processing, testing, laboratory safety, maintenance of laboratory records and media preparation. One or two laboratory supportive staff: With this minimum staff, routine diagnostic assays for several viral diseases can be performed. However, this would depend upon the load of clinical specimens and the range of diagnostic assays that the laboratory wishes to engage in. The most important aspect of human resource management in a virology laboratory is to ensure that roles and responsibilities of all the staff are clearly outlined and provide periodic training to upgrade the knowledge and skills of the laboratory personnel. This would ensure that the laboratory is abreast with contemporary diagnostic methodology as well as maintain quality in the services rendered. The virology laboratory should be provided with adequate equipment which should take into account certain general principles, i.e. it should be: designed to prevent or limit contact between the operator and the infectious material (e.g. biosafety cabinets, electronic pipetting aids, etc.) constructed of materials that are impermeable to liquids, resistant to corrosion and meet structural requirements. Should be free of sharp edges, burrs and unguarded moving parts. Designed, constructed and installed to facilitate simple operation and provide for ease of maintenance, cleaning, decontamination and certification testing. Glassware and other breakable materials should be avoided wherever possible.

### **Types of fire extinguishers:**

Types of fire are:

- Class A: wood, paper, fabric, cloth, trash and plastics
- Class B: flammable liquids-petroleum oil, paint, gasoline
- Class C: energized electrical equipments
- Class D: metal/Class K: cooking oil, grease

Types of fire extinguishers are:

- water and foam -class A - separate oxygen
- carbon dioxide- class B and C - separate oxygen and heat
- dry chemical - class A, B, C- interrupt chemical reaction
- wet chemical-class K – remove heat
- clean agents-class A, B and C (halogens) interrupt chemical reaction
- water mist- class A, remove heat

**Fire Exits:**

All doors on escape routes leading towards a final exit should be quick and easy to open without the need for a key. In most situations this is the case; for instance, you simply operate the door handle of the door leading from an office and pass through. In the case of a hotel, while a key is required to access a bedroom, it is only necessary to operate the door handle to get out. However, the final exit door of a building frequently presents problems because this type of door requires a higher degree of security while still having to be opened easily from within.

**Fire wardens:**

Fire wardens play an important role in ensuring your business is prepared for a fire emergency. Along with your emergency plan, fire wardens are an important risk control measure to ensure that your workplace is prepared should an emergency situation, potentially a fire, occur.

Key duties of fire wardens include:

- to assist in implementing and improving effective emergency procedures in your workplace;
- to help prevent emergencies by monitoring the adequacy of the fire risk control measures;
- to raise awareness with other staff about the fire hazards that exist in your workplace;
- to instruct workers in how to respond in an emergency;
- to lead the fire drills and real evacuation procedures – they must be familiar with all escape routes and exits from their designated area;
- to ensure all workers are accounted for during an evacuation; and
- to assist all people in the workplace should an emergency occur, including assisting people with special needs, e.g. helping someone in a wheelchair to evacuate.

**Fire assembly area:**

The areas of the Fire Assembly Points are to be large enough to accommodate the expected maximum occupancy of the building being evacuated (staff, visitors and users). Alternative locations of Fire Assembly Points should be considered if possible (recommended minimum of two locations) to allow adequate means of dispersion away from the passage of smoke and/or fire. You would have to take into consideration the type of persons involved and the likelihood of evacuation during inclement weather conditions and during the hours of darkness. The Fire Assembly Points should be safely and easily accessed especially for disabled persons, the elderly and children. The locations of the Fire Assembly Points should be marked with appropriate signs to clearly indicate its location. Note that in town centre/densely occupied regions it may not be possible to mark the location of the Fire Assembly Points by signage in all cases – in these instances; the Fire Assembly Points should be indicated on a publicly displayed diagram at the premises and notable landmarks used to signify the location of the Fire Assembly Points. The areas (i.e. the boundary and area on the ground) of the Fire Assembly Points should where possible be clearly marked and easily identified and should be far enough away from the building to afford protection from the heat and smoke in a fire situation but not so far away as to discourage people from assembling. The Fire Assembly Points should be at places, normally in the open air at ground level, in which persons are in no danger from fire, heat, falling debris/glass and/or smoke. The areas of the Fire Assembly Points are to be in positions that do not put staff, visitors and users of the building at risk from emergency vehicles responding to the incident, or from general/other traffic in the vicinity, therefore the Fire Assembly Points are to be located away from and off the vehicle access routes leading to the building. Ideally the Fire Assembly Points should be located so as not to require the crossing of the road or movement through trafficked areas. Ensure that if your assembly points are a long way away that there is someone around, located in a safe position, to meet and brief the fire service about the incident and to stop people re-entering the building. Good use of Fire Marshalls to direct people to the Fire Assembly Points is important. Fire Assembly Points are temporary gathering areas where it can be immediately determined if everyone is out of the building. Appropriate decisions should be made in regard to continuance of use of the Fire Assembly Points for longer durations. Management and staff should undertake fire drills so that they will be familiar with what should be done in the event of a fire occurring and the locations and use of the Fire Assembly Points.

**National biosafety rules:**

Recognizing the revolutionary economic potential of the new biotechnology in agriculture, health, industry, environment and energy sectors; and appreciating the concerns that mixing of genes from unrelated organisms might create natural imbalance that is not yet adequately understood; and considering the fears that manipulated genes or products thereof if allowed to move around freely in nature, may pose potential hazards; and realizing

the apprehensions that certain transgenic organisms may be harmful or become harmful to economic plants, animals and human being; and discharging the obligations of the Convention of Biological Diversity (CBD) and Cartagena Protocols to which Pakistan is a signatory; the Minister of Environment, constituted a National Biosafety Expert Committee to deliberate on these issues to regulate the safe release of Genetically Modified Organisms (GMOs) and products thereof. 2. Consequent upon extensive deliberations/consultation with all the stakeholders, the national committee concluded that there is a national need to develop biosafety guidelines to control laboratory research, field studies and commercial release of GMOs and products thereof, as have been done by all the developed countries and many developing countries. 3. Accordingly, a set of National Biosafety Guidelines have been developed through a national forum participated by all the stakeholders including the academic institutions, R&D organization, industry, non-government organizations and human right societies. 4. These guidelines have been prepared keeping in view the guidelines prepared by UNIDO, FAO, WHO, UNEP, and all the developed and developing countries with modification to suit our unique and specific socio-economic and geographic environment. 5. The objective of these guidelines is to prevent unintentional negligence leading to misuse and irresponsibility by laboratory workers/researchers as well as the endusers. 6. To define the bounds guidelines/regulatory jurisdiction of these guidelines, biotechnology has been defined as processes using living organisms or parts thereof to make or modify products; and to improve plants, animals, or microorganisms for specific uses. "Recombinant DNA" has been defined as molecules developed outside living cells by joining natural or synthetic DNA segments to DNA that can replicate in a living cell and those DNA molecules that result from the replication of such DNA. For the purposes of these guidelines, regulated material includes all genetically modified materials (DNA & RNA preparations, viroids, viruses, cells and organisms, modified or constructed through genetic engineering), derivatives thereof and wastes or by-products of genetic engineering practices (containing viable organisms or otherwise). 8. The scope of these guidelines embraces all works related to gene manipulation employing recombinant DNA technology for all purposes including the development of transgenic plants, animals and microorganisms; production of vaccines; industrial manufacturing of Genetically Modified Organisms and products thereof, and their release into the environment for field trials as well as for commercial uses. 9. The Guidelines consist of two parts; the first part relates to regulated work in laboratory research and field trials; and the second part deals with procedures for approvals which must be obtained to deregulate the regulated materials to allow their free movement and commercial uses. 10. All regulated laboratory research works are classified into (a) Minimal risk, (b) Low risk, (c) Considerable level of risk and laboratory containment conditions are accordingly prescribed. For regulated fieldwork, comprehensive containment conditions have been prescribed separately for genetically modified microorganisms plants and animals. 11. The mechanism of monitoring and implementation of the proposed guidelines is built on three tiers as specified in the Biosafety Rules, 2005, namely a National Biosafety Committee (NBC); a Technical Advisory Committee (TAC); and Institutional Biosafety Committees (IBCs) at the institutional levels. The NBC headed by the Secretary, Ministry of Environment will be responsible to oversee all laboratory work, field trials and allow commercial releases of GMOs and their products. 12. Enforcement of various clauses of the National Biosafety Guidelines will be administered by the three monitoring implementation bodies, as per legal authority under Clause 7(g) of the Pakistan Environment Protection Act 1997. 13. The IBC may recommend to NBC for awarding exempt status for Laboratory work/field work with genetically modified organisms, if there is sufficient information/grounds available to consider the work as having no risk and NBC may consider for formal approval. 14. Permission for deregulation granted by the NBC can be withdrawn if sufficient technical data/evidence becomes available after the approval, which warrants its deregulation. 15. To standardize processing, separate format for application/proposal for obtaining permission to undertake laboratory genetic manipulation work, field trial and commercialization have been designed. A separate application format has also been designed for the movement of regulated materials and/or exempt status. 17. Instructions for the preparation of applications as well as for its assessment have also been prescribed to streamline and standardize the procedures for assessment and evaluation. 18. These biosafety guidelines have been developed on the basis of technical information presently available and may change in the future as more know-how becomes available. Therefore, revision of these guidelines will be a continuous process. 19. These biosafety guidelines will be supplemented with annexures explaining/elaborating concepts, procedures and protocols required in monitoring/implementation of the guidelines.

#### **Applications of National biosafety rules:**

- manufacture, import and storage of microorganisms
- gene technological products for research
- field trial of GMOs
- import, export, sale and purchase of GMOs

**Establishment of National biosafety committee:**

Federal government establish director general, Pakistan- EPA –secretary. They hold office for term 3 years, frame its own rules and procedures. Secretary, Ministry of Environment, member - Pakistan Atomic Energy Commission, chairperson - institutional biosafety committee, Director-General, department of plant protection, chairman – PARC and representative Ministry of food and agriculture.

**Functions of National biosafety committee:**

- establish standards and procedures for risk assessment
- consider applications for the import, export or commercial release of GMOs – ban
- develop linkages with foreign committees
- cooperate with federal /provisional agencies
- advice of technical advisory committee
- facilitate exchange of technical expertise educate public
- implementation of biosafety guidelines
- inform institutions about new biosafety development
- coordinate efforts between private and government agencies
- certify labs, green / animal houses
- inspection of high-level laboratories
- inspect biosafety levels
- commercial - confidential from the public

**Functions of technical advisory committee:**

Members of technical advisory committee are director-general, EPA, director - national institute of biotechnology, Executive director-PMRC, director – PCSIR, director – HAS, director-NIH, representative of Pakistan atomic energy commission, center for molecular genetics – Karachi, CAMB, national commission on biotechnology, relevant technical representative animal sciences, PARC, relevant technical representative plant sciences, PARC, director – EPA and two experts from civil society.

Functions of technical advisory committee are to :

- examine applications and recommend to NBC
- review and control of safety measures
- review research methodologies
- monitor release of GMOs/products into environment
- provide information to NBC about approved projects
- supervise the implementation of terms and conditions

**Functions of institutional biosafety committee:**

Members of institutional biosafety committee are head of the institution, subject expert, social scientist / economist, and representative of civil society,

Functions of institutional biosafety committee are to:

- assist the activities of NBC and technical advisory committee
- assist researchers
- determine additional safeguards
- evaluate qualification of the researchers
- monitor work for biosafety guidelines
- serve as a gateway, there is a flow of opinions, ideas / information b/w NBC-research teams
- update directory - at every biosafety level
- health of lab and field personnel
- contact with NBC and technical advisory committee for import/export
- prepare/ implement emergency plans

- hold funds and to assess projects that under which category it falls
- Inspect and certify labs / plant glass houses / animal houses

**Prohibition and license requirement:**

License is required for import/export/sale/ purchase. They need approval from federal agency. For this they first submit application with prescribed fees. Furthermore they have to notify NBC / federal agency for and change or addition in the information.

**Confidential information:**

Information of the applicant is protected with article 21 of the Cartagena protocol as set forth in the biosafety guidelines.

**Risk assessment and management:**

According to Article 15/ Annex III of Cartagena protocol, NBC will ensure activities-biosafety guidelines as well as license. Risk assessment is done by auditing of risk assessment. Evaluation of risk management measures is also done through field trials.

**Decision making and communication of information:**

Final decision is made and communicated to the applicant. 60 days for risk category 2/3, 90 days for experimental release and 120 days for commercialization. Criteria of decision are based on information set forth in the application. Scientific risk assessment prior field experience with GMOs is also done. Final decision is recorded in a decision document as described in biosafety guidelines. No person can vary the license activity. This license is granted by federal agency under rule 11. License remains ineffective until applicant executes an undertaking. Otherwise applicant will follow biosafety guidelines.

**Grant of licence:**

Federal agency-rule 11 approved license for a specified time period. It cannot be exceeded for more than 4 years. It is renewable after every 2 years. They have the powers to revoke new information-harmful effects of GMOs such as damage to the nature, health, environment or any other condition. Terms and conditions include labeling, control - exercised by the applicant, supervision, restriction to use, layout of the enterprise, submission of information or any other condition deemed appropriate.

**Application of re-examination:**

Applicant may file application to the NBC. Application can be submitted after a minimum time of 6 months when there is change in circumstances, material effect on the outcome of risk assessment, change in scientific or technical information and material effect on decision, conditions, and limitations and on the need.

**Special requirement for import and export of modified living organisms:**

Import can be of GMOs, substances/cells, products. Reasons of import can be contained use, intentional introduction into the environment, direct use as a food or direct use as a feed. According to Article 18-Cartagena protocol, National plant quarantine regulations, International plant protection convention, IT and PO/ EP and PO rules and regulations must be followed. Information for export include risk assessment/field trials to the exporting country by following National plant quarantine regulations, International plant protection convention and IT and PO/ EP and PO regulations.

**Permission and approval for food stuff:**

Food stuff includes ingredients, additives or any other processing aid. All food stuffs containing GMOs produced, sold, and imported need permission from NBC under sub-rule 2 of rule 20.

**Responsibility to notify interruptions and accidents:**

Any discharge of GMOs in to the environment may have harmful effects to the nature / health. Such interruptions or accidents must be notified to technical advisory committee. This shall not lessen the duty of

person, institution, and of organization whether got license. Information related to off-side emergency plan must be given to the technical advisory committee.

### **Pakistan biosafety measures:**

Pakistan-implementing National and administrative measures. Designation of National focal point is important for oversight of biological research activities, inter-agency consultative process. There are guidelines on code of conduct for life scientists, confidence building measures and on the awareness on bio-risk management. Rules of National biosafety committee, National bioethics committee, Drug Act 1976 and rules, Plant quarantine Act 1976, Animal quarantine Act 1979, Anti terrorism Act 1997, Pakistan export control Act 2004, Pakistan export list 2005 and 2011 are followed. Pakistan biosafety rules 2005 have drafted biological and toxin weapon convention.

### **National legislations and implementation:**

Pakistan biosecurity is under increasing pressure from the rapid expansion of world trade and as the worldwide movement of people and goods becomes quicker and easier. All this creates challenges for biosecurity, including increased risks from exotic pests and new and re-emerging diseases, and raises concerns about national security. Therefore we must strengthen our biosafety and biosecurity system to ensure confidence building and harmonization with the rest of world. International consumers are demanding production systems that produce safe food while respecting the environment and animal welfare. Pakistan just has started work on a three-year project to introduce the system of Good Agricultural Practices (GAP) that will enable the country to upgrade its fruit and vegetable farming system in line with international standards. Faced with the threat of losing more international markets. Pakistan has been losing international markets of its agricultural produce - vegetables and fruits, particularly citrus due to its inability to comply with International Plant Protection Convention (IPPC) standards and Sanitary and Phyto-sanitary (SPS) regulations of the World Trade Organisation (WTO).

However Pakistan need to implement Hazard Analysis and Critical Control Points (HACCP) methods to ensure food safety, pharmaceutical safety, HACCP is used in the food industry to identify potential food safety hazards to reduce or eliminate the risk of the hazards being realized. Today to product related standards and technical regulations, system standards are rapidly gaining currency as more and more international buyers ask for the proof that internationally recognized, certified, operational systems and procedures are in place for the control of food contamination. Food Safety Management System (HACCP), quality management (ISO-9000), Environmental Management Standard (ISO-14000), Product Traceability, Social Accountability (SA-8000), Occupational Health and Safety so on. It is worth mentioning that public must not get confuse with ISO 9000 or ISO 9001 standards with biosafety as ISO standards only ensures for quality management systems; set of procedures that cover all key processes in the business and how properly it is documented not the safety of the product. On the other hand principles of GAPs and HACCP basically lead us to words biosecurity system.

In February 2008; Japan pledged to step up screening of food imports from China as hundreds of Japanese complaining of illness. Ten people were diagnosed with pesticide poisoning after eating the frozen meat - major food makers recall food products manufactured at the same factory in China. In August 2007; China has come under strong international pressure after millions of toys exported to the United States and Europe proved to have dangerous defects; millions of toys were recalled by many big businesses because of concern over toxic lead paints used in it. In 2004; Pakistan refused to receive three Australian wheat shipments; which were believed containing harmful fungus. According to National Academy of Sciences USA; few categories of Science & Technology advances that have potential to contribute to the future development of biological hazard products like acquisition of novel biological or molecular diversity, Understanding and manipulating biological systems, Production, delivery, and packaging. Although United States is just one of many countries that conduct research on infectious disease agents and maintain collections of dangerous pathogens but our neighboring countries also have either offensive or defensive biological warfare program. Today, many biological tech facilities located in the independent states of Russia have been converted to civilian uses. Since political instability in Afghanistan and economical uncertainty in the whole region there is big concern that certain individual or groups may have access to microbial technology and collect pathogens highly dangerous for human, animal and crops - could potentially diverted to destabilize the economy of a country.

Moreover trade in microbial cultures is poorly regulated both within and among developing countries therefore national biosecurity regulations must be strengthened to prevent terrorists from stealing deadly pathogens from

poorly protected facilities in those countries where laws and enforcement are lax. So improved security for collections of dangerous pathogens in the region is urgently needed many laboratories lack the necessary financial and technical resources to implement these measures for that reason foreign technical and financial assistance would be required. By helping to ensure that dangerous pathogens are used only for peaceful purposes global biosecurity standards would reinforce the prohibition on the state level development, production, and stockpiling of biological weapons enshrined in the 1972 Biological Weapons Convention (BWC); this treaty has been ratified by Pakistan and many other developing countries. More recently there has been a trend towards more sustainable measures such as safe trade rules for biosafety, an example of which is the Biosafety Protocol; although Pakistan is part to Convention on Biological Diversity (CBD) but it has not yet ratified Cartagena Protocol on Biosafety.

In the early 1980s, the government launched a program under which expatriates visited different research laboratories and participated in short-term courses and training workshops. In 1981 the Nuclear Institute of Agriculture and Biology (NIAB), Faisalabad, organised a course on recombinant DNA methodology and genetic engineering which marked the beginning of initiatives in biotechnology in the country. In Pakistan most biotech research institutes declared that they have the capacity to conduct biotech research and development in different disciplines, however only a few have adequate infrastructure and made noteworthy achievements. The major centres in the country are Pakistan Atomic Energy Commission (PAEC); National Institute for Biotechnology and Genetic Engineering (NIBGE), Faisalabad; National Centre of Excellence in Molecular Biology (NCEMB), University of the Punjab, Lahore; Nuclear Institute of Agriculture and Biology (NIAB), Faisalabad; The Centre for Molecular Genetics (CMG), University of Karachi; Biomedical and Genetic Engineering Division, Dr A.Q. Khan Research Laboratories, Islamabad; Centre of Agriculture, Biochemistry and Biotechnology (CABB), University of Agriculture, Faisalabad; Agriculture Biotechnology Institute, National Agriculture Research Centre (NARC), Islamabad; University of Arid Agriculture, Rawalpindi; Institute of Biotechnology and Genetic Engineering, Peshawar; Institute of Biochemistry, University of Balochistan, Quetta; Institute of Biotechnology and Genetic Engineering, University of Sindh, Jamshoro; and Dr. Punjwani Center for Molecular Medicine and Drug Research University of Karachi (HEJ).

The historical record suggests that bioterrorists are generally opportunistic and seek out the most accessible source of pathogens. Although some countries developed research programs in biological weapons as early as the 1930s; Japan had an offensive biological warfare program and performed human experiments similarly many believed Germany was experimenting with biological agents for purposes of war at the same time. The U.S. started offensive biological plan in 1943. It weaponized seven biological agents such as anthrax that could kill humans. In 1980, Sri Lankan Tamil secessionist group threatened to infect humans and crops with deadly pathogens. In October 2001 twenty-two people developed symptoms and five died from the intentional distribution of letters laced with anthrax in USA. There have been some accident in which food borne illness have been reported in many countries which badly effected business in the region in 1996 in USA Escherichia coli O157:H7 was reported in California lettuce similarly in 2003 Hepatitis A reported in Mexican green onions. In our country agricultural biosafety and biosecurity covering crops, trees and farm and aquatic animals is of even greater importance since it relates to the livelihood security of nearly seventy percent of the population and the food, health, and trade security of the nation. The world is truly becoming a global village with reference to communication and transport. Disease causing organisms can spread fast through airplanes and farm trade. Disruption of the agricultural sector can cause profound dislocation of societies. Direct losses of plants or animals can result in shortage of food supply, increase in food prices, and unemployment. All this, if severe, can bring about serious destabilizing effects on social and political structures. Many developing countries are potentially quite vulnerable to such destabilization, particularly if they depend heavily on a single food crop or animal. Nevertheless, the potential for immense economic damage is high in a well-planned attack.

In June 2002, US President Bush signed into law "The Bioterrorism Act of 2002". This Act is to be administered by the United States Food and Drug Administration (FDA) in collaboration with the Department of Homeland Security. The Animal and Plant Health Inspection Service (APHIS) has the primary responsibility for implementing the provisions of the Act within the Department of Agriculture (USDA). The Act and regulations there under are designed to improve the ability of the United States to prevent, prepare for, and respond to bioterrorism and other public health emergencies. The Act will impact not only on the food industry in the United States itself, but also those countries; which ship food, feed, etc. into or through the United States. In 2004 the federal "BioShield law provides \$5.6 billion over 10 years to procure vaccines, therapies and other products critical to protecting against bioterrorism. At present President Bush's has increases food safety and security funding \$264 million FY 2009 - USDA budget includes increased funding for food safety and security programs in order to improve the safety and security of America's food supply and agriculture; The budget increases funding for high priority for food and agriculture defense and emerging diseases in crops and

livestock.

It is worthy to know that according to recent research Global warming may trigger infectious diseases to spread more easily via pests like mosquitoes, cockroaches or ticks that are sensitive to temperature changes; the rise in temperatures in some areas like Europe, Canada or places at high altitude may bring diseases like malaria, dengue, where it has never been seen as long as anyone can remember. Similarly it is believed that higher temperatures would give rise to new pests and diseases of crops and livestock. Pakistan is the transitory home for many migratory birds especially during winter season; our country is also becoming a national village with reference to communication, transportation, and trade. Therefore, home quarantine assumes as much importance as international quarantine. Cross-border movement of farm goods and animals with neighboring countries is another area of biosecurity significance. Agriculture is the single largest sector and a dominant driving force for growth and development of the national economy of Pakistan; the economy very heavily depends on the production of major crops like cotton, wheat, rice and sugarcane. It accounts for 24 percent of the GDP and employs 46 percent of the total work force. Agriculture contributes to growth as a supplier of raw materials to industry as well as a market for industrial products and also contributes substantially to Pakistan's exports earnings. Almost 70 percent of country's population are living in rural areas and are directly or indirectly linked with agriculture for their livelihood. Any improvement in agriculture will not only help country's economic growth to rise at a faster rate but will also benefit a large segment of the country's population.

Cotton is the major cash crop of Pakistan considered as a backbone of our economy; it accounts for 8.2 percent of the value added in agriculture and about 3.2 percent to GDP; which earns nearly 60% of the foreign exchange; adds over \$3.1 billion to the national economy. This season cotton production has declined by about 15 percent which is around 10.6 million bales as compared to 13 million bales in 2007; a decline of over two million bales. Three main reasons are the cotton leaf curl virus (CLCV), pesticide-resistant mealy bugs and non approved Bt cotton varieties over 40 percent of cotton growing area adversely affected boll size, fiber quality and weight, however in some area harsh weather conditions also added problems for cotton growing farmers. It is believed that cotton leaf curl virus - Burewala strain, which resulted in huge losses to the cotton crop in the country, was due to the introduction of foreign non approved cotton varieties that were not suitable to our soil and climatic condition similarly Pakistan never had "Banana Bunchy virus" but after import of untested banana variety from Australia; Banana crop in Sindh never came out of its infestation and damages. Presently there are some trees having unknown pathogenic problems Mango Sudden Death Syndrome which need urgent attention by the authorities to evaluate its causes. Agriculture is our strategic asset, and must be protected from those who want to gamble on it just to make some money or ruin our economy. Since Livestock (Cattle, sheep, poultry etc) for us is as important as crops - need to be protected from diseases and plagues because it contributes 49 percent to the value added in the agriculture sector. Because of the huge financial stakes in the agricultural sector, and drug industry involves, organized crime may take an interest in bio-criminal activities with agricultural targets. 1950's in Kenya, Mau Mau used plant toxins to kill livestock. Some may be interested to destabilize important agriculture market sector to create shortage of food, cause trade barriers or capture market share. The European Union (EU) imposed restriction on the import of UK beef due to the outbreak of Bovine Spongiform Encephalopathy (BSE); as a result UK bear losses in million and it took years to convince EU to lift ban on the import of its beef. Similarly the threat to industry profits from diseases like foot-and-mouth disease and citrus canker which increasing globalization makes harder to control if there would not be any biosecurity in place. The present infrastructure and institutional framework in the area of agricultural biosecurity, including the World Trade Organization specifications of sanitary and phytosanitary measures but unfortunately so far Pakistan is too slow in its strengthening and implementation. The existing infrastructure for sanitary and phytosanitary measures will have to be reviewed and major gaps filled. While in developed countries, any disaster arising from invasive alien species like the H5N1 strain of the avian flu may be more of a human health problem.

In 2006 Poultry farming, an important sub-sector of livestock, has suffered a loss of over Rs3 billion in one month due to reduction in prices as well as low consumption of poultry meat due to fear of bird flu (H5N1 strain) in the country. So far eight cases of bird flu among people confirmed in Pakistan by the WHO; since 2003, 341 recorded cases among people in 14 nations; 210 were fatal. Scientists fear possible pandemic if virus mutates into more transmissible form human to human. In the last few years rapid spread of Dengue Fever – a viral infection spread by mosquitoes has caused concern among people in Pakistan as this disease was never heard before 1990's. In Pakistan, at least 27 deaths have been reported and the death rate from Dengue is significantly more than elsewhere. As many as 1900 cases have been confirmed and far more are expected. Travel services from PIA and Pakistan Railways are taking measures to contain the spread of the disease but look beyond their capacity to ensure biosecurity due to lack of reinforcement system.

Number of times Pakistani government has given assurance to world that its nuclear program is in the safe hand; in future if we failed to develop biosafety regulation and its implementation system; we may end-up with allegations of bridging biosecurity; it is notable that in March 2003, when Khalid Shaikh Mohammed was captured, claimed a key operational planner for Al Qaeda –authorities revealed that the organization had recruited a Pakistani microbiologist, acquired materials to manufacture botulinum toxin (neurotoxin protein), and developed a workable plan for anthrax production. The government of Pakistan should set their house in order related to biosafety and biosecurity at the earliest in order to avoid apologetic position at any international forum. Every country that transfers pathogens and toxins across national borders should establish rules for the safe and secure shipping of dangerous goods and import-export controls, and create a national body to enforce biosafety regulations. World of science and technology; research in modern biotechnology, nanotechnology and genetic engineering are amazing piece of art however the real concern is that it's another example of knowledge and skill delving into matters that have potentially dangerous consequences for mankind if issues of biosafety and biosecurity would be ignored. There is desperate need to engage public from all backgrounds in order to minimize possible biohazard dangerous to human health, agriculture and environment.

### **Efforts to mitigate biological threats:**

We are experiencing an unparalleled period of advancement and innovation in the life sciences globally that continues to transform our way of life. Whether augmenting our ability to provide health care and protect the environment, or expanding our capacity for energy and agricultural production towards global sustainability, continued research and development in the life sciences is essential to a brighter future for all people. The beneficial nature of life science research is reflected in the widespread manner in which it occurs. From cutting-edge academic institutes, to industrial research centers, to private laboratories in basements and garages, progress is increasingly driven by innovation and open access to the insights and materials needed to advance individual initiatives. We must support the ongoing revolution in the life sciences by seeking to ensure that resulting discoveries and their applications, used solely for peaceful and beneficial purposes, are globally available. At the same time, we must be mindful of the risks throughout history posed by those who sought to misuse the products of new technologies for harmful purposes. Specifically, we must reduce the risk that misuse of the life sciences could result in the deliberate or inadvertent release of biological material in a manner that sickens or kills people, animals, or plants, or renders unusable critical resources. The effective dissemination of a lethal biological agent within an unprotected population could place at risk the lives of hundreds of thousands of people. The unmitigated consequences of such an event could overwhelm our public health capabilities, potentially causing an untold number of deaths. The economic cost could exceed one trillion dollars for each such incident. In addition, there could be significant societal and political consequences that would derive from the incident's direct impact on our way of life and the public's trust in government.

Since 2001, the United States Government has significantly expanded its efforts to improve the Nation's ability to recognize and respond to acts of bioterrorism or other significant outbreaks of infectious disease; however, efforts targeted to prevent such threats have received comparatively limited policy focus or substantive guidance at the National level. Although it is entirely feasible to mitigate the impact of even a large-scale biological attack upon a city's population, doing so incurs a significant cost and effort. We therefore need to place increased priority on actions to further reduce the likelihood that such an attack might occur. This Strategy will guide our efforts to prevent such incidents by reducing the risk that misuse of the life sciences or derivative materials, techniques, or expertise will result in the use or intent to use biological agents to cause harm. It also complements existing policies, plans, and preparations to advance our ability to respond to public health crises of natural, accidental, or deliberate origin.

### **Threats of biological weapons:**

Gram-for-gram, biological weapons are the deadliest weapons ever produced. While few countries are suspected of maintaining offensive biological weapons, many possess the capability to rapidly produce and weaponize biological agents if they choose to do so. Following the 2001 anthrax letter attacks in the United States, the possibility of bioterrorism has reinvigorated efforts to criminalize activities associated with the misuse of biological materials. The Biological and Toxin Weapons Convention (BTWC), which prohibits the development, production, stockpiling, and acquisition of biological weapons, lacks verification provisions to ensure its members are not secretly maintaining biological weapons programs. The difficulty of detecting clandestine programs due to the dual-use nature of biotechnology and the uneven and often meager preparedness of many states' public health systems for a major disease outbreak pose ongoing challenges to the international community.

**Biosecurity challenges of the global expansion of high containment biological laboratories:**

Containment labs are no longer solely the province of “high resource” or developed countries. Low resource countries are also investing in labs to produce livestock vaccines matched to local strains, perform research on endemic diseases, and combat local human and animal disease outbreaks. Many nations are enhancing their laboratory and surveillance capabilities to comply with the World Health Organization’s (WHO) International Health Regulations (IHR) (2005), which require States Parties to have the capacity to detect unusual levels of disease or death in all parts of their territory and to be able to analyze samples either domestically or through a collaborative agreement (WHO, 2008). Furthermore, infectious diseases do not respect national borders (NRC, 2010a), and biocontainment labs often play an integral part in global disease surveillance efforts.

**Public participation and access to information:**

Access to information, public participation in decision-making and access to justice in environmental matters is governed at international level by the so-called Aarhus Convention, signed in Aarhus (Denmark) in 1998. This Convention binds Community institutions and bodies and has been implemented by means of Regulation (EC) No 1367/2006, which is also known as 'the Aarhus Regulation'. The Aarhus Regulation has itself been implemented by means of two Commission Decisions 2008/50/EC and 2008/401/EC, Euratom. The Aarhus Regulation grants the public rights and imposes obligations on Community institutions and bodies regarding access to environmental information (Section I), public participation concerning plans and programmes relating to the environment (section II) and access to review procedures (Section III). This guide is intended to assist members of the public in availing themselves of their rights under the Aarhus Regulation. It aims thereby to contribute to a more transparent and accountable functioning of the European Community. Even though the Aarhus Regulation applies to all Community institutions and bodies concerned, this Guide will, for practical reasons, focus primarily on the implementation and application of that Regulation by the European Commission.

**International framework on biosafety:**

Debate about the potential risks of genetically modified organisms (GMOs) to the environment or human health spurred attention to biosafety. Biosafety is associated with the safe use of GMOs and, more generally, with the introduction of non-indigenous species into natural or managed ecosystems. Biosafety regulation--the policies and procedures adopted to ensure the environmentally safe application of modern biotechnology--has been extensively discussed at various national and international forums. Much of the discussion has focused on developing guidelines, appropriate legal frameworks and, at the international level, a legally binding international biosafety protocol--the Cartagena Protocol on Biosafety. The Protocol is one among various international instruments and treaties that regulate specific aspects relevant to agricultural biotechnology. The present article presents the main international instruments relevant to biosafety regulation, and their key provisions. While international agreements and standards provide important guidance, they leave significant room for interpretation, and flexibility for countries implementing them. Implementation of biosafety at the national level has proven to be a major challenge, particularly in developing countries, and consequently the actual functioning of the international regulatory framework for biotechnology is still in a state of flux.

**Occupational health and immunoprophylaxis:**

The goal of medical support services in a biomedical research setting is to promote a safe and healthy workplace. This is accomplished by limiting opportunities for exposure, promptly detecting and treating exposures, and using information gained from work injuries to further enhance safety precautions. Occupational health and safety in biomedical research settings is a responsibility shared by healthcare providers, safety specialists, principal investigators, employers, and workplace personnel. Optimal worker protection depends on effective, ongoing collaboration among these groups. Supervisors, working with personnel representatives, should describe workers’ proposed tasks and responsibilities. First line supervisors and safety professionals should identify the potential worksite health hazards. Principal investigators may serve as subject matter experts. The health provider should design medical support services in consultation with representatives from the institutional environmental health and safety program and the principal investigators. Workers should be fully informed of the available medical support services and encouraged to utilize them. Requisite occupational medical services are described below and expanded discussions of the principles of effective medical support services are available in authoritative texts.<sup>1,2</sup> Services offered by the medical support team should be designed to be in compliance with United States Department of Labor (DOL), OSHA regulations, patient confidentiality laws, and the Americans with Disabilities Act of 1990.<sup>3-8</sup> Medical support services should be based upon detailed risk assessments and tailored to meet the organization’s needs. Risk assessments should define potential

hazards and exposures by job responsibility. They should be provided for all personnel regardless of employment status. Contracted workers, students, and visitors should be provided occupational medical care by their employer or sponsor equivalent to that provided by the host institution for exposures, injuries, or other emergencies experienced at the worksite. Occupational medical services may be provided through a variety of arrangements (e.g., in-house or community based) as long as the service is readily available and allows timely, appropriate evaluation and treatment. The interaction between worker, healthcare provider and employer may be complex, such as a contract worker who uses his own medical provider or uses contract medical services. Thus, plans for providing medical support for workers should be completed before work actually begins. The medical provider must be knowledgeable about the nature of potential health risks in the work environment and have access to expert consultation. Prevention is the most effective approach to managing biohazards. Prospective workers should be educated about the biohazards to which they may be occupationally exposed, the types of exposures that place their health at risk, the nature and significance of such risks, as well as the appropriate first aid and follow up for potential exposures. That information should be reinforced annually, at the time of any significant change in job responsibility, and following recognized and suspected exposures.<sup>9-11</sup> Medical support services for biomedical research facilities should be evaluated annually. Joint annual review of occupational injury and illness reports by healthcare providers and environmental health and safety representatives can assist revision of exposure prevention strategies to minimize occupational health hazards that cannot be eliminated.

### **Occupational health support service elements:**

Workers who may be exposed to human pathogens should receive a preplacement medical evaluation. Healthcare providers should be cognizant of potential hazards encountered by the worker. A description of the requirements for the position and an understanding of the potential health hazards present in the work environment, provided by the worker's supervisor, should guide the evaluation. The healthcare provider should review the worker's previous and ongoing medical problems, current medications, allergies to medicines, animals, and other environmental proteins, and prior immunizations. With that information, the healthcare provider determines what medical services are indicated to permit the individual to safely assume the duties of the position. Occasionally, it may be useful to review pre-existing medical records to address specific concerns regarding an individual's medical fitness to perform the duties of a specific position. If pre-existing medical records are unavailable or are inadequate, the healthcare provider may need to perform a targeted medical exam. Comprehensive physical examinations are rarely indicated. During the visit, the healthcare provider should inform the worker of potential health hazards in the work area and review steps that should be taken in the event of an accidental exposure. This visit also establishes a link with the medical support services provider. When occupational exposure to human pathogens is a risk, employers should consider collecting and storing a serum specimen prior to the initiation of work with the agent. It can be used to establish baseline sero-reactivity, should additional blood samples be collected for serological testing subsequent to a recognized or suspected exposure. Occasionally, it is desirable to determine an individual's vulnerability to infection with specific agents prior to assigning work responsibilities. Some occupational exposures present substantially more hazard to identifiable sub-populations of workers. Immunodeficient workers or non-immune pregnant female workers may experience devastating consequences from exposures that pose a chance of risk to pregnant women with prior immunity and other immunocompetent workers (e.g., cytomegalovirus or toxoplasmosis). Serologic testing should be used to document baseline vulnerability to specific infections to which the worker might be exposed, and non-immune workers should be adequately informed about risks. In specific settings, serologic documentation that individual workers have pre-existing immunity to specific infections also may be required for the protection of research animals.

Commercial vaccines should be made available to workers to provide protection against infectious agents to which they may be occupationally exposed.<sup>12-16</sup> The Advisory Committee on Immunization Practices (ACIP) provides expert advice to the Secretary of the DHHS, the Assistant Secretary for Health, and the CDC on the most effective means to prevent vaccine-preventable diseases and to increase the safe usage of vaccines and related biological products. The ACIP develops recommendations for the routine administration of vaccines to pediatric and adult populations, and schedules regarding the appropriate periodicity, dosage, and contraindications. The ACIP is the only entity in the federal government that makes such recommendations. The ACIP is available at the CDC Web site: [www.cdc.gov](http://www.cdc.gov). If the potential consequences of infection are substantial and the protective benefit from immunization is proven, acceptance of such immunization may be a condition for employment. Current, applicable vaccine information statements must be provided whenever a vaccine is administered. Each worker's immunization history should be evaluated for completeness and currency at the time of employment and re-evaluated when the individual is assigned job responsibilities with a new biohazard. When occupational exposure to highly pathogenic agents is possible and no commercial vaccine is available, it may be appropriate to immunize workers using vaccines or immune serum preparations that are investigational,

or for which the specific indication constitutes an off-label use. Use of investigational products, or of licensed products for off-label indications must be accompanied by adequate informed consent outlining the limited availability of information on safety and efficacy.

Routine, periodic medical evaluations generally are not recommended; however, limited periodic medical evaluations or medical clearances targeted to job requirements may occasionally be warranted (e.g., respirator usage).<sup>3</sup> In special circumstances, it may be appropriate to offer periodic laboratory testing to workers with substantial risk of exposure to infectious agents to detect pre-clinical or sub-clinical evidence for an occupationally acquired infection. Before asymptomatic workers without specific exposures are tested for seroreactivity, the benefit of such testing should be justified, plans for further investigation of indeterminate test results should be delineated, and clearly defined criteria for interpretation of results should be developed. Workers should be encouraged to seek medical evaluation for symptoms that they suspect may be related to infectious agents in their work area, without fear of reprisal. A high index of suspicion for potential occupational exposures should be maintained during any unexplained illness among workers or visitors to worksites containing biohazards. Modes of transmission, as well as the clinical presentation of infections acquired through occupational exposures, may differ markedly from naturally acquired infections. Fatal occupational infections have resulted from apparently trivial exposures. The healthcare provider should have a working understanding of the biohazards present in the workplace and remain alert for subtle evidence of infection and atypical presentations. A close working relationship with the research or clinical program in which the affected employee works is absolutely essential. In the event of injury, consultation between healthcare provider, employee, and the employee's supervisor is required for proper medical management and recordkeeping. All occupational injuries, including exposures to human pathogens, should be reported to the medical support services provider. Strategies for responding to biohazard exposures should be formulated in advance. Proper post-exposure response is facilitated by exposure-specific protocols that define appropriate first aid, potential post-exposure prophylaxis options, recommended diagnostic tests, and sources of expert medical evaluation. These protocols should address how exposures that occur outside of regular work hours are handled and these protocols should be distributed to potential healthcare providers (e.g., local hospital emergency departments). In exceptional cases, the protocols should be reviewed with state and community public health departments. Emergency medical support training should be provided on a regular basis for both employees and healthcare providers.

### ***Bacillus anthracis:***

*Bacillus anthracis*, a gram-positive, non-hemolytic, and non-motile bacillus, is the etiologic agent of anthrax, an acute bacterial disease of mammals, including humans. Like all members of the genus *Bacillus*, under adverse conditions *B. anthracis* has the ability to produce spores that allow the organism to persist for long periods until the return of more favorable conditions. Reports of suspected anthrax outbreaks date back to as early as 1250 BC. The study of anthrax and *B. anthracis* in the 1800s contributed greatly to our general understanding of infectious diseases. Much of Koch's postulates were derived from work on identifying the etiologic agent of anthrax. Louis Pasteur developed the first attenuated live vaccine for anthrax. Most mammals are susceptible to anthrax; it mostly affects herbivores that ingest spores from contaminated soil and, to a lesser extent, carnivores that scavenge on the carcasses of diseased animals. Anthrax still occurs frequently in parts of central Asia and Africa. In the United States, it occurs sporadically in animals in parts of the West, Midwest and Southwest. The infectious dose varies greatly from species to species and is routependent. The inhalation anthrax infectious dose (ID) for humans primarily has been extrapolated from inhalation challenges of nonhuman primates (NHP) or studies done in contaminated mills. Estimates vary greatly but the medium lethal dose (LD<sub>50</sub>) is likely within the range of 2,500-55,000 spores.<sup>1</sup> It is believed that very few spores (10 or less) are required for cutaneous anthrax.

Occupational infections are possible when in contact with contaminated animals, animal products or pure cultures of *B. anthracis*, and may include ranchers, veterinarians and laboratory workers. Numerous cases of laboratory-associated anthrax (primarily cutaneous) have been reported.<sup>3,4</sup> Recent cases include suspected cutaneous anthrax in a laboratory worker in Texas and a cutaneous case in a North Dakota male who disposed of five cows that died of anthrax. The clinical forms of anthrax in humans that result from different routes of infection are: 1) cutaneous (via broken skin); 2) gastrointestinal (via ingestion); and 3) inhalation anthrax. Cutaneous anthrax is the most common and readily treatable form of the disease. Inhalation anthrax used to be known as "Woolsorter disease" due to its prevalence in textile mill workers handling wool and other contaminated animal products. While naturally occurring disease is no longer a significant public health problem in the United States, anthrax has become a bioterrorism concern. In 2001, 22 people were diagnosed with anthrax acquired from spores sent through the mail, including 11 cases of inhalation anthrax with five deaths and 11 cutaneous cases.

*B. anthracis* may be present in blood, skin lesion exudates, cerebrospinal fluid, pleural fluid, sputum, and rarely, in urine and feces. The primary hazards to laboratory personnel are: direct and indirect contact of broken skin with cultures and contaminated laboratory surfaces, accidental parenteral inoculation and, rarely, exposure to infectious aerosols. Efforts should be made to avoid production of aerosols by working with infectious organisms in a BSC. In addition, all centrifugation should be done using aerosol-tight rotors that are opened within the BSC after each run. BSL-2 practices, containment equipment, and facilities are recommended for activities using clinical materials and diagnostic quantities of infectious cultures. ABSL-2 practices, containment equipment and facilities are recommended for studies utilizing experimentally infected laboratory rodents. BSL-3 practices, containment equipment, and facilities are recommended for work involving production quantities or high concentrations of cultures, screening environmental samples (especially powders) from anthrax-contaminated locations, and for activities with a high potential for aerosol production. Workers who frequently centrifuge *B. anthracis* suspensions should use autoclavable aerosol-tight rotors. In addition, regular routine swabbing specimens for culture should be routinely obtained inside the rotor and rotor lid and, if contaminated, rotors should be autoclaved before re-use.

Vaccines A licensed vaccine for anthrax is available. Guidelines for its use in occupational settings are available from the ACIP.<sup>8,9</sup> Worker vaccination is recommended for activities that present an increased risk for repeated exposures to *B. anthracis* spores including: 1) work involving production quantities with a high potential for aerosol production; 2) handling environmental specimens, especially powders associated with anthrax investigations; 3) performing confirmatory testing for *B. anthracis*, with purified cultures; 4) making repeated entries into known *B. anthracis*-spore-contaminated areas after a terrorist attack; 5) work in other settings in which repeated exposure to aerosolized *B. anthracis* spores might occur. Vaccination is not recommended for workers involved in routine processing of clinical specimens or environmental swabs in general diagnostic laboratories.

### **Brucella species:**

The genus *Brucella* consists of slow-growing, very small gram-negative coccobacilli whose natural hosts are mammals. Seven *Brucella* species have been described using epidemiologic and biological characteristics, although at the genetic level all brucellae are closely related. *B. melitensis* (natural host: sheep/goats), *B. suis* (natural host: swine), *B. abortus* (natural host: cattle), *B. canis* (natural host: dogs), and *B. "maris"* (natural host: marine mammals) have caused illness in humans exposed to the organism including laboratory personnel. Hypersensitivity to *Brucella* antigens is a potential but rare hazard to laboratory personnel. Occasional hypersensitivity reactions to *Brucella* antigens occur in workers exposed to experimentally and naturally infected animals or their tissues. Brucellosis has been one of the most frequently reported laboratory infections in the past and cases continue to occur. Airborne and mucocutaneous exposures can produce LAI. Accidental self-inoculation with vaccine strains is an occupational hazard for veterinarians. Brucellosis (Undulant fever, Malta fever, Mediterranean fever) is a zoonotic disease of worldwide occurrence. Mammals, particularly cattle, goats, swine, and sheep act as reservoirs for brucellae. Multiple routes of transmission have been identified, including direct contact with infected animal tissues or products, ingestion of contaminated milk, and airborne exposure in pens and stables.

*Brucella* infects the blood and a wide variety of body tissues, including cerebral spinal fluid, semen, pulmonary excretions, placenta, and occasionally urine. Most laboratory-associated cases occur in research facilities and involve exposures to *Brucella* organisms grown in large quantities or exposure to placental tissues containing *Brucella*. Cases have occurred in clinical laboratory settings from sniffing bacteriological cultures<sup>29</sup> or working on open bench tops.<sup>30</sup> Aerosols from, or direct skin contact with, cultures or with infectious clinical specimens from animals (e.g., blood, body fluids, tissues) are commonly implicated in human infections. Aerosols generated during laboratory procedures have caused multiple cases per exposure. Mouth pipetting, accidental parenteral inoculations, and sprays into eyes, nose and mouth result in infection. The infectious dose of *Brucella* is 10-100 organisms by aerosol route and subcutaneous route in laboratory animals. BSL-2 practices, containment equipment, and facilities are recommended for routine clinical specimens of human or animal origin. Products of conception containing or believed to contain pathogenic *Brucella* should be handled with BSL-3 practices due to the high concentration of organisms per gram of tissue. BSL-3 and ABSL-3 practices, containment equipment, and facilities are recommended, for all manipulations of cultures of pathogenic *Brucella* spp. listed in this summary, and for experimental animal studies. Human *Brucella* vaccines have been developed and tested in other countries with limited success. A human vaccine is not available in the United States.

### ***Campylobacter:***

*Campylobacters* are curved, S-shaped, or spiral rods associated with gastrointestinal infections (primarily *C. jejuni* subsp. *jejuni* and *C. coli*), bacteremia, and sepsis (primarily *C. fetus* subsp. *fetus* and *C. upsaliensis*).

Organisms are isolated from stool specimens using selective media, reduced oxygen tension, and elevated incubation temperature (43°C). These organisms rarely cause LAI, although laboratory-associated cases have been documented.<sup>44-47</sup> Experimentally infected animals also are a potential source of infection. Numerous domestic and wild animals, including poultry, pets, farm animals, laboratory animals, and wild birds are known reservoirs and are a potential source of infection for laboratory and animal care personnel. While the infective dose is not firmly established, ingestion of as few as 500-800 organisms has caused symptomatic infection.<sup>49-51</sup> Natural transmission usually occurs from ingestion of organisms in contaminated food or water and from direct contact with infected pets, farm animals, or infants. Pathogenic *Campylobacter* sp. may occur in fecal specimens in large numbers. *C. fetus* subsp. *fetus* may also be present in blood, exudates from abscesses, tissues, and sputa. The primary laboratory hazards are ingestion and parenteral inoculation of *C. jejuni*. The significance of aerosol exposure is not known. BSL-2 practices, containment equipment, and facilities are recommended for activities with cultures or potentially infectious clinical materials.

#### **Neurotoxin producing Clostridia species:**

*Clostridium botulinum*, and rare strains of *C. baratii* and *C. butyricum* are anaerobic spore-forming species that cause botulism, a life-threatening foodborne illness. The pathogenicity of these organisms results from the production of botulinum toxin, one of the most highly potent neurotoxins currently recognized. Purified botulinum neurotoxin is a 150 kDa protein that acts selectively on peripheral cholinergic nerve endings to block neurotransmitter release. The principal site of action is the neuromuscular junction, where blockade of transmission produces muscle weakness or paralysis. The toxin also acts on autonomic nerve endings where blockade of transmission can produce a variety of adverse effects. The toxin may also contain associated proteins that may increase its size to as high as 900 kDa. There has been only one report of botulism associated with handling of the toxin in a laboratory setting. However, concerns about potential use of the toxin as an agent of bioterrorism or biological warfare have led to increased handling of the substance by investigators studying mechanism of action and/or developing countermeasures to poisoning. Botulinum toxin occurs in seven different serotypes (A to G), but almost all naturally-occurring human illness is due to serotypes A, B, E, and F.<sup>58</sup> Botulism occurs when botulinum toxin is released into circulation following ingestion of preformed toxin. However, animal studies have shown that botulism may occur through inhalation of preformed toxin. Use of appropriate personal protective equipment should prevent potential exposure through mucous membranes. Symptoms and even death are possible by accidental injection of botulinum toxin. Risk to toxin exposure is dependent on both route of exposure and toxin molecular weight size. Exposure to neurotoxin producing Clostridia species does not cause infection; however, in certain rare circumstances (Infant Botulism, Wound Botulism, and Adult colonization), the organism can colonize the intestinal tract and other sites and produce toxin. In Wound Botulism, exposure to toxin is caused by introduction of spores into puncture wounds and in situ production by the organism. Infants less than 1 year of age may be susceptible to intestinal colonization and develop the syndrome of Infant Botulism as a result of in situ production of toxin. Similarly to Infant Botulism, ingestion of spores by adults with a compromised gastrointestinal tract (GI), such as following GI surgery or long-term administration of antibiotics, may increase risk for intestinal infection and in situ production of toxin.

Neurotoxin producing Clostridia species or its toxin may be present in a variety of food products, clinical materials (serum, feces) and environmental samples (soil, surface water).<sup>59</sup> In addition, bacterial cultures may produce very high levels of toxin.<sup>60</sup> In healthy adults, it is typically the toxin and not the organism that causes disease. Risk of laboratory exposure is due to the presence of the toxin and not due to a potential of infection from the organisms that produce the toxin. Although spore-forming, there is no known risk to spore exposure except for the potential for the presence of residual toxin associated with pure spore preparations. Laboratory safety protocols should be developed with the focus on prevention of accidental exposure to the toxin produced by these *Clostridia* species. BSL-2 practices, containment equipment, and facilities are recommended for activities that involve the organism or the toxin<sup>61</sup> including the handling of potentially contaminated food. Solutions of sodium hypochlorite (0.1%) or sodium hydroxide (0.1N) readily inactivate the toxin and are recommended for decontamination of work surfaces and for spills. Autoclaving of contaminated materials also is appropriate. Additional primary containment and personnel precautions, such as those recommended for BSL-3, should be implemented for activities with a high potential for aerosol or droplet production, or for those requiring routine handling of larger quantities of the organism or of the toxin. ABSL-2 practices, containment equipment, and facilities are recommended for diagnostic studies and titration of toxin. A pentavalent (A, B, C, D and E) botulinum toxoid vaccine (PBT) is available through the CDC as an Investigational New Drug (IND). Vaccination is recommended for all personnel working in direct contact with cultures of neurotoxin producing *Clostridia* species or stock solutions of Botulinum neurotoxin.

### ***Campylobacter diphtheriae*:**

*Corynebacterium diphtheriae* is a pleomorphic gram-positive rod that is isolated from the nasopharynx and skin of humans. The organism is easily grown in the laboratory on media containing 5% sheep blood. *C. diphtheriae* produces a potent exotoxin and is the causative agent of diphtheria, one of the most widespread bacterial diseases in the pre-vaccine era. Laboratory-associated infections with *C. diphtheriae* have been documented, but laboratory animal-associated infections have not been reported. Inhalation, accidental parenteral inoculation, and ingestion are the primary laboratory hazards. The agent may be present in exudates or secretions of the nose, throat (tonsil), pharynx, larynx, wounds, in blood, and on the skin. Travel to endemic areas or close contact with persons who have returned recently from such areas, increases risk. Transmission usually occurs via direct contact with patients or carriers, and more rarely, with articles contaminated with secretions from infected people. Naturally occurring diphtheria is characterized by the development of grayish white membranous lesions involving the tonsils, pharynx, larynx, or nasal mucosa. Systemic sequelae are associated with the production of diphtheria toxin. An effective vaccine has been developed for diphtheria and this disease has become a rarity in countries with vaccination programs. BSL-2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infected clinical materials or cultures. A BSL-2 facilities are recommended for studies utilizing infected laboratory animals. A licensed vaccine is available.

### ***Helicobacter* species:**

*Helicobacters* are spiral or curved gram-negative rods isolated from gastrointestinal and hepatobiliary tracts of mammals and birds. There are currently 20 recognized species, including at least nine isolated from humans. Since its discovery in 1982, *Helicobacter pylori* has received increasing attention as an agent of gastritis. The main habitat of *H. pylori* is the human gastric mucosa. Other *Helicobacter* spp. (*H. cinaedi*, *H. canadensis*, *H. canis*, *H. pullorum*, and *H. fennelliae*) may cause asymptomatic infection as well as proctitis, proctocolitis, enteritis and extraintestinal infections in humans. *H. cinaedi* has been isolated from dogs, cats and Syrian hamsters. Both experimental and accidental LAI with *H. pylori* have been reported. Ingestion is the primary known laboratory hazard. The importance of aerosol exposures is unknown. Chronic gastritis and duodenal ulcers are associated with *H. pylori* infection. Epidemiologic associations have also been made with gastric adenocarcinoma. Human infection with *H. pylori* may be long in duration with few or no symptoms, or may present as an acute gastric illness. Transmission, while incompletely understood, is thought to be by the fecal-oral or oral-oral route.

*H. pylori* may be present in gastric and oral secretions and stool. The enterohepatic helicobacters (e.g., *H. canadensis*, *H. canis*, *H. cinaedi*, *H. fennelliae*, *H. pullorum*, and *H. winghamensis*) may be isolated from stool specimens, rectal swabs, and blood cultures. Protocols involving homogenization or vortexing of gastric specimens have been described for the isolation of *H. pylori*. Containment of potential aerosols or droplets should be incorporated in these procedures. BSL-2 practices, containment equipment, and facilities are recommended for activities with clinical materials and cultures known to contain or potentially contain the agents. A BSL-2 practices, containment equipment, and facilities are recommended for activities with experimentally or naturally infected animals.

### ***Neisseria gonorrhoeae*:**

*Neisseria gonorrhoeae* is a gram-negative, oxidase-positive diplococcus associated with gonorrhea, a sexually transmitted disease of humans. The organism may be isolated from clinical specimens and cultivated in the laboratory using specialized growth media. Laboratory-associated gonococcal infections have been reported in the United States and elsewhere. These infections have presented as conjunctivitis, with either direct finger-to-eye contact or exposure to splashes of either liquid cultures or contaminated solutions proposed as the most likely means of transmission. Gonorrhea is a sexually transmitted disease of worldwide importance. The 2004 rate of reported infections for this disease in the United States was 112 per 100,000 population. The natural mode of infection is through direct contact with exudates from mucous membranes of infected individuals. This usually occurs by sexual activity, although newborns may also become infected during birth.

The agent may be present in conjunctival, urethral and cervical exudates, synovial fluid, urine, feces, and CSF. Accidental parenteral inoculation and direct or indirect contact of mucous membranes with infectious clinical materials are known primary laboratory hazards. Laboratory-acquired illness due to aerosol transmission has not been documented. BSL-2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of clinical materials or cultures. Gloves should be worn when handling infected laboratory animals and when there is the likelihood of direct skin contact with infectious materials. Additional primary containment and personnel precautions such as those described for BSL-3 may be indicated

when there is high risk of aerosol or droplet production, and for activities involving production quantities or high concentrations of infectious materials. Animal studies may be performed at ABSL-2.

### **Salmonella serotypes:**

Salmonellae are gram-negative enteric bacteria associated with diarrheal illness in humans. They are motile oxidase-negative organisms that are easily cultivated on standard bacteriologic media, although enrichment and selective media may be required for isolation from clinical materials. Recent taxonomic studies have organized this genus into two species, *S. enterica* and *S. bongori*, containing more than 2500 antigenically distinct subtypes or serotypes.<sup>123</sup> *S. enterica* contains the vast majority of serotypes associated with human disease. *S. enterica* serotypes Typhimurium and Enteritidis (commonly designated *S. typhimurium* and *S. enteritidis*) are the serotypes most frequently encountered in the United States. This summary statement covers all pathogenic serotypes except *S. typhi*. Salmonellosis is a documented hazard to laboratory personnel.<sup>4,26,124-125</sup> Primary reservoir hosts include a broad spectrum of domestic and wild animals, including birds, mammals, and reptiles, all of which may serve as a source of infection to laboratory personnel. Case reports of laboratory-acquired infections indicate a presentation of symptoms (fever, severe diarrhea, abdominal cramping) similar to those of naturally-acquired infections, although one case also developed erythema nodosum and reactive arthritis. Salmonellosis is a food borne disease of worldwide distribution. An estimated 5 million cases of salmonellosis occur annually in the United States. A wide range of domestic and feral animals (poultry, swine, rodents, cattle, iguanas, turtles, chicks, dogs, cats) may serve as reservoirs for this disease, as well as humans.<sup>128</sup> The most common mode of transmission is by ingestion of food from contaminated animals or contaminated during processing. The disease usually presents as an acute enterocolitis, with an incubation period ranging from 6 to 72 hours.

The agent may be present in feces, blood, urine, and in food, feed, and environmental materials. Ingestion or parenteral inoculation is the primary laboratory hazards. The importance of aerosol exposure is not known. Naturally or experimentally infected animals are a potential source of infection for laboratory and animal care personnel, and for other animals. Strict compliance with BSL-2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious clinical materials or cultures. This includes conducting procedures with aerosol or high splash potential in primary containment devices such as a BSCs or safety centrifuge cups. Personal protective equipment should be used in accordance with a risk assessment, including splash shields, face protection, gowns, and gloves. The importance of proper gloving techniques and frequent and thorough hand washing is emphasized. Care in manipulating faucet handles to prevent contamination of cleaned hands or the use of sinks equipped with remote water control devices, such as foot pedals, is highly recommended. Special attention to the timely and appropriate decontamination of work surfaces, including potentially contaminated equipment and laboratory fixtures, is strongly advised. ABSL-2 facilities and practices are recommended for activities with experimentally infected animals.

### ***Treponema pallidum*:**

*Treponema pallidum* is a species of extremely fastidious spirochetes that die readily upon desiccation or exposure to atmospheric levels of oxygen, and have not been cultured continuously in vitro. *T. pallidum* cells have lipid-rich outer membranes and are highly susceptible to disinfection with common alcohols (i.e., 70% isopropanol). This species contains three subspecies including *T. pallidum* spp. pallidum (associated with venereal syphilis), *T. pallidum endemicum* (associated with endemic syphilis), and *T. pallidum pertenue* (associated with Yaws). These organisms are obligate human pathogens. *T. pallidum* is a documented hazard to laboratory personnel. Pike lists 20 cases of LAI.<sup>4</sup> Syphilis has been transmitted to personnel working with a concentrated suspension of *T. pallidum* obtained from an experimental rabbit orchitis. *T. pallidum* is present in the circulation during primary and secondary syphilis. The ID<sub>50</sub> of *T. pallidum* needed to infect rabbits by subcutaneous injection has been reported to be as low as 23 organisms. The concentration of *T. pallidum* in patients' blood during early syphilis, however, has not been determined. No cases of laboratory animal-associated infections are reported; however, rabbit-adapted *T. pallidum* retains virulence for humans.

Humans are the only known natural reservoir of *T. pallidum* and transmission occurs via direct sexual contact (venereal syphilis), direct skin contact (Yaws), or direct mucous contact (endemic syphilis). Venereal syphilis is a sexually transmitted disease that occurs in many areas of the world, whereas Yaws occurs in tropical areas of Africa, South America, the Caribbean, and Indonesia. Endemic syphilis is limited to arid areas of Africa and the Middle East. The agent may be present in materials collected from cutaneous and mucosal lesions and in blood. Accidental parenteral inoculation, contact with mucous membranes or broken skin with infectious clinical materials are the primary hazards to laboratory personnel. BSL-2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of blood or other clinical samples from humans or infected rabbits. Gloves should be worn when there is a likelihood of direct skin contact with

infective materials. Periodic serological monitoring should be considered in personnel regularly working with these materials. A BSL-2 practices, containment equipment, and facilities are recommended for work with infected animals. Vaccines are currently not available for use in humans.

### ***Cryptococcus neoformans*:**

*Cryptococcus neoformans* is a monomorphic fungal pathogen existing in nature, in laboratory cultures at room temperature and in vivo as a budding yeast. The sexual stage is grouped with the Basidiomycetes and is characterized by sparse hyphal formation with basidiospores. Both basidiospores and asexual yeasts are infectious. Accidental inoculation of a heavy inoculum of *C. neoformans* into the hands of laboratory workers has occurred during injection or necropsy of laboratory animals. Either a local granuloma or no lesion was reported, suggesting low pathogenicity by this route. Respiratory infections as a consequence of laboratory exposure have not been recorded. The fungus is distributed worldwide in the environment and is associated with pigeon feces. Infections are not transmissible from person-to-person, but require common exposure via the respiratory route to a point source.

Accidental parenteral inoculation of cultures or other infectious materials represents a potential hazard to laboratory personnel, particularly to those who may be immunocompromised. Bites by experimentally infected mice and manipulations of infectious environmental materials (e.g., pigeon feces) may also represent a potential hazard to laboratory personnel. *C. neoformans* has been isolated from bedding of cages housing mice with pulmonary infection indicating the potential for contamination of cages and animal facilities by infected animals.<sup>22</sup> Reports of cutaneous cryptococcal infection following minor skin injuries suggests that localized infection may complicate skin injuries incurred in laboratories that handle *C. neoformans*. BSL-2 and ABSL-2 practices, containment equipment, and facilities are recommended for activities with known or potentially infectious clinical, environmental or culture materials and with experimentally infected animals. This agent and any samples that may contain this agent should also be handled in a Class II BSC.

### **Blood and tissue protozoal parasites:**

Blood and tissue protozoal parasites that pose greatest occupational risk include Babesia, Leishmania, Plasmodium, Toxoplasma, and Trypanosoma. Other tissue protozoa of potential concern include free-living ameba (Acanthamoeba, Balamuthia mandrillaris, Naegleria fowleri) and some species of microsporidia including Encephalitozoon cuniculi that commonly cause extraintestinal infection. Leishmania spp. cause human leishmaniasis; Plasmodium spp. cause human malaria, or some, such as P. cynomolgi cause nonhuman primate malaria; Toxoplasma gondii causes toxoplasmosis; Trypanosoma cruzi causes American trypanosomiasis or Chagas disease; and Trypanosoma brucei gambiense and T. b. rhodesiense cause African trypanosomiasis or (African) sleeping sickness. With the exception of Leishmania and Toxoplasma, these agents are classically thought of as bloodborne and have stages that circulate in the blood. Although not always recognized, both Leishmania and Toxoplasma may have stages that circulate in the blood. Some, such as Plasmodium and Trypanosoma cruzi, also have tissue stages. Leishmania spp. are well recognized to have skin and deep tissue stages and Toxoplasma gondii forms tissue cysts, including in the central nervous system.

Laboratory-acquired infections with Leishmania spp., Plasmodium spp., Toxoplasma gondii, and Trypanosoma spp. have been reported; the majority of these involved needle-stick or other cutaneous exposure to infectious stages of the organisms through abraded skin, including microabrasions.<sup>1,2</sup> Laboratory-acquired infections may be asymptomatic. If clinically manifest, they may exhibit features similar to those seen in naturally acquired infections, although bypassing natural modes of infection could result in atypical signs and symptoms. Cutaneous leishmaniasis could manifest as various types of skin lesions (e.g., nodules, ulcers, plaques), while visceral leishmaniasis may result in fever, hepatosplenomegaly, and pancytopenia. However, only one of the laboratorians known to have become infected with L. (L.) donovani, an organism typically associated with visceral leishmaniasis, developed clinical manifestations of visceral involvement (e.g., fever, splenomegaly, leukopenia).<sup>1</sup> The other laboratorians developed skin lesions. Laboratory-acquired malaria infections may result in fever and chills, fatigue, and hemolytic anemia. Laboratorians can become infected with T. gondii through accidental ingestion of sporulated oocysts, but also may become infected through skin or mucous membrane contact with either tachyzoites or bradyzoites in human or animal tissue or culture. Symptoms in laboratory-acquired T. gondii infections may be restricted to flu-like conditions with enlarged lymph nodes, although rash may be present. Trypanosoma cruzi infection could manifest initially as swelling and redness at the inoculation site, fever, rash, and adenopathy. Myocarditis and electrocardiographic changes may develop. Infection with T. b. rhodesiense and T. b. gambiense also may cause initial swelling and redness at the inoculation site, followed by fever, rash, adenopathy, headache, fatigue and neurologic signs. Blood and tissue protozoal infections associated with exposure to laboratory animals are not common. Potential direct sources of infection for laboratory personnel include accidental needle-stick while inoculating or bleeding animals, contact with lesion

material from cutaneous leishmaniasis, and contact with blood of experimentally or naturally infected animals. In the case of rodents experimentally inoculated with *Toxoplasma gondii* via the intraperitoneal route, contact with peritoneal fluid could result in exposure to infectious organisms. Mosquito-transmitted malaria infections can occur under laboratory conditions as nearly half of the occupationally acquired malaria infections were reported to be vector borne, and contact with body fluids (including feces) of reduviids (triatomines) experimentally or naturally infected with *T. cruzi* poses a risk to laboratory personnel. *Babesia microti* and other *Babesia* spp. can cause human babesiosis or piroplasmiasis. Under natural conditions, *Babesia* is transmitted by the bite of an infected tick, or by blood transfusion; in the United States, hard ticks (*Ixodes*) are the principal vectors. Although no laboratory infections with *Babesia* have been reported, they could easily result from accidental needle-stick or other cutaneous exposure of abraded skin to blood containing parasites. Persons who are asplenic, immunocompromised, or elderly have increased risk for severe illness if infected.

Leishmaniasis is endemic in parts of the tropics, subtropics, and southern Europe, while malaria is widely distributed throughout the tropics. However, the prevalence of these diseases varies widely among endemic areas; the diseases can be very focal in nature. The four species of malaria that infect humans have no animal reservoir hosts. Some *Leishmania* spp. may have a number of important mammalian reservoir hosts, including rodents and dogs. Only cats and other felines can serve as definitive hosts for *Toxoplasma gondii*, which is distributed worldwide. Birds and mammals, including sheep, pigs, rodents, cattle, deer, and humans can be infected from ingestion of tissue cysts or fecal oocysts and subsequently develop tissue cysts throughout the body. Chagas disease occurs from Mexico southward throughout most of Central and South America, with the exception of the southern-most tip of South America. It has been characterized in some accounts as a zoonotic infection, yet the role of animals in maintaining human infection is unclear. A variety of domestic and wild animals are found naturally infected with *T. cruzi*, but human infection undoubtedly serves as the major source of infection for other humans. African trypanosomiasis is endemic in sub-Saharan Africa but is extremely focal in its distribution. Generally, *T. b. gambiense* occurs in West and Central Africa while *T. b. rhodesiense* occurs in East and Southeast Africa. *T. b. rhodesiense* is a zoonotic infection with cattle or, in a more limited role, game animals serving as reservoir hosts, whereas humans are the only epidemiologically important hosts for *T. b. gambiense*. *Leishmania*, *Plasmodium*, and both American and African trypanosomes are all transmitted in nature by blood-sucking insects. Sandflies in the genera *Phlebotomus* and *Lutzomyia* transmit *Leishmania*; mosquitoes in the genus *Anopheles* transmit *Plasmodium*; reduviid (triatomine) bugs such as *Triatoma*, *Rhodnius*, and *Panstrongylus* transmit *T. cruzi* (in the feces rather than the saliva of the bug), and tsetse flies in the genus *Glossina* transmit African trypanosomes.

Infective stages may be present in blood, CSF, bone marrow, or other biopsy tissue, lesion exudates, and infected arthropods. Depending on the parasite, the primary laboratory hazards are skin penetration through wounds or microabrasions, accidental parenteral inoculation, and transmission by arthropod vectors. Aerosol or droplet exposure of organisms to the mucous membranes of the eyes, nose, or mouth are potential hazards when working with cultures of *Leishmania*, *Toxoplasma gondii*, or *T. cruzi*, or with tissue homogenates or blood containing hemoflagellates. Immuno-compromised persons should avoid working with live organisms. Because of the potential for grave consequences of toxoplasmosis in the developing fetus, women who are or might become pregnant and who are at risk for infection with *T. gondii* should receive counseling from their personal physician and employer regarding appropriate means of mitigating the risk (including alternate work assignments, additional PPE, etc.). Working with infectious oocysts poses the greatest risk of acquiring infection; needle-sticks with material containing tachyzoites or bradyzoites also pose a significant risk. Infection with tachyzoites or bradyzoites through mucous membranes or skin abrasions is also possible. Kittens and cats that might be naturally infected with *Toxoplasma* pose some risk to personnel.<sup>5</sup> Good hygiene and use of personal protection measures would reduce the risk. One laboratory infection with microsporidia has been reported, associated with conjunctival exposure to spores leading to the development of keratoconjunctivitis. Infection could also result from ingestion of spores in feces, urine, sputum, CSF, or culture. No laboratory-acquired infections have been reported with *Acanthamoeba* spp., *Balamuthia mandrillaris* or *Naegleria fowleri*; however, the possibility of becoming infected by inhalation, by accidental needlesticks, or through exposure to mucous membranes or microabrasions of the skin should be considered. BSL-2 and ABSL-2 practices, containment equipment, and facilities are recommended for activities with infective stages of the parasites listed. Infected arthropods should be maintained in facilities that reasonably preclude the exposure of personnel or the escape of insects. Personal protection (e.g., lab coat, gloves, face shield), in conjunction with containment in a BSC, is indicated when working with cultures, tissue homogenates, or blood containing organisms.

### **Intestinal protozoal parasites:**

Intestinal protozoal parasites that pose greatest occupational risk include *Cryptosporidium*, *Isospora*, *Entamoeba histolytica*, and *Giardia*. Other intestinal pathogens of concern are some species of microsporidia, specifically *Septata intestinalis* and *Enterocytozoon bieneusi*. *Cryptosporidium parvum*, *C. hominis*, and *Isospora belli* cause

intestinal coccidiosis, most often referred to as cryptosporidiosis and isosporiasis, respectively. *Entamoeba histolytica* can cause both intestinal and extraintestinal infection (e.g., liver abscess) called amebiasis, and *Giardia intestinalis* causes giardiasis. Laboratory-acquired infections with *Cryptosporidium* spp., *E. histolytica*, *G. intestinalis*, and *I. belli* have been reported.<sup>1-3</sup> The mode of exposure in laboratory-acquired infections in this group of agents mimics the natural infection routes for the most part, and consequently, clinical symptoms are typically very similar to those seen in naturally acquired infections. For *Cryptosporidium*, *E. histolytica*, *G. intestinalis*, and *I. belli*, the common clinical manifestations are symptoms of gastroenteritis (e.g., diarrhea, abdominal pain and cramping, loss of appetite). Infection with *E. histolytica* may result in bloody stools. Laboratory animal-associated infections with this group of organisms have been reported and provide a direct source of infection for laboratory personnel who are exposed to feces of experimentally or naturally infected animals.<sup>3</sup> Handling *Cryptosporidium* oocysts requires special care, as laboratory-acquired infections have occurred commonly in personnel working with this agent, especially if calves are used as the source of oocysts. Other experimentally infected animals pose potential risks as well. Circumstantial evidence suggests that airborne transmission of oocysts of this small organism (i.e., 4-6 µm diameter) may occur. Rigid adherence to protocol should reduce the occurrence of laboratory-acquired infection in laboratory and animal care personnel.

All of these intestinal protozoa have a cosmopolitan distribution, and in some settings, including developed countries, the prevalence of infection can be high. The natural mode of infection for this group of organisms is typically ingestion of an environmentally hardy oocyst (for the coccidia) or cyst (for *E. histolytica* and *G. intestinalis*). The ID<sub>50</sub>, best established for *Cryptosporidium*, has been shown for some strains to be 5-10 oocysts. This suggests that even a single oocyst might pose a risk for infection in an exposed laboratorian. The infectious dose for other parasites in this group is not as well established, but is probably in the same range. Further, because these protozoa multiply in the host, ingestion of even small inocula can cause infection and illness. The role for animal reservoir hosts is diverse in this group of organisms. In the case of *C. hominis*, principally humans are infected, whereas for *C. parvum*, humans, cattle, and other mammals can be infected and serve as reservoir hosts for human infection. In the case of *E. histolytica*, humans serve as the only significant source of infection, and there is no convincing evidence that any animal serves as reservoir host for *I. belli*. The extent to which *Giardia* spp. parasitizing animals can infect humans is only now becoming better understood, but most human infection seems to be acquired from human-to-human transmission. The organisms in this group do not require more than one host to complete their life cycle because they infect, develop, and result in shedding of infectious stages all in a single host. Ingestion of contaminated drinking or recreational water has also been a common source of cryptosporidiosis and giardiasis. Infective stages may be present in the feces or other body fluids and tissues. Depending on the parasite, ingestion is the primary laboratory hazard. Immunocompromised persons should avoid working with live organisms. Laboratorians who work only with killed or inactivated parasite materials, or parasite fractions, are not at significant risk. Similarly, no accidental laboratory infection with *Sarcocystis* has been reported. BSL-2 and ABSL-2 practices, containment equipment, and facilities are recommended for activities with infective stages of the parasites.

### ***Hepatitis A and E virus:***

*Hepatitis A virus* is a positive single-stranded RNA virus, the type species of the Hepatovirus genus in the family *Picornaviridae*. *Hepatitis E virus* is a positive single-stranded RNA virus, the type species of the genus *Hepevirus*, a floating genus not assigned to any family. Laboratory-associated infections with hepatitis A or E viruses do not appear to be an important occupational risk among laboratory personnel. However, hepatitis A is a documented hazard in animal handlers and others working with naturally or experimentally infected chimpanzees and other nonhuman primates.<sup>29</sup> Workers handling other recently captured, susceptible primates (owl monkeys, marmosets) also may be at risk for hepatitis A infection. Hepatitis E virus appears to be less of a risk to personnel than hepatitis A virus, except during pregnancy, when infection can result in severe or fatal disease. Most infections with hepatitis A are foodborne and occasionally water-borne. The virus is present in feces during the prodromal phase of the disease and usually disappears once jaundice occurs. Hepatitis E virus causes acute enterically transmitted cases of hepatitis, mostly waterborne. In Asia, epidemics involving thousands of cases have occurred.

The agents may be present in feces and blood of infected humans and nonhuman primates. Feces, stool suspensions, and other contaminated materials are the primary hazards to laboratory personnel. Care should be taken to avoid puncture wounds when handling contaminated blood from humans or nonhuman primates. There is no evidence that aerosol exposure results in infection. BSL-2 practices, containment equipment, and facilities are recommended for the manipulation of hepatitis A and E virus, infected feces, blood or other tissues. ABSL-2 practices and facilities are recommended for activities using naturally or experimentally-infected nonhuman primates or other animal models that may shed the virus. A licensed inactivated vaccine against hepatitis A is available. Vaccines against hepatitis E are not currently available.

### ***Hepatitis B and C virus:***

*Hepatitis B virus (HBV)* is the type species of the *Orthohepadnavirus* genus in the family *Hepadnaviridae*. *Hepatitis C virus (HCV)* is the type species of the *Hepacivirus* genus in the family *Flaviviridae*. *Hepatitis D virus (HDV)* is the only member of the genus *Deltavirus*. These viruses are naturally acquired from a carrier during blood transfusion, vaccination, tattooing, or body piercing with inadequately sterilized instruments. Non-parenteral routes, such as domestic contact and unprotected (heterosexual and homosexual) intercourse, are also major modes of transmission. Individuals who are infected with the HBV are at risk of infection with HDV, a defective RNA virus that requires the presence of HBV virus for replication. Infection with HDV usually exacerbates the symptoms caused by HBV infection. Hepatitis B has been one of the most frequently occurring laboratory-associated infections, and laboratory workers are recognized as a high-risk group for acquiring such infections.<sup>30</sup> Hepatitis C virus infection can occur in the laboratory situation as well. The prevalence of antibody to hepatitis C (anti-HCV) is slightly higher in medical care workers than in the general population. Epidemiologic evidence indicates that HCV is spread predominantly by the parenteral route.

HBV may be present in blood and blood products of human origin, in urine, semen, CSF and saliva. Parenteral inoculation, droplet exposure of mucous membranes, and contact exposure of broken skin are the primary laboratory hazards.<sup>33</sup> The virus may be stable in dried blood or blood components for several days. Attenuated or avirulent strains have not been identified. HCV has been detected primarily in blood and serum, less frequently in saliva and rarely or not at all in urine or semen. It appears to be relatively unstable to storage at room temperature and repeated freezing and thawing. BSL-2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious body fluids and tissues. Additional primary containment and personnel precautions, such as those described for BSL-3, may be indicated for activities with potential for droplet or aerosol production and for activities involving production quantities or concentrations of infectious materials. ABSL-2 practices, containment equipment and facilities are recommended for activities utilizing naturally or experimentally infected chimpanzees or other NHP. Gloves should be worn when working with infected animals and when there is the likelihood of skin contact with infectious materials. In addition to these recommended precautions, persons working with HBV, HCV, or other bloodborne pathogens should consult the OSHA Bloodborne Pathogen Standard. Licensed recombinant vaccines against hepatitis B are available and are highly recommended for and offered to laboratory personnel.<sup>35</sup> Vaccines against hepatitis C and D are not yet available for use in humans, but vaccination against HBV will also prevent HDV infection.

### ***Human Herpes virus:***

The *herpesviruses* are ubiquitous human pathogens and are commonly present in a variety of clinical materials submitted for virus isolation. Thus far, nine *herpesviruses* have been isolated from humans: *herpes simplex virus-1 (HSV-1)*, *HSV-2*, *human cytomegalovirus (HCMV)*, *varicella-zoster virus (VZV)*, *EpsteinBarr virus (EBV)*, and *human herpesviruses (HHV) 6A, 6B, 7, and 8*.<sup>41</sup> *HSV* infection is characterized by a localized primary lesion. Primary infection with HSV-1 may be mild and unapparent occurring in early childhood. In approximately 10% of infections, overt illness marked by fever and malaise occurs. HSV-1 is a common cause of meningoencephalitis. Genital infections, usually caused by *HSV-2*, generally occur in adults and are sexually transmissible. Neonatal infections are most frequently caused by HSV-2 but HSV-1 infections are also common. In the neonate, disseminated disease and encephalitis are often fatal. EBV is the cause of infectious mononucleosis. It is also associated with the pathogenesis of several lymphomas and nasopharyngeal cancer.<sup>42</sup> EBV is serologically distinct from the other *herpesviruses*; it infects and transforms B-lymphocytes. HCMV infection is common and often undiagnosed presenting as a nonspecific febrile illness. HCMV causes up to 10% of all cases of mononucleosis in young adults. The most severe form of the disease is seen in infants infected in utero. Children surviving infection may evidence mental retardation, microencephaly, motor disabilities and chronic liver disease.<sup>42</sup> HCMV is one of the most common congenital diseases.

VZV is the causative agent of chickenpox and herpes zoster. Chickenpox usually occurs in childhood and zoster occurs more commonly in adults. HHV-6 is the causative agent of exanthema subitum (roseola), a common childhood exanthem. Nonspecific febrile illness and febrile seizures are also clinical manifestations of disease. HHV-6 may reactivate in immunocompetent individuals during pregnancy or during critical illness. Two distinct variants, HHV-6A and HHV-6B, exist, the latter causing roseola. HHV-7 is a constitutive inhabitant of adult human saliva. Clinical manifestations are less well understood but the virus has also been associated with roseola. HHV-8, also known as Kaposi's sarcoma-associated virus, was first identified by Chang and co-workers in 1994. HHV-8 is believed to be the causative agent of Kaposi's sarcoma and has been associated with primary effusion lymphoma. The natural history of HHV-8 has not been completely elucidated. High risk groups for HHV-8 include HIV-infected men who have sex with men and individuals from areas of high endemicity, such

as Africa or the Mediterranean. The prevalence of HHV-8 is also higher among intravenous drug users than in the general population. At least one report has provided evidence that in African children, HHV-8 infection may be transmitted from mother to child. While few of the human herpesviruses have been demonstrated to cause laboratory-acquired infections, they are both primary and opportunistic pathogens, especially in immunocompromised hosts.

Few of the human herpesviruses have been documented as sources of laboratory acquired infections. In a limited study, Gartner and co-workers have investigated the HHV-8 immunoglobulin G (IgG) seroprevalence rates for healthcare workers caring for patients with a high risk for HHV-8 infection in a non-endemic area. Healthcare workers in contact with risk group patients were infected more frequently than healthcare workers without contact with risk groups. Workers without contact with risk group patients were infected no more frequently than the control group. Although this diverse group of indigenous viral agents has not demonstrated a high potential hazard for laboratory-associated infection, frequent presence in clinical materials and common use in research warrant the application of appropriate laboratory containment and safe practices. Given the wide array of viruses included in this family, the natural modes of infection vary greatly, as does the pathogenesis of the various viruses. Some have wide host ranges, multiply effectively, and rapidly destroy the cells they infect (*HSV-1*, *HSV-2*). Others have restricted host ranges or long replicative cycles (HHV-6).<sup>41</sup> Transmission of human *herpesviruses* in nature are, in general, associated with close, intimate contact with a person excreting the virus in their saliva, urine, or other bodily fluids. VZV is transmitted person-to-person through direct contact, through aerosolized vesicular fluids and respiratory secretions, and indirectly transmitted by fomites. Latency is a trait common to most *herpesviruses*, although the site and duration vary greatly. For example, EBV will persist in an asymptomatic, latent form in the host immune system, primarily in EBV-specific cytotoxic T cells while latent HSV has been detected only in sensory neurons.<sup>48,49</sup> HHV-8 has been transmitted through organ transplantation<sup>50</sup> and blood transfusion;<sup>51</sup> some evidence suggests non-sexual horizontal transmission.

Clinical materials and isolates of *herpesviruses* may pose a risk of infection following ingestion, accidental parenteral inoculation, and droplet exposure of the mucous membranes of the eyes, nose, or mouth, or inhalation of concentrated aerosolized materials. HHV-8 may be present in human blood or blood products and tissues or saliva. Aerosol transmission cannot be excluded as a potential route of transmission. Clinical specimens containing the more virulent *Herpesvirus simiae* (B-virus) may be inadvertently submitted for diagnosis of suspected herpes simplex infection. HCMV may pose a special risk during pregnancy because of potential infection of the fetus. All human *herpesviruses* pose an increased risk to persons who are immunocompromised. BSL-2 practices, containment equipment, and facilities are recommended for activities utilizing known or potentially infectious clinical materials or cultures of indigenous viral agents that are associated or identified as a primary pathogen of human disease. Although there is little evidence that infectious aerosols are a significant source of LAI, it is prudent to avoid the generation of aerosols during the handling of clinical materials or isolates, or during the necropsy of animals. Primary containment devices (e.g., BSC) should be utilized to prevent exposure of workers to infectious aerosols. Additional containment and procedures, such as those described for BSL-3, should be considered when producing, purifying, and concentrating human *herpesviruses*, based on risk assessment.

### ***Influenza virus:***

Influenza is an acute viral disease of the respiratory tract. The most common clinical manifestations are fever, headache, malaise, sore throat and cough. GI tract manifestations (nausea, vomiting and diarrhea) are rare but may accompany the respiratory phase in children. The two most important features of influenza are the epidemic nature of illness and the mortality that arises from pulmonary complications of the disease.<sup>54</sup> The influenza viruses are enveloped RNA viruses belonging to the *Orthomyxoviridae*. There are three serotypes of influenza viruses, A, B and C. Influenza A is further classified into subtypes by the surface glycoproteins that possess either hemagglutinin (H) or neuraminidase (N) activity. Emergence of completely new subtypes (antigenic shift) occurs at irregular intervals with Type A viruses. New subtypes are responsible for pandemics and can result from reassortment of human and avian influenza virus genes. Antigenic changes within a type or subtype (antigenic drift) of A and B viruses are ongoing processes that are responsible for frequent epidemics and regional outbreaks and make the annual reformulation of influenza vaccine necessary. Influenza viral infections, with different antigenic subtypes, occur naturally in swine, horses, mink, seals and in many domestic and wild avian species. Interspecies transmission and reassortment of influenza A viruses have been reported to occur among humans and wild and domestic fowl. The *human influenza viruses* responsible for the 1918, 1957 and

1968 pandemics contained gene segments closely related to those of avian influenza viruses.<sup>55</sup> Swine influenza has also been isolated in human outbreaks.

LAI have not been routinely documented in the literature, but informal accounts and published reports indicate that such infections are known to have occurred, particularly when new strains showing antigenic shift or drift are introduced into a laboratory for diagnostic/research purposes. Occupationally-acquired, nosocomial infections are documented. Laboratory animal-associated infections have not been reported; however, there is possibility of human infection acquired from infected ferrets and vice versa. Airborne spread is the predominant mode of transmission especially in crowded, enclosed spaces. Transmission may also occur through direct contact since influenza viruses may persist for hours on surfaces particularly in the cold and under conditions of low humidity. The incubation period is from one to three days. Recommendations for treatment and prophylaxis of influenza are available. The agent may be present in respiratory tissues or secretions of humans and most infected animals and birds. In addition, the agent may be present in the intestines and cloacae of many infected avian species. Influenza viruses may be disseminated in multiple organs in some infected animal species. The primary laboratory hazard is inhalation of virus from aerosols generated by infecting animals or by aspirating, dispensing, mixing, centrifuging or otherwise manipulating virus-infected samples. In addition, laboratory infection can result from direct inoculation of mucus membranes through virus-contaminated gloves following handling of tissues, feces or secretions from infected animals. Genetic manipulation has the potential for altering the host range, pathogenicity, and antigenic composition of influenza viruses. The potential for introducing influenza viruses with novel genetic composition into humans is unknown. BSL-2 facilities, practices and procedures are recommended for diagnostic, research and production activities utilizing contemporary, circulating human influenza strains (e.g., H1/H3/B) and low pathogenicity avian influenza (LPAI) strains (e.g., H1-4, H6, H8-16), and *equine and swine influenza viruses*. ABSL-2 is appropriate for work with these viruses in animal models. All avian and swine influenza viruses require an APHIS permit. Based on economic ramifications and source of the virus, LPAI H5 and H7 and *swine influenza viruses* may have additional APHIS permit-driven containment requirements and personnel practices and/or restrictions.

Non-contemporary, wild-type human influenza (H2N2) strains should be handled with increased caution. Important considerations in working with these strains are the number of years since an antigenically related virus last circulated and the potential for presence of a susceptible population. BSL-3 and ABSL-3 practices, procedures and facilities are recommended with rigorous adherence to additional respiratory protection and clothing change protocols. Negative pressure, HEPA filtered respirators or positive air-purifying respirators (PAPRs) are recommended for use. Cold-adapted, live attenuated H2N2 vaccine strains may continue to be worked with at BSL-2. Any research involving reverse genetics of the 1918 influenza strain should proceed with extreme caution. The risk to laboratory workers is unknown, but the pandemic potential is thought to be significant. Until further risk assessment data are available, the following practices and conditions are recommended for manipulation of reconstructed 1918 *influenza viruses* and laboratory animals infected with the viruses. These practices and procedures are considered minimum standards for work with the fully reconstructed virus. BSL-3 and ABSL-3 practices, procedures and facilities. Large laboratory animals such as NHP should be housed in primary barrier systems in ABSL-3 facilities. Rigorous adherence to additional respiratory protection and clothing change protocols. Use of negative pressure, HEPA-filtered respirators or PAPRs. Use of HEPA filtration for treatment of exhaust air. Amendment of personnel practices to include personal showers prior to exiting the laboratory

### **SARS:**

SARS is a viral respiratory illness caused by a previously undescribed coronavirus, SARS-associated coronavirus (SARS-CoV) within the family Coronaviridae. SARS was retrospectively recognized in China in November 2002. Over the next few months, the illness spread to other south-east. Asian countries, North America, South America, and Europe following major airline routes. The majority of disease spread occurred in hospitals, among family members and contacts of hospital workers. From November 2002 through July 2003, when the global outbreak was contained, a total of 8,098 probable cases of SARS were reported to the WHO from 29 countries.<sup>89</sup> In general, SARS patients present with fever (temperature greater than 100.4°F [ $>38.0^{\circ}\text{C}$ ]), malaise and myalgias quickly followed by respiratory symptoms including shortness of breath and cough. Ten to 20 percent of patients may have diarrhea. Review of probable cases indicates that the shortness of breath sometimes rapidly progresses to respiratory failure requiring ventilation. The case fatality rate is about 11%.

Healthcare workers are at increased risk of acquiring SARS from an infected patient especially if involved in pulmonary/respiratory procedures such as endotracheal intubation, aerosolization or nebulization of medications, diagnostic sputum induction, airway suctioning, positive pressure ventilation and highfrequency oscillatory ventilation. Two confirmed episodes of SARS-CoV transmission to laboratory workers occurred in research laboratories in Singapore and Taiwan.<sup>89,90</sup> Both occurrences were linked to breaches in laboratory

practices. Laboratory-acquired infections in China during 2004 demonstrated secondary and tertiary spread of the disease to close contacts and healthcare providers of one of the employees involved.<sup>91</sup> Although no laboratory-acquired cases have been associated with the routine processing of diagnostic specimens, SARS coronavirus represents an emerging infectious disease for which risk to the medical and laboratory community is not fully understood. The mode of transmission in nature is not well understood. It appears that SARS is transmitted from person-to-person through close contact such as caring for, living with, or having direct contact with respiratory secretions or body fluids of a suspect or probable case.<sup>92</sup> SARS is thought to be spread primarily through droplets, aerosols and possibly fomites. The natural reservoir for SARS CoV is unknown.

SARS-CoV may be detected in respiratory, blood, or stool specimens. The exact mode of transmission of SARS-CoV laboratory-acquired infection has not been established, but in clinical settings the primary mode of transmission appears through direct or indirect contact of mucous membranes with infectious respiratory droplets.<sup>93,94</sup> In clinical laboratories, whole blood, serum, plasma and urine specimens should be handled using Standard Precautions, which includes use of gloves, gown, mask, and eye protection. Any procedure with the potential to generate aerosols (e.g., vortexing or sonication of specimens in an open tube) should be performed in a BSC. Use sealed centrifuge rotors or gasketed safety carriers for centrifugation. Rotors and safety carriers should be loaded and unloaded in a BSC. Procedures conducted outside a BSC must be performed in a manner that minimizes the risk of personnel exposure and environmental release. The following procedures may be conducted in the BSL-2 setting: pathologic examination and processing of formalin-fixed or otherwise inactivated tissues, molecular analysis of extracted nucleic acid preparations, electron microscopic studies with glutaraldehyde-fixed grids, routine examination of bacterial and fungal cultures, routine staining and microscopic analysis of fixed smears, and final packaging of specimens for transport to diagnostic laboratories for additional testing (specimens should already be in a sealed, decontaminated primary container). Activities involving manipulation of untreated specimens should be performed in BSL-2 facilities following BSL-3 practices. In the rare event that a procedure or process involving untreated specimens cannot be conducted in a BSC, gloves, gown, eye protection, and respiratory protection (acceptable methods of respiratory protection include: a properly fit-tested, National Institute for Occupational Safety and Health [NIOSH]-approved filter respirator [N-95 or higher level] or a PAPR equipped with HEPA filters) should be used. All personnel who use respiratory protective devices should be enrolled in an appropriately constituted respiratory protection program.

#### **Agriculture pathogen biosafety:**

Risk assessment and management guidelines for agriculture differ from human public health standards. Risk management for agriculture research is based on the potential economic impact of animal and plant morbidity, and mortality, and the trade implications of disease. Agricultural guidelines take this difference into account. Worker protection is important but great emphasis is placed on reducing the risk of agent escape into the environment. This Appendix describes the facility parameters and work practices of what has come to be known as BSL-3-Ag. BSL-3-Ag is unique to agriculture because of the necessity to protect the environment from an economic, high risk pathogen in a situation where studies are conducted employing large agricultural animals or other similar situations in which the facility barriers now serve as primary containment. Also described are some of the enhancements beyond BSL-3 that may be required by USDA/APHIS when working in the laboratory or vivarium with veterinary agents of concern. This Appendix provides guidance and is not regulatory nor is it meant to describe policy. Conditions for approval to work with specific agricultural agents are provided at the time USDA/APHIS permits a location to work with an agent. In agriculture, special biocontainment features are required for certain types of research involving high consequence livestock pathogens in animal species or other research where the room provides the primary containment. To support such research, USDA has developed a special facility designed, constructed and operated at a unique animal containment level called BSL- 3-Ag. Using the containment features of the standard ABSL-3 facility as a starting point, BSL-3-Ag facilities are specifically designed to protect the environment by including almost all of the features ordinarily used for BSL-4 facilities as enhancements. All BSL-3-Ag containment spaces must be designed, constructed and certified as primary containment barriers. 344 Biosafety in Microbiological and Biomedical Laboratories The BSL-3-Ag facility can be a separate building, but more often, it is an isolated zone within a facility operating at a lower biosafety level, usually at BSL-3. This isolated zone has strictly controlled access with special physical security measures and functions on the “box within a box” principle.

#### **Foot and mouth disease virus:**

FMD is a severe, highly communicable viral disease of cloven-hoofed animals (cattle, swine, sheep, and goats), causing fever, malaise, vesicular lesions in affected livestock and in some cases death in young animals due to myocardial lesions.<sup>22</sup> It can also affect a variety of wild ruminants (e.g., deer, bison). FMD is one of the most devastating diseases of livestock, causing large economic losses when introduced to FMD-free countries. The

etiologic agent, FMD virus (FMDV), is a member of the aphthovirus genus, family picornaviridae with seven serotypes (A, O, C, Asia1, SAT1, SAT2 and SAT3).<sup>23</sup> Humans are considered accidental hosts for FMDV and rarely become infected or develop clinical disease. Historically, humans have been exposed to large quantities of FMDV both during natural outbreaks among large herds of animals and in laboratory settings. Despite this, there has been an extremely low incidence of human infections reported and many have been anecdotal. Reports of fever, headaches and vesicles in the skin (especially at an accidental inoculation site) and oral mucosa have been associated with documented FMDV infections. The symptoms can be easily mistaken with those of Hand, Foot and Mouth Disease caused by coxsackie A viruses. On the other hand, humans have been shown to carry virus in their throats for up to three days after exposure to aerosols from infected animals, potentially making them carriers of FMDV. Humans and their clothing and footwear have been implicated as fomites for transmission of FMDV during outbreaks. Therefore, most FMDV laboratories impose a five day period of contact avoidance with susceptible species for personnel working with the viruses.

Laboratory practices for FMDV are principally designed to prevent transmission to susceptible livestock, but also to protect workers. The greatest risk of working with FMD is the escape of the organism into susceptible animal populations, which would necessitate USDA emergency procedures to contain and eradicate the disease. The virus is considered a cause of a foreign animal disease in the United States. Due to the highly contagious nature and the severe economic consequences of disease presence in the United States, this virus should only be handled in vitro in a BSL-3 laboratory with enhancements as required by the USDA (see Section IV of this Appendix) and in vivo in USDA-approved BSL-3-Ag animal facilities. Infected animals are handled with standard protection (gloves, protective clothing). Change of clothing, personal showers and clearing of the throat and nose are required upon exiting contaminated areas in order to minimize virus transmission to susceptible species. Laboratory workers should have no contact with susceptible hosts for five days after working with the agent. In the United States, the Plum Island Animal Disease Center in New York is the only laboratory authorized to possess and work with this agent.

#### ***Newcastle disease virus:***

ND is one of the most serious infectious diseases of poultry worldwide. It is primarily a respiratory disease, but nervous and enteric forms occur. All bird species are probably susceptible to infection with ND virus (*NDV*). The severity of the disease caused by any given *NDV* strain can vary from an unapparent infection to 100% mortality. The chicken is the most susceptible species. The biocontainment requirements for working with a particular strain are based on the virulence of the virus as determined by chicken inoculation and more recently by determination of amino acid sequence of the fusion protein cleavage site (as defined by the World Organization for Animal Health).<sup>35</sup> The virus is shed in respiratory secretions and in feces. Natural transmission among birds occurs by aerosol inhalation or by consumption of contaminated feed or water. *NDV* is classified in the *Avulavirus* genus within the family *Paramyxoviridae*, subfamily *Paramyxovirinae*, in the order Mononegavirales. All *NDV* isolates are of a single serotype avian *paramyxovirus* type 1 (APMV-1) that includes the antigenic variants isolated from pigeons called pigeon *paramyxovirus1*. All strains are readily propagated in embryonated chicken eggs and a variety of avian and mammalian cell cultures although special additives may be required to propagate the low virulence (lentogenic) viruses in some cell types. The most common infection is a self-limiting conjunctivitis with tearing and pain that develops within 24 hours of an eye exposure by aerosol, splash of infective fluids, or eye contact with contaminated hands. The occurrence of upper respiratory or generalized symptoms is rare. *NDV* isolates may be recovered from any infected bird, but on occasion may be recovered from humans infected by contact with infected poultry. Humans treated with live *NDV* in experimental cancer therapies, or those who are exposed by laboratory contamination also are sources of the virus. The greatest risk is for susceptible birds that may be exposed to *NDV*. If isolates of moderate to high virulence for chickens are used for human cancer therapies, those isolates are probably of greater risk for inadvertent exposure of birds and poultry than they are to the humans handling or being treated with those viruses.

#### **Integrated pest management:**

Integrated pest management, or IPM, is a process you can use to solve pest problems while minimizing risks to people and the environment. IPM can be used to manage all kinds of pests anywhere—in urban, agricultural, and wildland or natural areas. IPM focuses on long-term prevention of pests or their damage by managing the ecosystem. With IPM, you take actions to keep pests from becoming a problem, such as by growing a healthy crop that can withstand pest attacks, using disease-resistant plants, or caulking cracks to keep insects or rodents from entering a building. Rather than simply eliminating the pests you see right now, using IPM means you'll look at environmental factors that affect the pest and its ability to thrive. Armed with this information, you can create conditions that are unfavorable for the pest. In IPM, monitoring and correct pest identification help you

decide whether management is needed Monitoring means checking your field, landscape, forest, or building—or other site—to identify which pests are present, how many there are, or what damage they've caused. Correctly identifying the pest is a key to knowing whether a pest is likely to become a problem and determining the best management strategy. After monitoring and considering information about the pest, its biology, and environmental factors, you can decide whether the pest can be tolerated or whether it is a problem that warrants control. If control is needed, this information also helps you select the most effective management methods and the best time to use them. The most effective, long-term way to manage pests is by using a combination of methods that work better together than separately. Approaches for managing pests are often grouped in the following categories.

- Biological control is the use of natural enemies—predators, parasites, pathogens, and competitors—to control pests and their damage. Invertebrates, plant pathogens, nematodes, weeds, and vertebrates have many natural enemies.
- Cultural controls are practices that reduce pest establishment, reproduction, dispersal, and survival. For example, changing irrigation practices can reduce pest problems, since too much water can increase root disease and weeds.
- Mechanical and physical controls kill a pest directly or make the environment unsuitable for it. Traps for rodents are examples of mechanical control. Physical controls include mulches for weed management, steam sterilization of the soil for disease management, or barriers such as screens to keep birds or insects out.
- Chemical control is the use of pesticides. In IPM, pesticides are used only when needed and in combination with other approaches for more effective, long-term control. Also, pesticides are selected and applied in a way that minimizes their possible harm to people and the environment. With IPM you'll use the most selective pesticide that will do the job and be the safest for other organisms and for air, soil, and water quality; use pesticides in bait stations rather than sprays; or spot-spray a few weeds instead of an entire area.

These IPM principles and practices are combined to create IPM programs. While each situation is different, five major components are common to all IPM programs and these are pest identification, Monitoring and assessing pest numbers and damage, Guidelines for when management action is needed, preventing pest problems and using a combination of biological, cultural, physical/mechanical and chemical management tools.

#### **BSC Class I:**

Class I cabinets provide personnel and environmental protection but no product protection. In fact, the inward flow of air can contribute to contamination of samples. Inward airflow is maintained at a minimum velocity of 75 ft/min (0.38 m/s). These BSCs are commonly used to enclose specific equipment (*e.g.* centrifuges) or procedures (*e.g.* aerating cultures) that potentially generate aerosols. BSCs of this class are either ducted (connected to the building exhaust system) or unducted (recirculating filtered exhaust back into the laboratory).

#### **BSC Class II:**

Class II cabinets provide both kinds of protection (of the samples and of the environment) since makeup air is also HEPA-filtered. There are four types: Type A1 (formerly A), Type A2 (formerly A/B3), Type B1, and Type B2. Each type's requirements are defined by NSF International Standard 49, which in 2002 reclassified A/B3 cabinets (classified under the latter type if connected to an exhaust duct) as Type A2. About 95% of all biosafety cabinets installed are Type A2 cabinets. The principle of operation involves using a fan mounted in the top of the cabinet to draw a curtain of sterile air over the products that are being handled. The air is then drawn underneath the work surface and back up to the top of the cabinet where it passes through the HEPA filters. The air that is exhausted is made up by air being drawn into the front of the cabinet underneath the work surface. The air being drawn in acts as a barrier to potentially contaminated air coming back out to the operator. The Type A1 cabinet, formerly known as Type A, has a minimum inflow velocity of 75 ft/min. The filtered makeup air is divided equally over the work surface at about two to six inches above the work surface. Exhaust is drawn at the bottom of the cabinet where it rises to the top. At the top of the cabinet, 70% of the air recirculates through the supply HEPA filter, the other 30% of air exhausted through the exhaust HEPA filter. This is due to the relative sizes of the two filters, and dampers typically allow the adjustment of this ratio. This type is not safe for work with hazardous chemicals except when ducted, usually with a "thimble" or canopy hood to avoid disturbing internal air flow.

The Type A2 cabinet, formerly designated A/B3, has a minimum inflow velocity of 100 ft/min. A negative air pressure plenum surrounds all contaminated plenums that are under positive pressure. In other respects, the

specifications are identical to those of a Type A1 cabinet. The Type B1 and B2 cabinets have a minimum inflow velocity of 100 ft/min, and these cabinets must be hard-ducted to an exhaust system rather than exhausted through a thimble connection. In contrast to the type A1 and A2 cabinets, 60% of air from the rear grille is exhausted and only 40% is recirculated. Since exhaust air is drawn from the rear grille, the CDC advises that work with chemicals be conducted in the rear of the cabinet. The Type B2 cabinet is expensive to operate because no air is recirculated within. Therefore, this type is mainly found in such applications as toxicology laboratories, where the ability to safely use hazardous chemicals is important. Additionally, there is the risk that contaminated air would flow into the laboratory if the exhaust system for a Type B1 or B2 cabinet were to fail. To mitigate this risk, cabinets of these types generally monitor the exhaust flow, shutting off the supply blower and sounding an alarm if the exhaust flow is insufficient. Class II cabinets are the commonly used cabinets in clinical and research laboratories.

### **BSC Class III:**

The Class III cabinet, generally only installed in maximum containment laboratories, is specifically designed for work with BSL-4 pathogenic agents, providing maximum protection. The enclosure is gas-tight, and all materials enter and leave through a dunk tank or double-door autoclave. Gloves attached to the front prevent direct contact with hazardous materials (Class III cabinets are sometimes called glove box). These custom-built cabinets often attach into a line, and the lab equipment installed inside is usually custom-built as well.

### **Biosafety and biosecurity in hematology:**

Biosafety guidelines in hematology lab are:

- lab workers should wear personal protective equipment
- work surfaces should be decontaminated on completion of work --disinfectants
- all disposable waste should be autoclaved
- procedure / process cannot be conducted in BSC
- performed while wearing gloves, gown, goggles and a fit tested N-95 mask
- acceptable methods of respiratory protection include
- approved filter respirator, powered air-purifying respirator
- HEPA filters
- appropriate physical containment devices (e.g. centrifuge safety cups; sealed rotors) should also be used
- rotors and cups should be loaded and unloaded in a BSC
- blood samples will arrive in an EDTA vial or in a non-EDTA vial
- storage of any specimen for future testing must be done with the utmost caution
- specimen - placed in a disposable rack
- rack placed into a biohazard bag and sealed
- specimens taken out of the bag on arrival to the lab
- outside of container should be wiped with a disinfectant
- cells / plasma will be separated by a Blood Bank staff member
- designated Blood Bank staff member will wear all barrier protection
- minimizes the risk of exposure from aerosol/ spills
- lab workers should receive training on the appropriate Biosafety level for the type of work being performed
- disposable hemacytometers will be used
- lab biosecurity training
- roles, responsibilities and authorities of staff
- maintenance and cleaning personnel, and to external first-responders
- responsible staff involved in ensuring the security of the laboratory facility
- lab biosecurity elements

### **Biosafety and biosecurity in Nanotechnology:**

There is research and development in life sciences. Science has a potential to bring transformational change for the betterment of society. One of the fields is Nanotechnology. Risks-misuse of the technological advances cannot be ignored. Development of technology / applications based on understanding of nanoscale processes such as borrows techniques from molecular biology, bioconjugation, synthetic chemistry, and extension-biotechnology. This improves healthcare, increase agricultural/industrial productivity. These enable effective environmental policies should be developed for biosafety and biosecurity concerns. The development of nanotechnology has resulted need to identify and implement appropriate safety mechanisms to protect the health of workers and the public biosafety programs now include a nanotechnology program. When there is a potential health threat to humans from the inhalation, ingestion, or skin contact with nano-sized materials. Strength durability, flexibility, performance, physical properties are associated with NP has been exploited in a multitude of industries. Treatment modalities - detection of tumors, targeted drug delivery, and prognostic visual monitoring of therapy. Workplace exposures in combination with other toxic agents may cause unpredictable adverse health effects. Nanotechnology has a failure to address these human health issues. Inhalation NPs may evade phagocytosis, cross cell- membrane, and redistribute to other sites of the body cause systemic health effects.

### **Biosafety and biosecurity in Cybernetics:**

Concepts of safety and security used are interchangeably. Inappropriate--defining features and emerging properties of cybernetic systems. Safety is a human focused concept reflecting the degree of freedom from unacceptable harm to people. Safety is predominately measured in terms of risk. Concepts of safety and security are examined across cybernetic systems. Contexts include from advanced control systems to information systems. The proposed framework addresses safety as well as security of such systems employing a systemic suite of principles. Proposed framework provide an integrated regulated aspects to modern complex systems, systematic/systemic treatment of environmental and sustainability facets, comprises systems assurance concepts founded on faults, errors, failures, hazards and consequences. Advanced system security concepts comprise vulnerability. Unlike safety-security many interpretations and contextual implications are for its stakeholder. Security is lack of susceptibility to vandalism/sabotage, theft and fraud, terrorism.

### **Biosecurity education for the next generation of life scientists:**

Changing international context has generated increased interest in biosecurity education. Very little exists in terms of biosecurity related education. There are a variety of reasons such as material is irrelevant, teaching may serve to unnerve students or unfamiliar with these issues, unqualified to teach. Consider development promulgation, adoption of biosecurity education. There is clear need for balance and proportionality. Biosecurity education is a part of the core, compulsory curriculum for life scientists to develop self-sustaining and self promulgating culture of responsibility. Value of compulsory biosecurity education should be in accordance with national requirements and circumstances. Significant and effective contributions in conjunction with measures have taken a lead including national legislation. There appears to be a heightened sense of awareness of the concerns of the security community. Various initiatives on biosecurity education and related projects have been taken in Pakistan. Biosecurity related education is not a silver bullet for ensuring biosecurity. Yet it is an important component in the web of prevention.

### **Conclusion:**

Due to health and social benefits to individual and families living free of mitochondrial disorders, parents having the preference to have genetically related children. This novel technique proves to be safe, acceptable and effective as treatments. Would be ethical for parents to use them? Yes but there is need to gather ethical information regarding pronuclear transfer and maternal spindle transfer. The emergence of biosecurity has focused on the critical policy area in 21<sup>st</sup> century. Revolutionary changes have transformed government approaches. Biosafety is the prevention of large-scale loss-biological integrity such as ecology-human health. Today man made unicellular organisms have an effect on biomass, enter into food chain, reproduction and create competition between the species.

### **Problem 1:**

A person on life-support machine has no chance of recovery. Whether machine should go on or turn it off?

Answer: Healthy life depends on the normal functions of the organs. Machine though which patient can breathe artificially is the biggest pro-hope and solution of the problem. Many ethical issues are there like one group of people say that If we remove the patient from ventilator then it is morally wrong. We are allowing the patient to die without his consent. If brain is alive then patient is also alive. In Western society four factors influence ethical thinking such as pluralist, post – Christian, post modernism and rights.

**Problem 2:**

If human embryo that has a genetic defect that the child will develop cancer in adult life. Then whether embryo should be destroyed or allow to have a baby.

Answer: First look what is most virtuous best / right decision. Give weight age to all the factor involved in arriving at the balance depends on the viewpoint of those making decisions. Principles should be considered like autonomy “Its my right to have a child”, responsibility “I have a responsibility to care for it and bring it up”. justice: our responsibility to look to the wider results of our decision. Ethical issues are raised like human embryos are equal to human child. Human embryos have rights, values of human life, human dignity, human liberty as well as human physical integrity.

**Problem 3:**

If new missiles and bombs are used by government to target the enemy site then this will minimize civil casualties. Considering this advantage, government should remain embark on war or not.

Answer: Lets take an example of Drone which is smarter, nimbler, critics fear, autonomous weapon and more efficient. There is common saying for this weapon “fire and forget”. Many ethical issues have been raised keeping in view this problem like drone attacks against Al-Qaeda had killed innocent civilians. Thus this creates ethical doubts against this weapon. Decision of death and life be left over to a machine thus it will function-ethically in a correct manner. Act in accordance to international humanitarian law. It differentiates between combatants and defenceless.

Bradley J Strawser said:

“Using them to go after terrorists not only ethically permissible but also might be ethically obligatory, because of their advantages in identifying targets and striking with precision.

**Problem 4:**

Why does the environment have intrinsic values?

Answer: intrinsic value is ascribed to the environment. So yes it is there.

**Problem 5:**

Is anthropocentrism a tenable position-face of environmental problems?

Answer: It is agreed by almost all scientists and philosophers that scientific knowledge cannot resolve questions of value. That is, science can only reveal what is, not what should or shouldn't be, which the realm of values or morality is. Therefore, although some value debates involve facts provided by science, they are not scientific debates. Scientific research cannot resolve them and scientists do not speak in them with special authority. The debates about anthropocentrism and other value systems are of this type. There are a number of implications of the anthropocentric view, which strongly influence the ways in which humans interpret their relationships with other species and with nature and ecosystems. Some of these are as follows:

1. The anthropocentric view suggests that humans have greater intrinsic value than other species. A possible result of this attitude is that any species that are of potential use to humans are a “resource” to be exploited. This has, historically, usually occurred in an unsustainable fashion that results in degradation, sometimes to the point of extinction, of nonhuman species, as has occurred with the dodo, great auk, and other animals.
2. The view that humans have greater intrinsic value than other species also influences ethical judgments about interactions with other organisms. These ethics are often used to legitimize treating other species in ways that would be considered morally unacceptable if humans were similarly treated. For example, animals are often treated cruelly in medical research and agriculture. This treatment of other species has been labeled “speciesism” by some ethicists.
3. Another possible implication or assumption of the anthropocentric view is the belief that humans are the height of the natural evolutionary progression of species and of life. This belief is often said to be in contrast to the modern biological theory of evolution, which does not find any scientific use for ranking

some species as “higher” than any others (although such language has often been used by biologists over the last two centuries).

Thus, anthropocentric views can be, and often have been, used to justify unlimited violence against the nonhuman world. However, it should also be noted that such violence does not follow as a logical necessity from all forms of anthropocentrism.

**Problem 6:**

Is radical biocentrism compatible with living in technology dependent?

Answer: According to Biocentric universe theory there is a radical change in a way we view the world. For example, position / appearance of rainbow is according to the person seeing it. Thus, universe exists in relation to us. Today universe exist in a highly defined, rich form because of the development in technology. In a biocentric approach, life is complex. “Life creates the universe than the other way around”-Robert lanze. In biocentricity, the universe consists fundamentally of information, world of object, space and time. There are two postulates:

- raw / uninterpreted information is all that known for certain
- every observation is consistent with any other observation

**Problem 7:**

Can we sustain a population of 6.3 billion if we adopt an accocentric approach to the environment?

Answer: accocentric is a relationship b/w human species and natural environment. *Homo sapiens* are taken as community of individuals (population) whose forms of life cause alteration to the ecosystem with or without human influence. At the end of Neolithic period, agriculture revolution had taken place. The earth was inhabited by 4 million individuals and in 12 thousand years, the world population exceeded to 6 billion. So sustainable development is required. Change in human behavior can make possible for the ecosystem to self-regulate. Biologically it is not possible- ecosystem adapt for a limited time period. Humankind has colonized the whole world even those regions which are very cold, very hot, and very dry and also fight against dangerous predators. The main problem is that human development is not sustainable. Life of many species threatened so there must be fundamental equilibrium that regulates life will be altered. In Environmental sustainability some limits have to respected. Earth has become a great natural park-survival of *homo sapiens*. Ethical commitment of responsibility is essential to preserve life on the planet. Sustainability is a concept of natural science which is also objective. Secondly, cooperation among scientists is essential for the accurate definitions of limits. It will be impossible without considering level of culture / economic /political evolution. For example, human activity like fishing is sustainable but if allows reproduction of species fished on an unchanged scale.

**Problem 8:**

Is sustainability compatible with development?

Answer: Yes, sustainable development promotes economic growth, environmental sustainability and also social development.

**Problem 9:**

How to reduce global warming?

Answer: Global warming can be reduced by many ways like reduce, reuse, recycle, use less heat and air conditioning, change a light bulb, drive less and drive smart, buy energy efficient products, use less hot water, use “off” switch, plant a tree, get a report card from utility companies and encourage others to conserve energy.

**Problem 10:**

Compare sets of priorities between pressures to generate from renewable resources with the pressure to conserve wild environment?

Answer: Increasing scarcity or overuse of renewable natural resources cause problems such as air and water pollution. This can cause damage to the atmosphere or the ozone layer

Environmental policy aims at the environmental resources under a common property regime which are clear and enforceable rules. The access to these resources may be limited, their use may be limited that made subject to specific conditions. Benefits of environmental policy include adjustment of economic structures, net effects on the welfare, cost-effective and benefits of action have been estimated.

**Problem 11:**

What is so wrong about extinction?

Answer: Extinction is a part of the natural order. The process of evolution involved new species gaining ground and others losing out - Charles Darwin. Extinction has always been with us in fact, it has quite often been good for us as our streets are safer with no sabre-toothed tigers. If we look on the other side of the mirror, there is need to worry about extinction rather than its consequences in order to save endangered species from the devastating effects of trade. The most famous mass wipe-out was loss of the dinosaurs.

**Problem 12:**

Are there any organisms whose extinction would not be a matter of concern?

Answer: No, human populations depend on plants and animals for food, medicines, clothing, and shelter.

**Problem 13:**

Animal rights supporters can justify threatening the lives of scientists and their families, releasing lab animals and targeting the financial basis-pharmaceutical company.

Answer: Why should animals suffer pain, or even die. But people want to see progress in medicine so physiological/pathological and therapeutic processes require animal experimentation. Scientists are developing and testing new drugs to reduce pain even developing new treatments for life-threatening diseases. Conducting experiments on live animals can make more rapid progress. But activists see themselves as a modern-day. They are removing animals from laboratories and farms, arranging safe houses and veterinary care. Critics have classified scientists as terrorists.

**Problem 14:**

Comment on the LD<sub>50</sub> test using dioxin

Answer: Chemical that kills one-half - test population-organisms over a period of several days.

**Problem 15:**

Is it ethical to breed and train for such sports as racing and eventing?

Answer: Yes, it is acceptable to use animals for sport or entertainment if animals are not harmed such as horse race-dolphin show. In these examples people are entertained.

**Problem 16:**

Is it always wrong to pamper a pet?

Answer: Yes, pampered pets are the silly creatures. Over feeding, lack of exercise, socialization and inappropriate diet are all serious issues.

**Problem 17:**

Describe ethical issues raised by the interest of a dairy farmer, a dairy cow in terms of well-being, justice, autonomy. Would these issues be different in a developing country?

Answer: There must be a balance between animals, environment and the farmer. Secondary, political challenges should be controlled.

**Problem 18:**

Is there any intrinsic ethical objection to genetic modification?

Answer: Yes, there are intrinsic concerns.

**Problem 19:**

Can non-GM version is less effective and safe?

Answer: Non - GMO Project is a non-profit organization. Protecting the non-GM food supply and giving consumers an informed choice. Non - GMO Project also verify products that have a low risk of containing GMOs.

**Problem 20:**

Can any GMO be said to be risk free? Is it possible to prove absence of risk?

Answer: Risks to GMOs have yet to consider or discover by the scientists but of course risks are there. Nothing in this life is risk-free but this is not an enough reason to reject valuable scientific advances.

**Problem 21:**

What ethical issues are raised by cybernetics?

Answer: who regulates? Society needs to focus on regulatory framework

Pink Floyd:

“Another brick come to mind; we don’t need any thought control”

**Problem 22:**

Young adult diagnosed with insulin-dependent diabetes. He has intrinsic objections to GM techniques and doctor has started recombinant human insulin. Now he wants to start pig insulin. How the physicians cope with the patient?

Answer: Physician will try to explain the importance of recombinant Human insulin. Recombinant human insulin could be less contaminated. Secondly, duration of action of human insulin is slightly shorter than animal insulin. Furthermore, switching from one source of insulin to another can cause difficulties in controlling BSL.

**Problem 23:**

Should misuse of technology lead us to consider banning it?

Answer: Coin has two faces one is good and another one is bad that no one accept it. God has gifted us with brain having capability to imagine. For example, cloning is not some evil as it helps in preventing many diseases, making organ transplantation an easy process, with less chances of rejection and the main motive of cloning is that it does not regenerate the human but the body parts.

**Problem 24:**

Is there any concern about conducting trials with GM crops than with GM microorganism?

Answer: GM crops are faster than conventional breeding (sorting/re-crossing/re-selection). Unlike microbes, crops grow outside and therefore not contained.

**Problem 25:**

What are the key points against the use of GM plants in agriculture?

Answer: Moving genes between organisms is intrinsically wrong. There is risk to the environment, risks to socio-economic as well as risk to human health.

**Problem 26:**

What are the key points in favor of GM crops used in agriculture?

GM technology is used widely in the production of foods and medicines. GM crops have drastically cut the use of pesticides for example, GM cotton, containing a built in insecticide, uses 50% less chemical insecticides. No doubt, antibiotic resistance genes can be transferred to bacteria but the risk is so small that it cannot be quantified.

**Problem 27:**

Does GM of mammals raise any ethical issues that are not raised by GM of microorganism or of plants?

Answer: Success rate of *in vitro* fertilization is lower with GM embryo than with non-modified embryo. Level of expression of foreign gene varies among different individuals. If we are using high expression genes then there is no guarantee that foreign gene will be expressed highly in later stages.

**Problem 28:**

Give ethical suggestions for the use of pig organs for transplantation?

Answer: Through this type of transplantation, animal virus can be passed on to a human patient. There is increased chance of transplantation rejection. Furthermore this may create psychological impacts for patients as well as social impact. Ethically, exploitation of animals for human use is cruel and inhumane. No doubt a scientist is killing piglets under anaesthesia but is this acceptable? Pigs are already reared and killed for meat. Pig cell transplants will be influenced by cultural, spiritual and religious background. Most religions find xenotransplantation acceptable.

**Problem 29:**

In a world where resources are limited, what would be your priorities in biological research?

Answer: Discuss the problems of organizational structure, research prioritization. Discuss the policies that address conservation and management of natural resources reflect societal values. Discuss the scientific information on the development and implementation of effective policies and management actions.

**Problem 30:**

What is your attitude towards new maize variety?

Answer: Maize is a major food crop. It accounts about 75% of the total value of small holder crop production. New maize variety adoption is found among farmers located in high rainfall regions. Secondly, young farmers are more likely to adopt new technology. Our attitude towards new maize variety depends on the agro ecological region, attitude towards production traits, as well as on their advantages and disadvantages.

**Problem 31:**

Does HGP have any implication in relation to racialist attitudes?

Answer: Race has been used as a human label with far reaching implications. HGP opened the door for better understanding of genetic disease; shape the future practices of medicine. HGP provided us the detailed map of our DNA sequence. Now scientists have revealed human genetic variation and its correlation with race and ethnicity.

**Problem 32:**

Evaluate the practice of compulsory sterilization on eugenic grounds

Answer: Limitations of consequentiality morality is the key to avoid a repetition of the evils of negative eugenics. There are exceptions like emergency cases (drunkenness, crime, poverty, unemployment, broken marriages), a collective version of the logic of preventive self-defence and a moral status of judgments (reproductive rights).

**Problem 33:**

Give comments on abortion in case of severe genetic conditions?

Answer: Prevention of suffering is worthy ideal under all ethical systems. Abortion is a fundamental right the pregnant woman. Children never to be born rather than to live a life burdened with a serious handicap. The question is not whether a handicapped individual is born or unborn, but whether handicapped human life should be protected equally with healthy human life. Such child can give both society and the family. This gives an opportunity to exercise true compassion, love, charity, and kindness.

**Problem 34:**

Discarding affected embryo is ethically acceptable than aborting a fetus with genetic disease?

Answer: Ethically acceptable but issues of PGD are there. All human life deserves respect, in law this respect is reserved for a child after birth. The embryo and fetus have no legal status, at least before viability. As the pregnancy proceeds it gives ethical status to the fetus as it develops in utero and not in the lab.

**Problem 35:**

Discuss ethical dilemmas regarding genetic screening?

Newborn screening technology has been improved by tandem mass spectrometry that can detect more than 20 different genetic conditions. Still specific cure long-term prognosis for some patients is uncertain and inaccurate. Genetic screening raises many ethical issues

- should the knowledge go outside the family
- religious groups raise many ethical issues.
- expensive/emotional distress for the patient
- done for common diseases / part of medical record

**Problem 36:**

Discuss eugenics with a smiling face?

Answer: In the large Ashkenazi Jewish population in USA, the frequency of Tay-Sachs disease is much lower than the expected one. System of genetic testing was initiated by Rabbi Joseph in New York. Religious authorities have organized genetic test of every member of the community. Later results of the test are kept in coded form. If two people want to marry, genetic test will be performed. If both are carriers then they are advised not to marry. If they want to marry, decision will be difficult because every time they have to terminate pregnancy. This program is also known as "Hebrew Dor Yeshorim" that means the generation of righteous. This is still a matter of debate but it can't be underestimated.

**Problem 37:**

Is it justified to perform essential experiments on life-threatening diseases as they have potential benefits but are also very risky?

Answer: If a patient has a disease caused by malfunctioning gene then gene transplant may be a good way of curing the disease but it has three problems. One is that there is no way for the functioning genes transplanted in all cells. Then gene correction is limited to one generation only, in other words correctly functioning gene is not heritable. Secondly delivering the gene requires the use of vectors. For this modified virus will carry the gene to the target cell. The last main problem is that whether or not gene will work. For example, gene therapy in case of Cystic Fibrosis raises many issues like symptom relief is poor. Then lung lining are constantly renewed so repeated treatments are required. But in case of SCID – self renewing stem cell of the bone marrow is there so need of repeated treatments but develop another side effect that is leukemia. It is believed that insertion of functioning gene into chromosome activate oncogene.

**Problem 38:**

Discuss ethical objections to germ-line gene therapy?

Answer: The idea of germ-line gene therapy is controversial. People who would be affected by germ-line gene therapy are not yet born. Due to these ethical concerns, U.S. government does not allow federal funds for germ-line gene therapy.

**Problem 39:**

Are there ethical objections to genetic enhancement?

Answer: In the language of genetics what is meant by normal? genetic intervention is rather "enhancing" or "therapeutic?" How should the benefit of genetic enhancement be calculated in comparing its risks and benefits? Would genetically enhanced enjoy an unfair advantage in competing for scarce resources? Will genetic enhancement be available to all or only to the few who can afford it? Questions of social inequality will also be raised. Genetic enhancement might affect human evolution. There is no certainty- that genetically enhanced individuals have greater biological fitness, as measured by reproductive success.

**Problem 40:**

How to distinguish between therapy and enhancement?

Answer: Line between therapy and enhancement is the line where medical necessity stops and optional procedures begin.

**Problem 41:**

What are the applications of GM crops in world's poorer countries?

Answer: GM crops increase agricultural productivity in tropical areas because climatic conditions are such that it favours the proliferation of insect pests and disease vector. GM crops increase food production in a reduce cost and fight against famine, hunger, malnutrition.

**Problem 42:**

Is a gene an invention or a discovery?

Answer: Patents are designed to protect the commercial interests arising from an invention. Keep in mind that gene is natural so how it can be patented. Scientists say that gene isolation is an inventive step. Opposition replied that chemical structure of the gene copy in test tube and remain same as the chemical structure of the gene in the person.

**Problem 43:**

What are the ethical issues for and against gene patents?

Answer: In favour of gene patents, it covers 3 distinct types of invention these are diagnostics, compositions of matter and the functional use. One of the ethical issues against human gene patent is that it makes research more difficult. There will be delay in discovery and development of diagnostics and therapeutics. The role patents in motivating academic researchers are less clear. Human gene patents are not simply that they confuse legally patentable genes with naturally occurring genes. Gene patents can threaten people's jobs, careers as well as their health/wellbeing. Genes should be thought of as property at all.

**Problem 44:**

Did the cloning of frog by nuclear transfer raise ethical issues?

Answer: Animal reproductive cloning suggests more ethically troubling issues such as early implantation of clones always result in death, maternal death and morbidity.

**Problem 45:**

Does the cloning of mammals raise issues that cloning of an amphibian does not?

Answer: Many serious safety concerns of individuality, family integrity are there. By cloning we are reating children as objects. Careful assessment of response revealed fears about harms to the children such as moral harms and psychological harms. Cloning will diminish the sense of individuality and personal autonomy. There will be degradation in the quality of parenting and family life. This undermine important social values by opening the door to a form of eugenics. Some religious thinkers argue to create a child is intrinsically immoral. Other religious thinkers believe that to create a child could be morally justified under some circumstances but it should be strictly regulated in order to prevent serious issues.

**Problem 46:**

Is animal welfare a greater concern with mammals cloning?

Answer: This can be justified by three reasons like to cope with unchanged environment, reduction in animals required for breeding programmes and to cope with changes in farming conditions.

**Problem 47:**

How open should be the scientific research?

Answer: scientific research should be open as it requires description, prediction and complete explanation as well as understanding.

**Problem 48:**

Can misuse of a research may be a reason for not doing it?

Answer: Common ways by which research findings are misrepresented are

- flawed research
- using findings out of context
- stretching findings
- distorting findings
- rejecting or ignoring findings

These are not acceptable in research. Instead of dishonest contribution it will be better not to do research. For this reason it is the duty of supervisor to keep a check on the student.

**Problem 49:**

Should there be a legal ban on human cloning?

Answer: Ban should cover just reproductive cloning or therapeutic cloning. Cloning is somewhat incompatible with human dignity and protection of human life. It lacks precision and also lacks clarity.

**Problem 50:**

Is the treatment of fertility problems an acceptable application of cloning?

Answer: According to Law, embryos can be created for fertility treatment, excess embryos can be frozen for future use but in such circumstances licence is required for each research project

Religious view:

- God has the power to 'open' the wombs of the infertile
- it is ultimately he who 'settles the barren woman in her home as a happy mother of children'

**Problem 51:**

Does selection of specific genotype for cloning may be regarded as a eugenic activity?

Answer: Cloning allow genetic manipulation that sets the stage for increased efforts at eugenics not by improving their economic, social, and educational opportunities but by altering the genes with which they are born. Keep in mind that threat of eugenics is inherent in technologies because it allows individuals to modify inherited traits. It is impossible to embark on human cloning without opening the door to eugenics. Cloning in animals by "improving" inherited characteristics is a deliberate form of animal eugenics.

**Problem 52:**

Does the use of adult stem cells have advantage over the use of embryonic stem cells?

Answer: Embryonic stem cells offer the potential for wider therapeutic application but adult stem cells avoid the ethical issues roused by embryonic stem cell research. Adult stem cells offer the potential for autologous stem cell donation. It helps to avoid issues of immune rejection. Injection into mice with compromised immune systems undifferentiated ESC form teratoma. This tumor formation creates doubt of the therapeutic applicability of ESCs. Not yet known similar results are observed with adult stem cells. ESCs have an immuno-privileged, highly undifferentiated state so this removes one of the main barriers of stem cell therapies. ESCs appear to be immortal *in vitro* while adult stem cells cannot be cultured indefinitely in the lab; once differentiated, stem cells seem to die off like typical tissue cells.

**Problem 53:**

What are the arguments for and against donor insemination treatment of the couple?

Answer: Risks associated with donor insemination treatment are multiple gestation pregnancies, ovarian hyperstimulation syndrome. There are number of side effects of donor insemination treatment like nausea, vomiting, ovarian enlargement and ovarian cysts formation. It is not therapeutic in its nature and do not cure infertility. It raises many issues like should the identity of the donor who provided sperm for couples be revealed? What information will be given to the child in the future? Sperm bank is there so same material will be used for multiple inseminations and thus the consequences of consanguineous marriages increases. What are

the criteria for choosing a donor? What is his relation with the unborn child? Should the husband or partner give a formal consent that the woman will be inseminated with donor semen?

**Problem 54:**

Discuss ethical issues related to intracytoplasmic sperm injection?

Answer: Most objections to ICSI are same as put forward for the new reproductive technologies. Objections can be classified as religious, feminist, and 'health and safety' objections.

**Problem 55:**

A wanted child can be a stem cell donor for sick sibling?

Yes, but ethical issues are involved

**Problem 56:**

Is it ethical to fertilize human eggs outside the uterus for infertility treatment?

Answer: Laboratory mix-ups misidentified gametes, this lead to the transfer of wrong embryos thus leading to legal action against the IVF provider. So double witnessing system was developed. Uptil now no consensus exists in science, religion, and philosophy over discarding unwanted embryos.

**Problem 57:**

Can failed embryos be described as human beings?

Answer: No

**Problem 58:**

What are arguments for and against only the woman having to give consent to a termination of pregnancy?

Answer: There are two standpoints one is pro-life that women should not have the ability to abort a human life while pro-choice is that woman carrying the fetus should be given the right to decide to carry the baby to term or abort it.

**Problem 59:**

Is compassion an adequate reason for ending the life of a person who is suffering terribly and who has no prospect of recovery?

Answer: A person who killed the patient without compassion wanted only to relieve the suffering. Here voluntary euthanasia can be involved ending person's life at their request.

**Problem 60:**

If voluntary euthanasia is made lawful in England then who should administer it? Are there any problems if doctors do it?

Answer: voluntary euthanasia was considered in Britain in 1994. House of Lords select a committee who rejected it as it accepts the right of every person. It can restrict the freedom for others to make their own decisions about their lives; this is the central point about banning smoking in public places. If voluntary euthanasia became lawful, it would threaten the weak, the vulnerable and those without capacity.

**Problem 61:**

Should bioscientists be required to sign up to a professional code of ethical practice?

Answer: this is a "Hippocratic oath for scientists". It helps scientists in performance of their work, ease public distrust of scientists, prevent conflict of interest where research is exploited for profit, protect scientists from discrimination by employers, causes no harm & wholly truthful in public pronouncements, being honest & open with challenges and the public, reducing experiments on animals, safeguarding the environment and not plagiarizing other scientists work.

**Problem 62:**

Describe principles of the practice of science?

Answer: there are six principles of the practice of science such as objectivity, questioning certitude, research freedom, research reproducibility, respect for subjects and of the community of science.

**Problem 63:**

Discuss the ethical issues related to nanomedicine?

Answer: Assessing the safety of nanomaterials can be a difficult because nanomaterials are not a unified class of compounds. Each type of material must be assessed on its own terms. Risks are associated with nanoscale materials that depend on the route of exposure as it accumulates in different parts of the body and produce adverse effects. Thus ethical guidelines and regulations are required. Social & regulatory aspects of nanomedicine need to be discussed.