Legal and Regulatory Issues in Biotechnology
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Module - 01
Regulation of Biotechnology Research
Lecture - 03
Ethics in Animal and Human Research

Hello, all. Welcome to the 3rd lecture of this series of Legal and Regulatory Issues in Biotechnology. So, in continuation to our module 1 discussion on Regulation of Biotechnology Research. Today, we would be dealing with the Ethics in Animal and the Human Research particularly with respect to biotechnology.

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So, here in this module we would be dealing with the core meaning of ethics or bioethics and also the ethics in the area of the clinical research particularly in the development of the biomedicine sector. And the history, as well as little bit theoretical aspects means the various theories with respect to animal research ethical theories with respect to animal research.

Also, the timeline on historical perspective and current development with respect to the principles, with respect to ethical research and the various course of ethics and regulation that is guiding the ethical research of the biotechnology.

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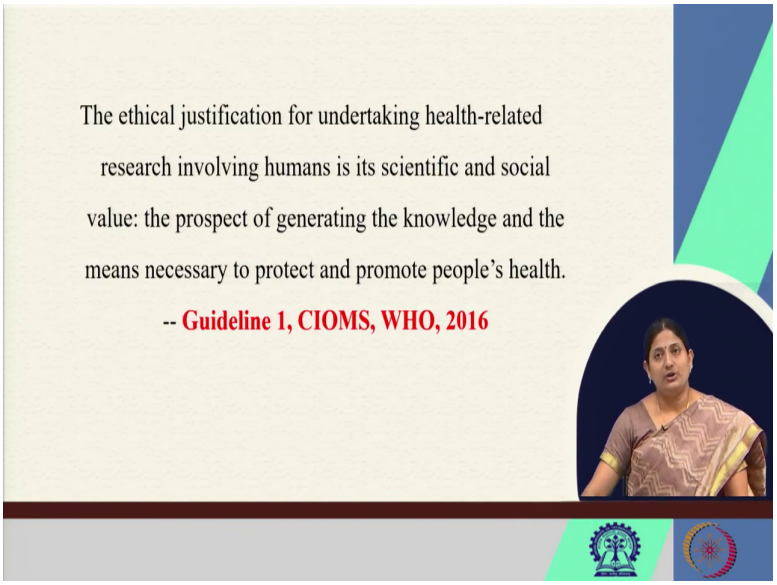

So, in our earlier discussion, we saw that the application of the biotechnology is multi fold. So, the concerns or apprehensions with respect to the biotechnologically developed product their quality, efficacy and the efficiency of the product is also another is another point of concern for major stakeholders or general public.

As we saw the development of the biotechnology is a critical process and this technology is not only a scientific development, but it is at the interaction of the scientific development and the ethics. Why I am saying so, because biotechnology has the inherent power to manipulate the living organism and some of the consequences are known and some of the consequences are not known as yet.

So, it may modify which might have a harmful effect modify the organisms or the product in such a way that it might have a harmful effect on the society or the consumer at the last at the end. So, all these apprehensions where we are not sure about the result of the research leads to the thinking that the scientific development which we are carrying out through the application of the biotechnology must be justified through the ethical notion.

So, what is that ethically justifying scientific development? So, if you go by the guideline of the CIOMS that is the Conference of International Organization of Medical Sciences and World Health Organization. So, it mentions that the ethical justification for undertaking the

health related research which involves human is basically depends upon the scientific as well as the social value. The prospect of generating the knowledge and the means necessary to protect the, protect as well as the promote public health.

So, when we are developing something, it is not only the scientific endeavour, but the societal value of the research must or should be taken into account.

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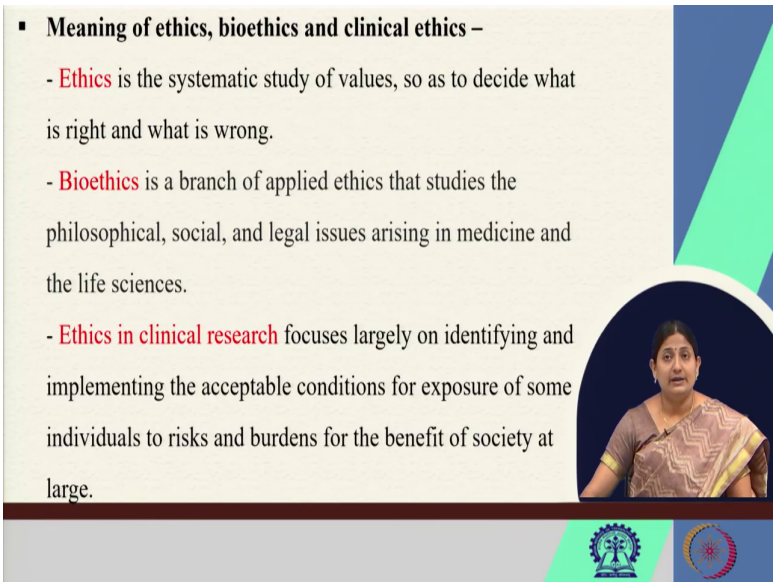

So, and where we are talking about the ethics, so, what is this ethics? So, ethics in general or in a dictionary meaning is the systematic study of the values or so as to the way we decide what is right or what is wrong. And, specifically when we talk about bioethics, so, it is basically a branch of the applied ethics that studies the philosophical social as well as the legal issue arising in the medicine as well as in the field of the life sciences.

So, the bioethics, because we know biotechnology has a greater utilization in the field of biomedicines or in the public health. So, bioethics remains a critical issue in the area of the biotechnological research.

Further, when we talk about the ethics in the clinical research, so this ethics in the clinical research majorly focuses on identifying and implementing the acceptable conditions for

exposure of some individuals to the risk and burden for benefit of the society at large means we are developing a risky product.

So, that is why as I mentioned in my earlier lecture the biotechnological process is a long and risky process. It involves number of steps starting from the preclinical to clinical to other areas. So, unless and until it has been experimentally proved you have this data which is able to satisfy the regulatory authority regarding the safety and efficacy of the product, we are not going to use it.

So, when we were talking about the ethics in the clinical research particularly. So, it is basically the focus on identifying or implementing the acceptable conditions of exposure of to some of the individuals to the risk or the burdens of which the biotechnological research may pose and which is carried out for the benefit of the larger society.

So, as I mentioned in my previous classes that biotechnologically biotechnological research is a long and risky process. It involves number of steps to prove this efficiency, as well as the safety of the product. So, we need certain parameters to test those and in generally, animals and humans are the experimental objects on which basically these are carried out.

So, now that is there arises the question of the ethics. So, is it really justified to use animals and some human beings for ascertaining something that whether it is good or bad? How and why and how we can justify the usage of these animals or the humans during the development of the biotechnologically biotechnological product. So, all these issues now centres around the ethical concept in the biotechnology.

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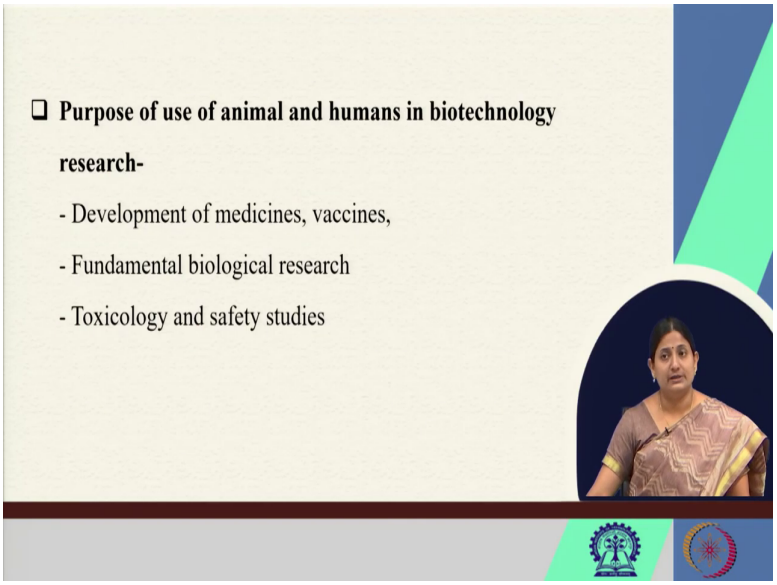

This is a process through which animals and humans' samples are used for establishing the products parameters and it is also essential. Because you know as the world is progressing with different technologies, we are being susceptible to various diseases. So, we need to develop more and more medicines and vaccines to protect the human race from different communicable as well as the non communicable diseases.

Further, there is a need to enhance the understanding of the fundamentals of the life as well as the fundamentals of the biological research that would be helpful for us. And, we need to also carry out this toxicology or the safety analysis for the products which is going to be a miracle maybe in the newer future so that the human race can be protected from the various hazards.

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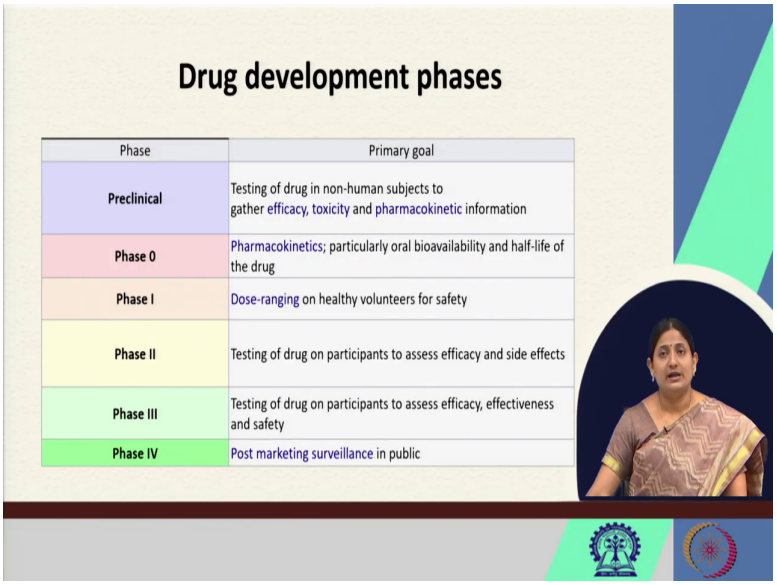

So, as I mentioned during the, if you take the biomedicine development process, the biomedicine development has many phases of development. So, it is basically the preclinical trial phases, as well as the clinical trial phases. And, during the preclinical phase basically the drugs are tested in the non-human subjects to gather the efficacy toxic and as well as the pharmacokinetic information's.

After that, once it is established in the non-human subject then some then the scientists go forward with the human clinical trials. So, again the human clinical trials are majorly divided into four phases – phase I, phase II, phase III, as well as phase IV. So, in different phases; these number of samples of the human population as well as the parameters which are tested are specified.

Or for example, in phase I basically the dose ranging studies are being carried out. In phase II is basically to assess the efficacy as well as the side effect of a particular medicine. And in the phase III, particularly it is a large-scale human trial where the drugs are tested on the participants to assess their efficacy, effectiveness as well as the safety.

And, phase IV comes into the picture once the drug is marketed in marketed or accessible by the public. So, if there is any post marketing effect or adverse effect so, those are reported

basically in phase IV studies. So, during this, so, you saw in the pre preclinical phases animals are used and in the other phases humans are used.

Now, again for the benefit of the humans is it justified to use the animals? Why the animal should be tortured to gain the safety or efficacy study for an unknown medicine? Yes, we may say that it is better to sacrifice a human than an animal, but again, is it again justified?

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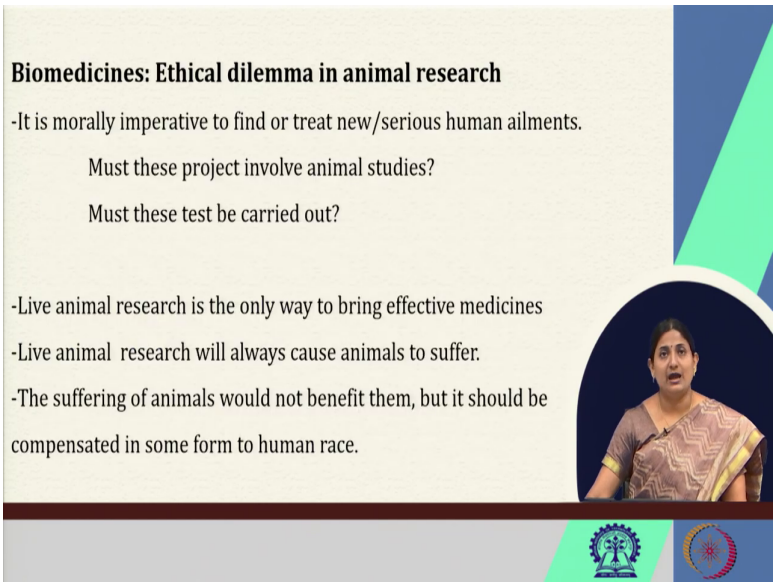

So, these issues have been these moral issues or ethical dilemma in the animal research is there since the beginning of the medical sciences. So, when initially when the physicians or the doctors have started understanding how the human body functions, what is the physiology of the human body? So, they started with experimenting with the animals and that gave them the background of understanding the physiology of the body.

So, we may have certain justification, but again there are different kinds of thought. Like live animal research is the only way to bring effective medicine or it will definitely cause some suffering to the animals, but at the end of the day it will be beneficial for the larger human society. And, yes, it is true it is not going to benefit them, but again it is compensated in some form to the human race.

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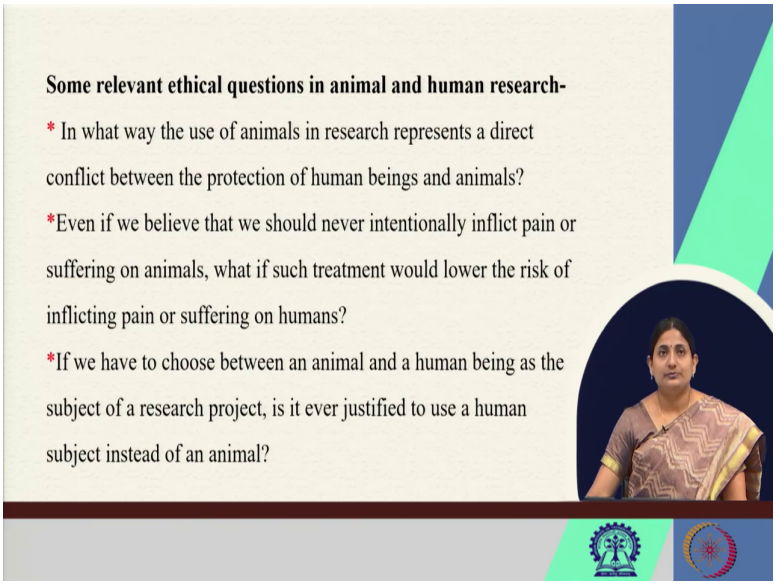

So, that has again laid to number of questions like in what way the use of the animals in the research presents a direct conflict between the protection of the human being and animals? And, even if we believe that we should never intentionally hurt or inflict the pain or suffering in an animal, what if such treatment would lower the risk of pain or suffering in the human beings.

And, if you have chosen between an animal or a human, then who can be a better or initial research subject matter and is it ever justified to use a human subject instead of an animal. So, these are the various questions, but again the answers would be different by different stakeholders like the proponent of the animal ethics and other things. So, it might have different connotation for different group of the people.

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And, all these had led to the creation of three different types of the theories. So, if we look into the ethical theories in the animal research it can be majorly classified into three categories: 1st; the contractarianism.

So, here this contractarianism is basically is basically coming from the Hobbesian line of the social contract thoughts and it primarily holds that persons are primarily self-interested, and that a rational assessment of the best strategy for attaining the maximization of their self interest would lead them to act morally.

So, it is basically talking or saying that humans basically always want to carry out their self interest. So, something which is majorly accepted by the humans to achieve some goals or which is beneficial to them and if majority of the society consent to them as well as we get the consent of the governmental authority, then we give a go ahead to those kinds of the thoughts.

So, the people who believe in this theory basically belongs to one kind of a moral community where this realization of the self interest is the main object. And, so, animal experimentation is not an ethical issue for this kind of believers of this kind of theory.

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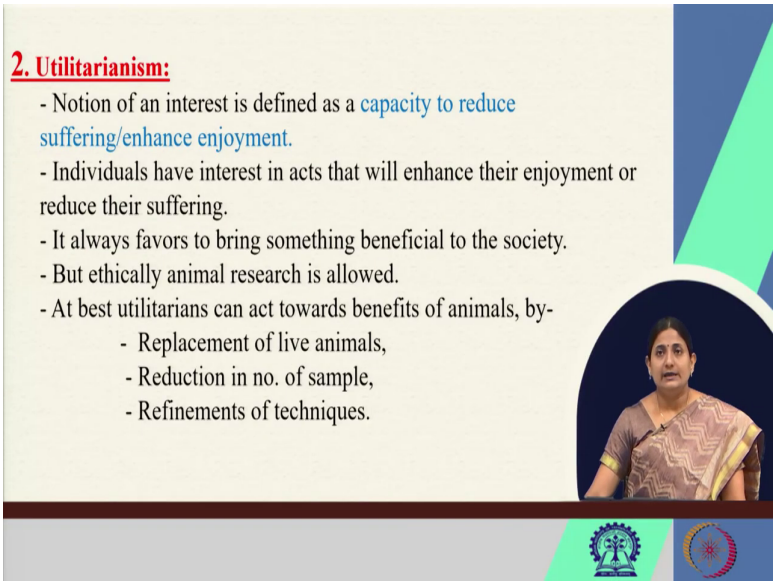

The 2nd theory is the utilitarianism. So, this theory basically defines the notion of an interest is like as a capacity to reduce suffering or enhance enjoyment. So, like as an individual, we always have the interest in those activities which will basically enhance our enjoyment or reduce our sufferings. So, which is beneficial to the society or something which may favour the society or reduce the suffering of the society is largely accepted by the society.

But, here a rational justification of the ethics is applied and the use of the animals in the research is allowed. But again, they somehow also give a thought towards the benefit of the animals like there are three R's theories like replacement of the live animal instead of the, if in some experiments instead of using the live animals we may use some other models or you may use a previous data. So, that is acceptable.

Or they may think about reducing the number of samples. So, instead of using 5 animals so, you may use and go for 3 animals if the analysis could be done with that. So, the way by which the number of animals used in the experiment can be reduced. So, they give a thought in that direction too.

And, refinements of the technique: so, these days with the advent of technologies number of alternatives are available simulation modelling or bioinformatics data. So, if any alternative is

available through which the use of the animal can be reduced or replaced so, those theory or aspects are generally taken in by this proponent of this theory.

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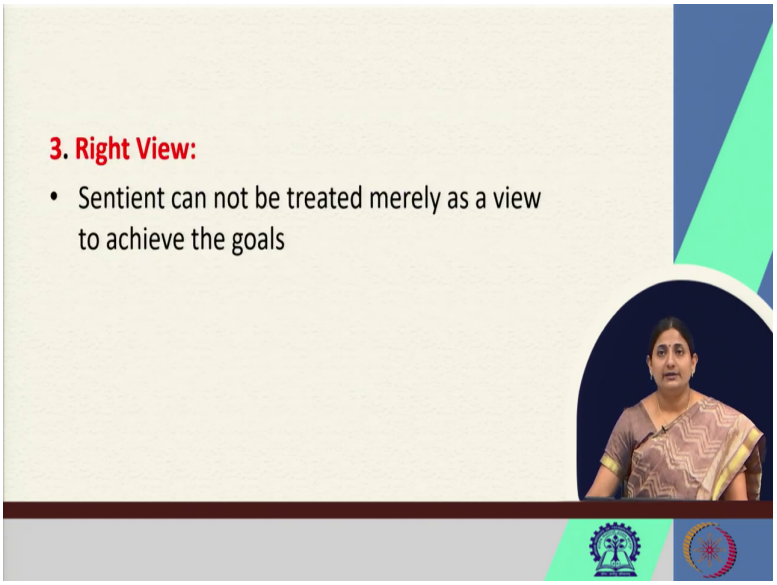

And, the 3rd theory is the right view, who are strictly against the use of the animals. So, they directly mention that the sentient cannot be treated merely as a view to achieve the goals. So, the use of the animals in for human benefit is never justified by the believers of this theory. So, these are the three theories which generally discuss or describes the thought process of various category of the people towards the use of the animal in clinical research.

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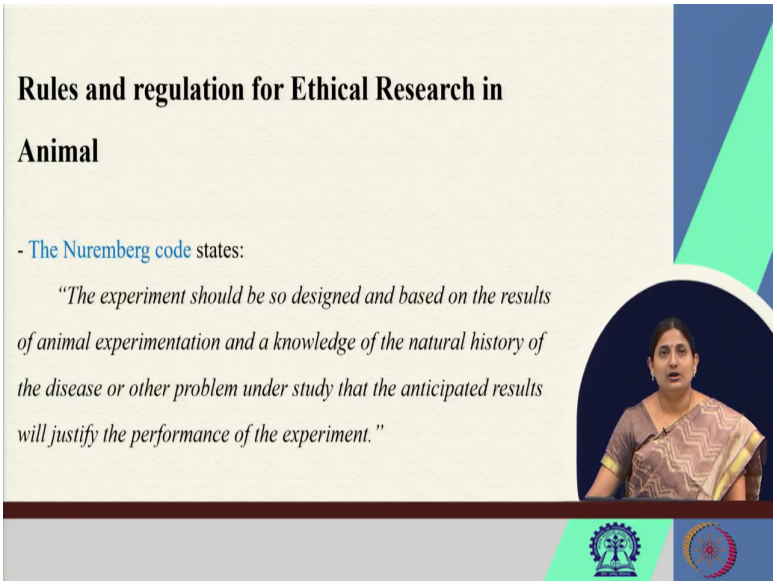

So, with this kind of conflict or delay ethical dilemma now we are in a situation where we cannot stop about developing something which is a beneficial to the human race, at the same time we need to think about the ethical justification of using animals in the research.

So, number of rules and regulations are in place which regulates basically the use of the animals in ethical way in the biotechnological research. One of them is the Nuremberg code. So, the Nuremberg code states that states that: The experiment should be so designed and based on the results of the animal experimentation and a knowledge of the natural history of the disease or other problems under the study that the anticipated results will justify the performance of the experiment.

So, all the experiments which are carried out in the area of development of biomedicine must be based on the animal experimentation, but at the same time it should be justified the performance of the experiment. So, undue experimentation is or should not be allowed as per the Nuremberg code.

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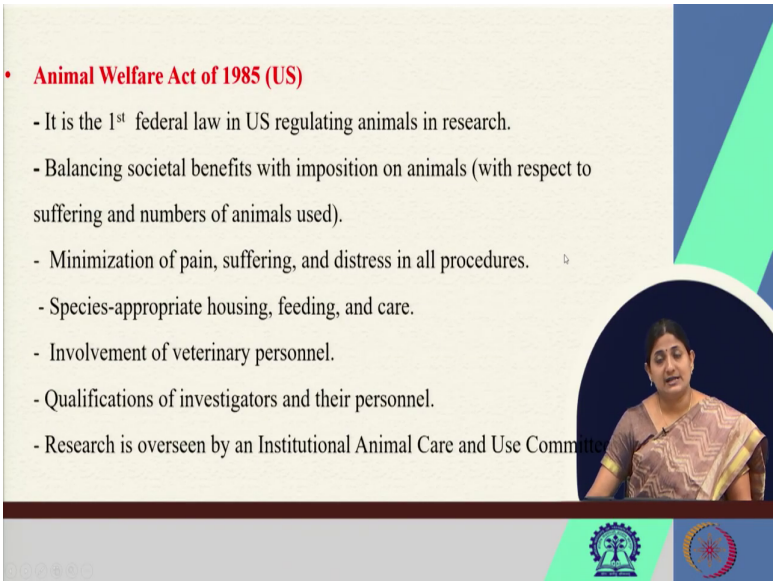

And, a number of other acts and regulations are placed in different countries. For example, I have taken few examples for in the developed nation like United States. We have the Animal Welfare Act of 1985, so, which is the first federal law in the United States which regulates the animals in the research.

And, it tries to balance the societal benefit with the imposition benefits with the imposition of the animals like how much suffering the animals are having or how many animals are used during the course of study. Also, it emphasizes on minimization of the pain, suffering and distress in all the procedures.

Then the animals must be taken care of appropriately like the species-appropriate housing, feeding and care must be given. Involvement of the veterinary personnel's and the persons who are investigating certain research must have adequate qualification and all these activities are generally overseen by the institutional animal care and use committee.

So, basically this act brings about the provision where justified use of animals in the research could be carried out and appropriate use of animals can be done.

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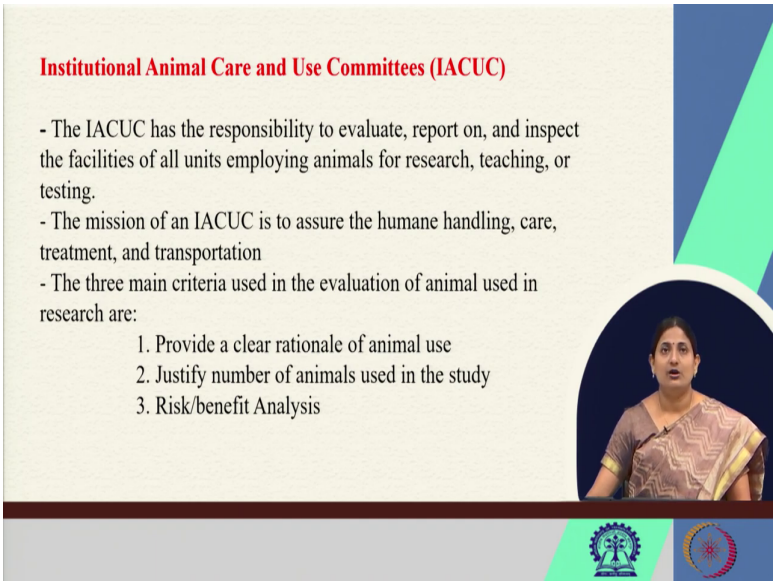

And, so, this institutional animal care and use committee or IACUC has the basic function or responsibility to evaluate or report or inspect the facilities of all the units employed for animal research or teaching or testing. And, it basically assures that the human handling or care or the treatment or the transportation for the animals are properly done.

And, there are three main criteria used in the evaluation of the animals used in the research. They are, 1st – a clear rational for the animal use must be provided; 2nd – the number of animals used for the research must be justified and proper risk benefit analysis must be carried out. So that the new experimentation or the proper experimentation which is carried out could be rational and it can be justified.

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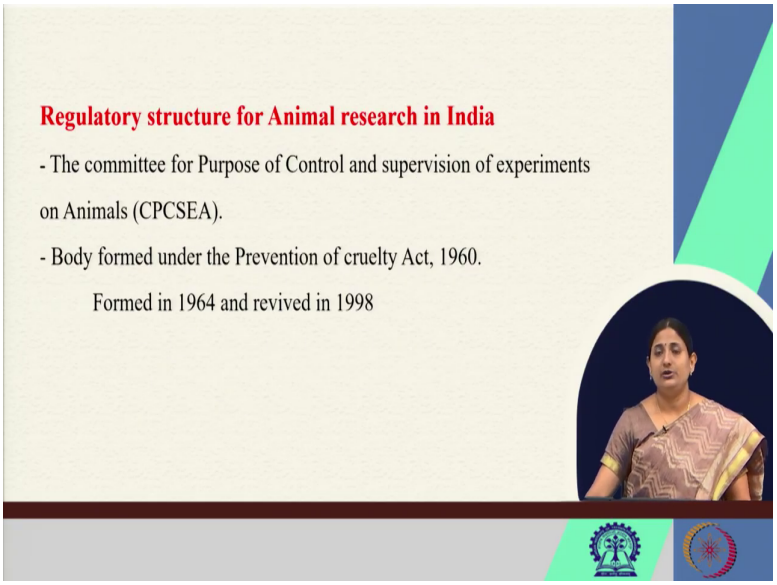

Similarly, if we come to India, we have this committee for the purpose of control and supervision of experiments of on animal or CPCSEA. So, basically this is a body formed under the prevention of cruelty act of 1960 and this body was formed in the year 1964 and it has been like revived you may say in 1998.

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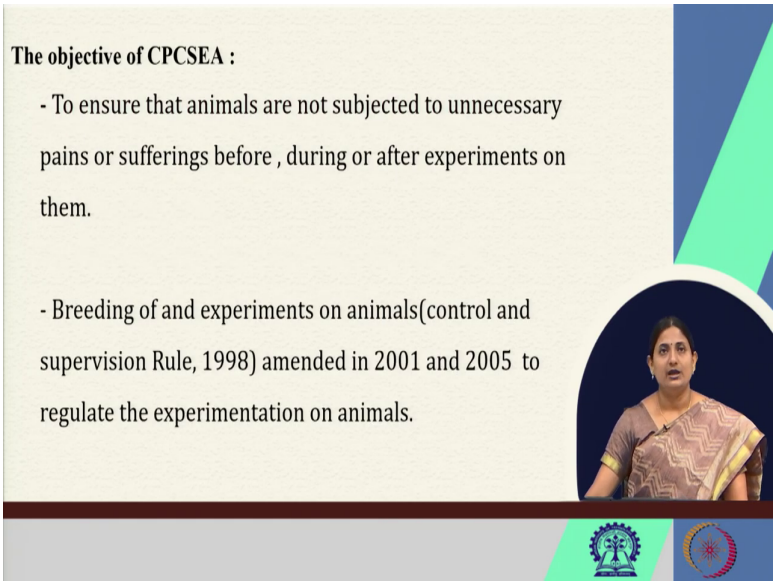

And, the object of this committee is that to ensure that the animals are not subjected to unnecessary pain or suffering, during, before or after the experiments. 2nd – breeding and

experiments on the animals like they have this control and supervision rule of 1998 which was amended in 2001 and 2005 and which basically regulates the experimentation on the animals. So, we have also some provisions in India which basically looks into the use of animals in the whole research process.

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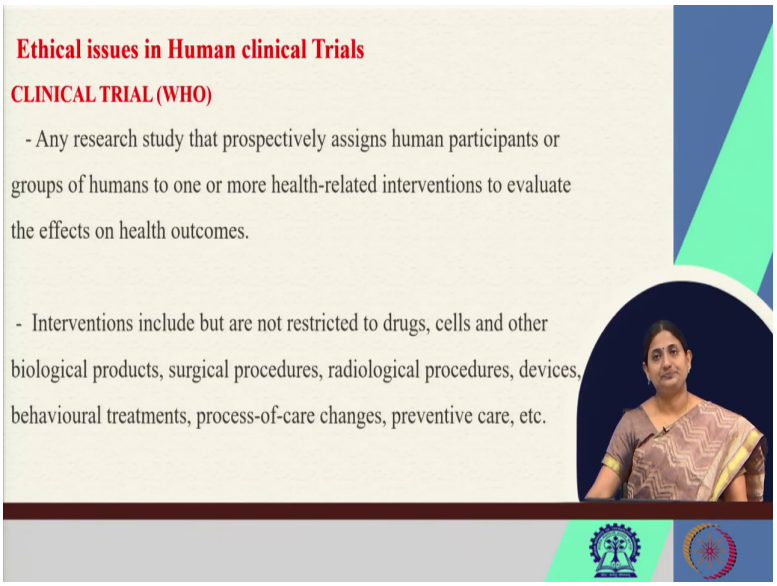

So, that is one part where we are using the animals in the human development of the biomedicines for the human beings. When we come to the next part that is the human clinical trials, so, again so, we may ask so what is the problem? It is the same human beings for whom the medicines are being produced. So obviously, humans are the samples for testing those medicines which are being developed from them.

But it is not so easy as said. Like the clinical trial process which is defined as the any research study which prospectively assigns human participants or group of humans to one or more health related interventions to evaluate the effect of the health outcome is not that simple to carry out as reason being the same.

So, these are the experimental medicine or something which is still in the development phase and we are not sure about the effect of the medicine. So, those things cannot be you just cannot experiment something on the human or any individual if he or she does not know what is going to or what are the consequences that that is going to happen.

And, particularly, if we look into the dark history of the human clinical trials then we can understand the situation in a better way like why we need ethical consideration for using humans in the human clinical trials.

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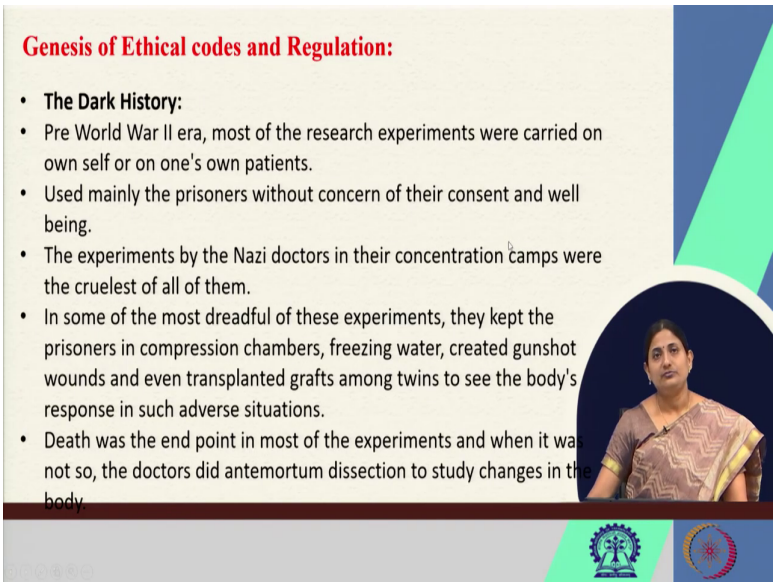

So, this the dark history which I am mentioning goes back to the pre-Second World War times. Most of the research experiments were carried out on own self or by the doctors' patients.

So, during the World War II time and second World War time the prisoners were the samples for testing different kinds of the drugs and the concern point of concern is that the prisoners did not know like why or to which drug they are subjected to and they do not know what are the consequences going to be.

And, this the in famous case of these Nazi doctors during the in their concentration camps where like they have treated the persons in the concentration camps with all sorts of possible experiments to understand their learning or to improve their learning of the science or physiology.

So, in one of the most dreadful experiments like the prisoners were kept in the compression chambers or they were allowed to stay inside the freezing water to see if how the body is responding to that or deliberate gunshots or wounds were created to see the development in

the wound if left untreated. How the patient or how the prisoner is going to survive that wound or not or deliberately tried to transplant grafts among the twins to see the body how it is responding to the adverse situation.

So, these deadly experimentation has like when it came to the forefront it gained a lot of attention and that lead to the thinking of yes, we need certain regulations or guidelines that would ethically ensure and would create a notion of ethics while conducting the experimentation for the sake of learning or understanding the science we cannot or one cannot do any sort of experiments on the subject or human subjects.

So, even in those cases like the death even the death was considered as an end point, but when it was not so, the doctors did the antemortem dissections to study the changes in the body. So, you can understand how deadly are those experimentation. So, finally, do after this World War II when these issues came to forefront and so, it was prosecuted in a US court.

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So, the Carl Branch versus in the United States case. So, there the doctor this doctor Brandt, as well as 22 other doctors were convicted of using this deadliest experiment deadliest experiment in the prisoners and they were found guilty of the wrongdoings and that led to the development or the genesis of the ethical codes and regulation.

So, it was this incidence this dark is this is not a single incident, there are many others. So, however, those incidents lead to the thinking or notion of the research should be ethically permissible and the research should always have certain social value as well as the scientific advantages.

So, now how you understand that some research is having a justified social value or justified scientific advancement? So, even there is no particular parameter to calculate the societal value we have three different factors generally which is taken into account to understand the scientific as well as the social value of the research.

First, we have to understand what kind or what is the quality of the information we are we will be getting by conducting some kind of study. And how significant is it going to in solving the health problems and its contribution to the creation or evaluation of the interventions policies or practices that is promoting the individual or the public health.

So, by evaluating all these three factors one can go ahead with a plan or an experimentation which is overall beneficial for the human society and giving or generating a meaningful information which can be used in future for benefit of the human society.

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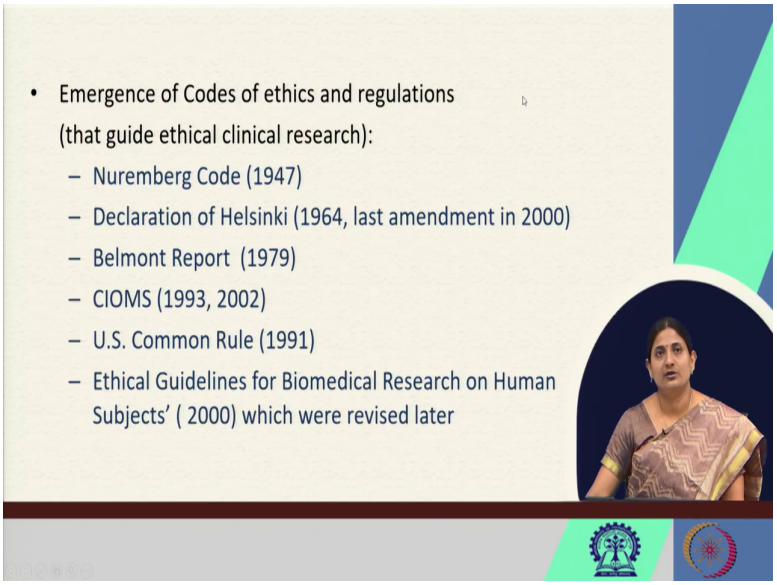

So, with this we have number of codes or provisions in place like Nuremberg Code, then we have the Declaration of Helsinki, we have this Belmont Report of the United States then we

have the CIOM guideline. We have U S Common Rules and also the Ethical Guidelines of the Biomedical Research on the Human Subject which is a modified version of the CIOM guideline in the year 2000. So, number of regulations or ethical codes has developed after particularly Nuremberg incident or the trials in the Nazi camps.

So, so, in this session we will stop here and in the next session I will briefly describe about all these codes. So, we will meet in the next session.

Thank you.