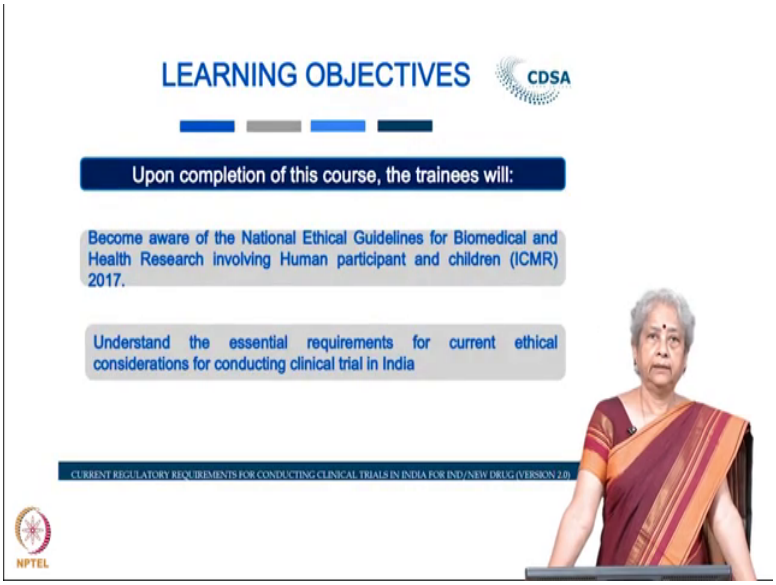
Current Regulatory Requirements for Conducting Clinical Trials in India for IND/NEW Drug Version 2.0
Department of Biotechnology
Indian Institute of Technology, Madras

Lecture – 12
Ethical Considerations

[FL] Welcome to the session on Current Regulatory Requirements for Conducting Clinical Trials in India for the Investigational New Drug. This is lecture 10 where we would be talking about Ethical Considerations related to this particular area.

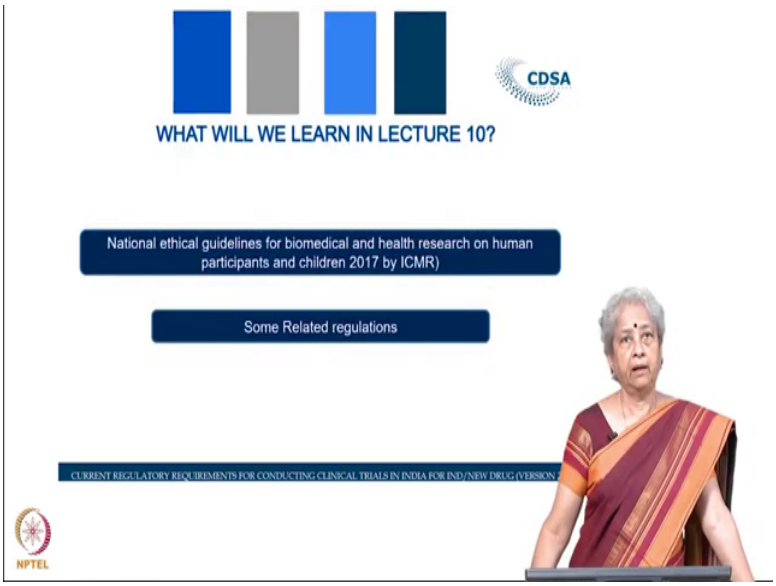
(Refer Slide Time: 00:31)



The learning objectives are actually upon completion of this course. The trainees will actually become aware of the national ethical guidelines for biomedical and health research involving human participant and children.

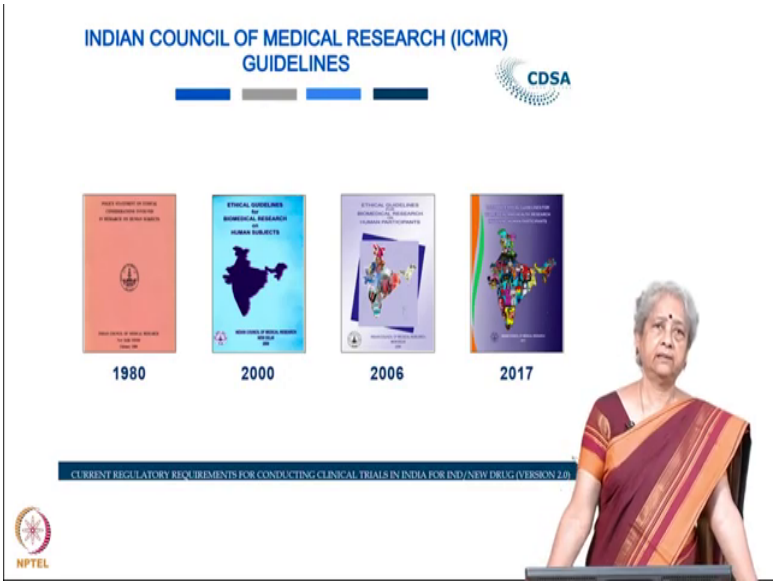
And also understand the essential requirements for current ethical considerations for conducting clinical trial in India.

(Refer Slide Time: 00:54)



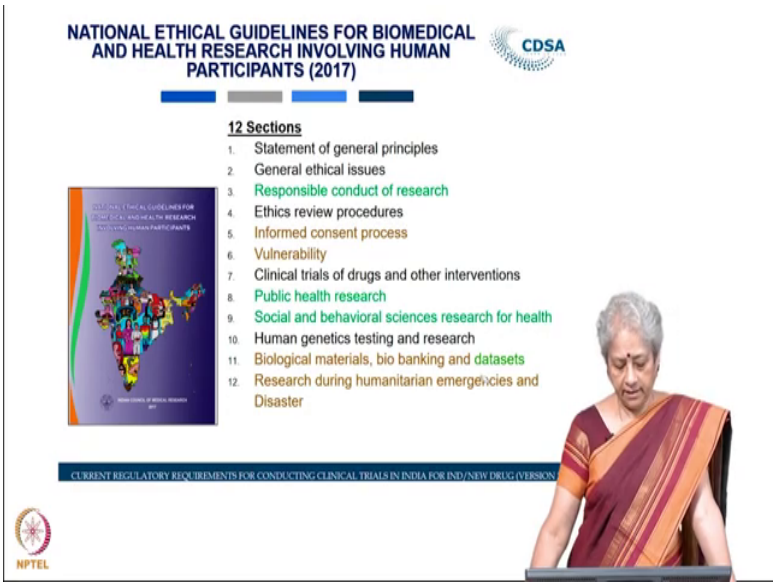
What will we learn in this lecture? One is about the guidelines and some of the related regulations.

(Refer Slide Time: 01:06)



To start with the first guidelines came out in 1980 followed by first revision in 2000 and second in 2006 and the last one in 2017.

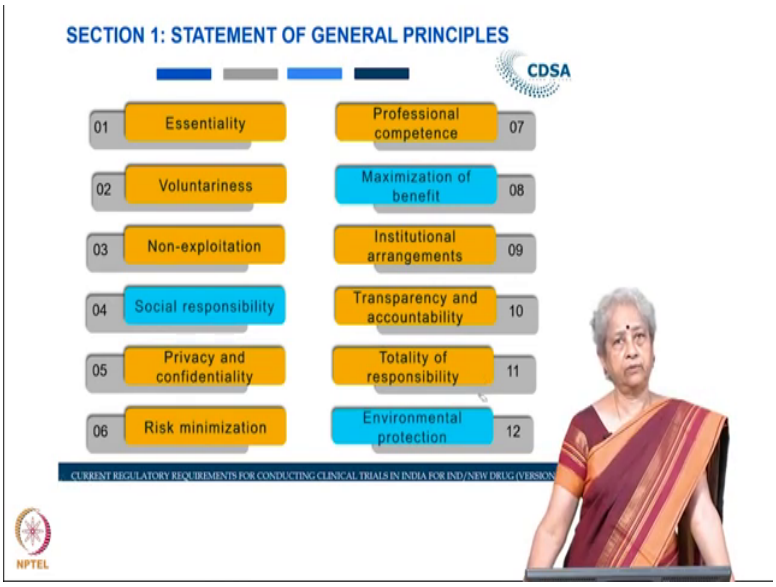
(Refer Slide Time: 01:20)



This national ethical guidelines actually has 12 sections. The green ones that you see are the new editions to this particular revision and the ones that you see in brown already there in the 2006 version but actually got expanded to certain extent that they have to be brought out as a separate section by itself.

So, the new ones are responsible contact of research, public health research, social and behavioral sciences research for health and also small portion data sets which is added to the section on biological materials and bio banking.

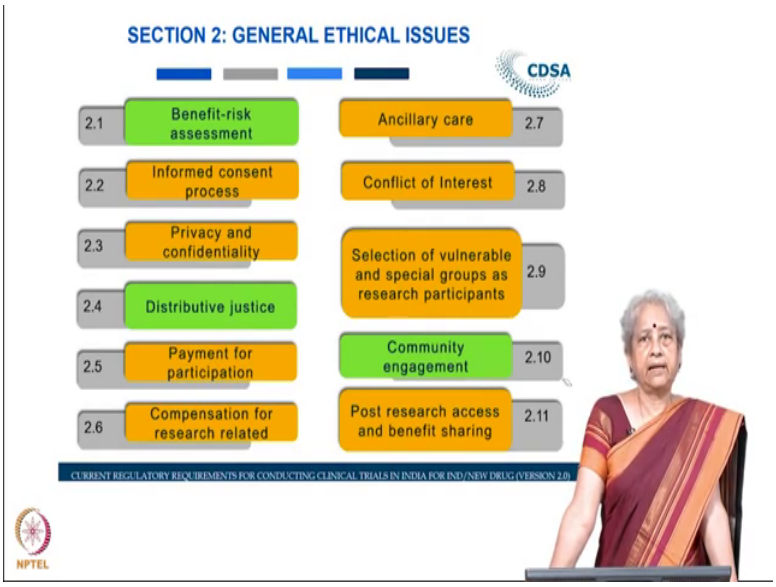
(Refer Slide Time: 02:06)



So, let us start with a section 1, The Statement of General Principles. They are 12 in number and in this revision actually we have replaced 3 of the past versions by social responsibility the ones that you see in bluish green, if social responsibility, maximization of benefit and environmental protection.

And the language of all these principles have been made simplified to such an extent that anybody interested could understand the meaning well.

(Refer Slide Time: 02:44)

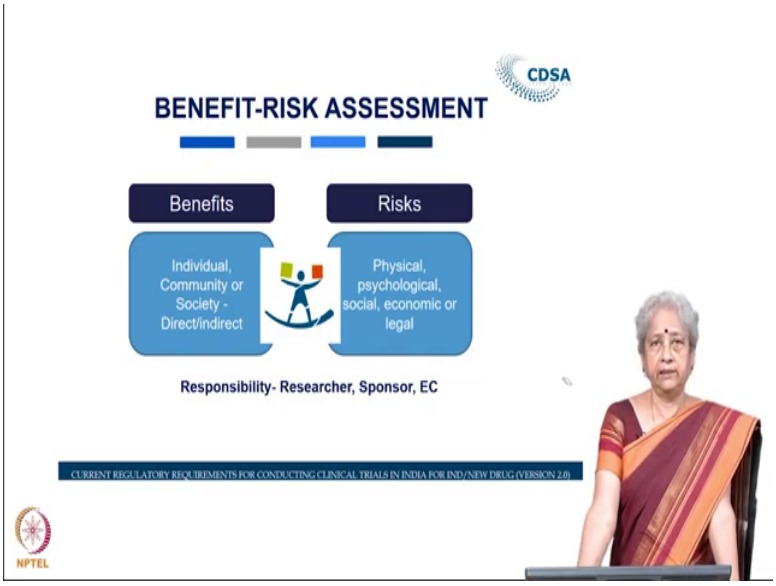


Then you come to the section 2 which is General Ethical Issues. And here again, we have actually added the ones that you see in green, we have added that in this particular section in greater detail; for example, the benefit risk assessment, distributive justice and community engagement.

The other ones in form concern process, privacy and confidentiality, payment for participation, compensation for research related injury, ancillary care, conflict of interest, selection of vulnerable and special groups as research participants and post research access and benefit sharing will be dealt separately.

And to talk about the post research access and benefit sharing this will be coming again and again in the ICMR guidelines in various sections.

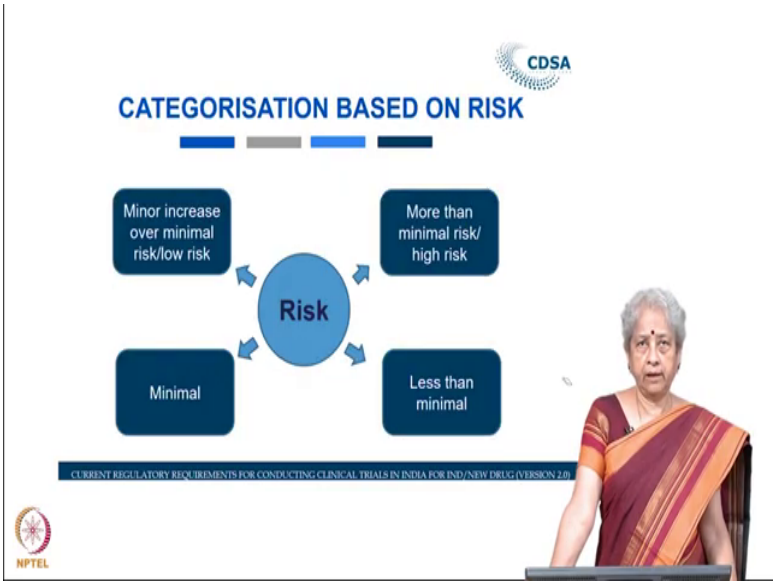
(Refer Slide Time: 03:34)



When you talk about the benefits and risk when you talk about benefits especially, it could be to the individual or to the community or the society and these could be direct or in direct.

And when you talk about risk, it is generally the physical risk that we actually note; but there are other types of risk as well the psycho socials, economic and legal which many a times we actually fail to recognize. And this is a responsibility of the researcher and the sponsor as well as the ethics committee.

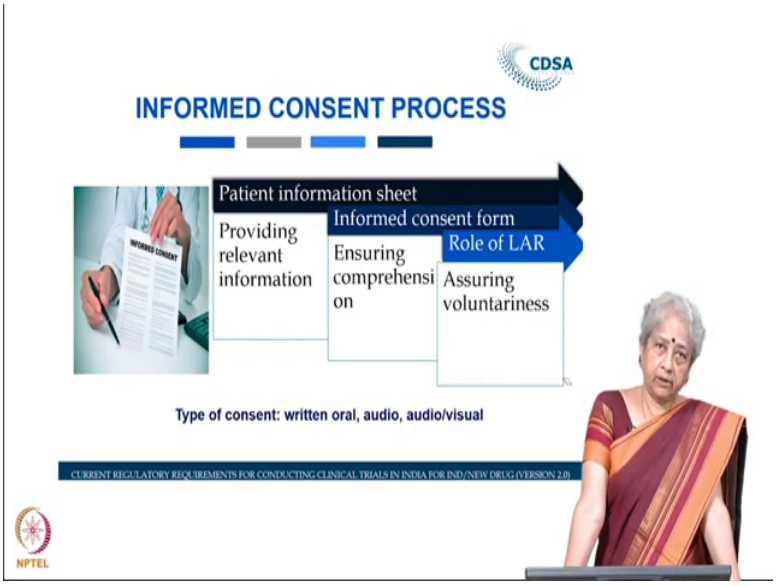
(Refer Slide Time: 04:15)



Now, in when we talk about categorization of risk we classify them into 4: minimal, starting with less than minimal; minimal, minor increase over minimal risk or low risk and more than minimal risk or high risk.

When we talk about less than minimal risk it means that the data or the details are unidentifiable. Minimal risk is what you encounter in daily life and as invasiveness increases you get this other two, minor increase over minimal risk and more than minimal risk.

(Refer Slide Time: 04:55)



Now, why is this important is mainly because you need to the it is actually helpful for the ethics committees to categorize the proposals into different types of reviews which we will talk about later.

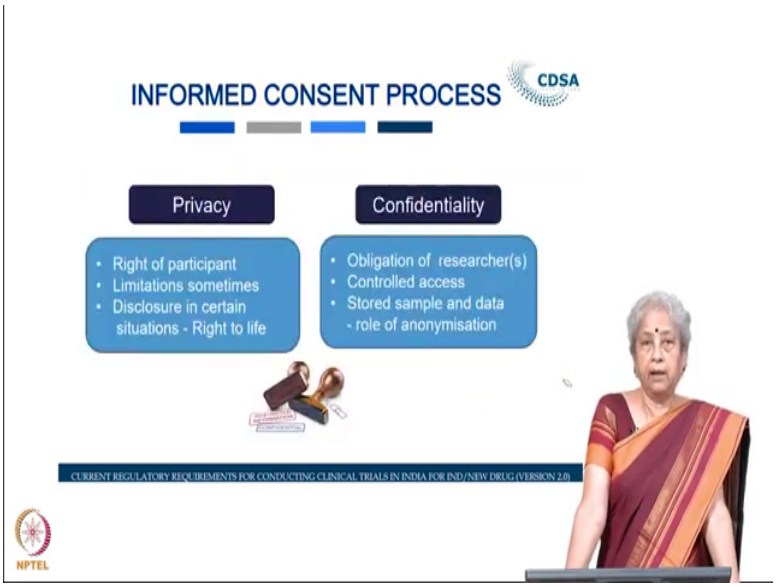
Coming to the informed consent, it actually talks about the informed consent documents which is patient information sheet as well as the informed consent form combine together which we call as informed consent document.

Now, when you talk about patient information sheet is actually providing the whole lot of information which is relevant for that project and the participant is expected to know all the details.

And thereafter, it is not enough that you communicate the information, it is also important to know whether the participant has understood that or not.

And many a times if the person does not understand he is cognitively impaired, then the role of the legally authorized or acceptable representative becomes very important which we term in short as LAR and this is all a means to assure that this voluntariness in the participant getting into enrolled in the clinical trial. The types of consent that we talk of could be either written or audio or audio visual.

(Refer Slide Time: 06:25)



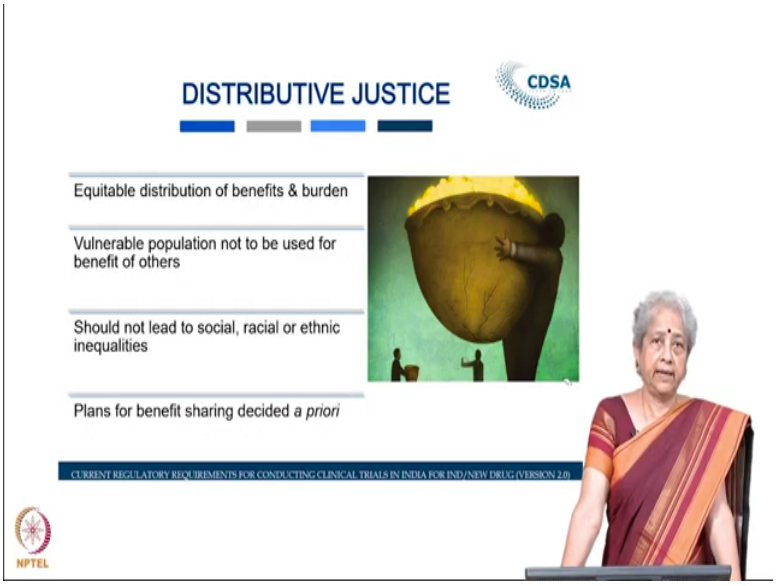
Now, when we talk of privacy and confidentiality one should understand that privacy actually is the right of the participant. But sometimes this can be limited especially in circumstances where there is risk to life not only own life, but also to others.

So, the right to life principle plays a great role here. So, in certain circumstances we may have to disclose it, for example, suicidal ideation or risk to another person or the community or when required by the court this right can be actually breezed.

When we talk of confidentiality, it is actually the obligation of the researcher to keep the information private and one should actually have the mechanism to have controlled access to this information and that is actually described in the document which is presented to the participant to sign or agree to become a participant.

When it comes to stored sample and data, the role of a anonymization becomes very important in order to preserve this confidentiality and we will come to that a little while later.

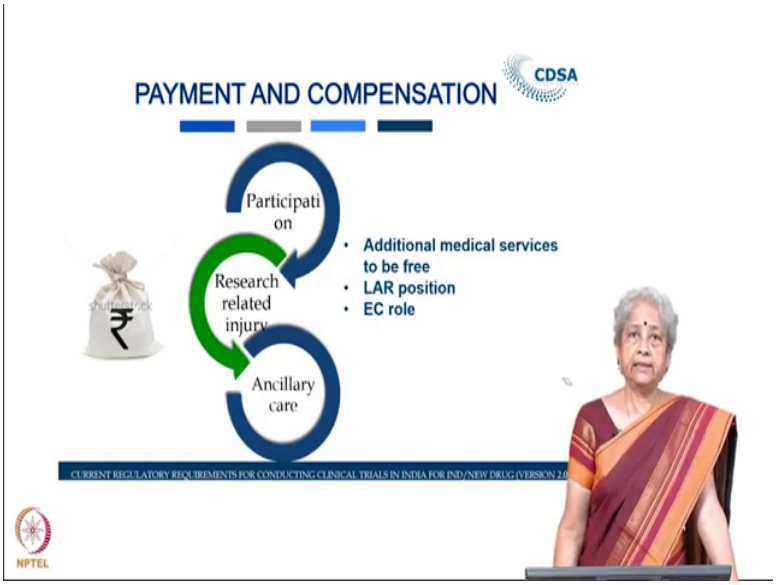
(Refer Slide Time: 07:46)



When we talk about distributive justice: as you can see from the picture each to his need. So, it has to be actually equitable distribution of benefits and burden. And when vulnerable population is used they should not be used for the benefit of others.

And you should not lead to social, racial or ethnic inequalities. There should also be plans for benefit sharing which should be decided before the project is initiated, what we say a priori.

(Refer Slide Time: 08:19)



Now, when it comes to payment, it could be of three types: for participating in the project you may pay a small sum reasonable sum for the travel expenses, incidental expenses or the time taken the extra time needed for such participation.

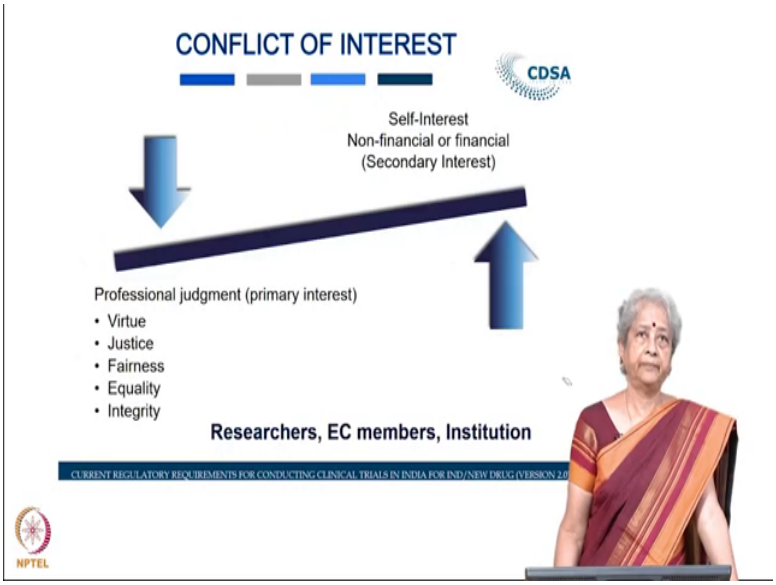
If it is research related injury, it is also bigger obligation of the researcher to compensate in terms of medical management and over and above that financial management if that that is

required. But if it is non-research related injury, then also you have to take care of the participant which is in other words termed as ancillary care.

Now, whenever any additional medical services are to be provided during the period of project then that should be made free for the participant. The position of the LAR is very important in such cases because always where money is involved ones intentions should be also taken care of.

And needless to say, the ethics committee's role in determining these aspects while reviewing a proposal is very important.

(Refer Slide Time: 09:43)



Coming to conflict of interest, always whenever we plan a project professionally, it all the adjectives like virtue, justice, fairness, equality, integrity all these values play a role.

But when one's self interest actually clouds that judgment it is called secondary interest and this could be non financial or financial. The researchers have to take care of this, the EC members as well as the institution. The institution is supposed to have policies addressing these issues.

(Refer Slide Time: 10:27)

When it comes to vulnerable and special groups as research participants, one has to see whether there could be situations where the participant may not have a legal position to give consent. For example, in children or cognitively impaired individuals they could be also legal aspects to that.

So, whenever we have projects related to the this special group of vulnerable group one has to have that particular project addressed addressing the health needs of that population and also try to bring benefits to the community.

Ethics role is of course is very important in deciding this and what are the safeguards that could be employed to protect the interest of this particular group.

(Refer Slide Time: 11:16)

The other general ethical issues which have been covered under this particular section is the investigator initiated research and student research where the student can never be the principle investigator. One has to note that it is the guide who has to the principle investigator and the student has to be termed as student researcher.

And also, there are issues related to investigator initiated research, who will pay the compensation such instances, how to apply for it and things like that. Whenever community engagement community is involved one has to actually engage them in active dialogue before the project is initiated.

Communication of research findings is also important, certain circumstances do you communicate do you not communicate that has to be decided a priori. Again, we mention about post research access and benefit sharing in this section.

(Refer Slide Time: 12:26)

Now, coming to section 3, Responsible Conduct of Research is the new section added to the ICMR guidelines. And this is actually one which can which means that you have to actively promote honesty, accuracy, efficiency, objectivity and transparency in research. And for that

purpose you have to abide by the ethical principles and the professional standards which are essential for the responsible practice of research.

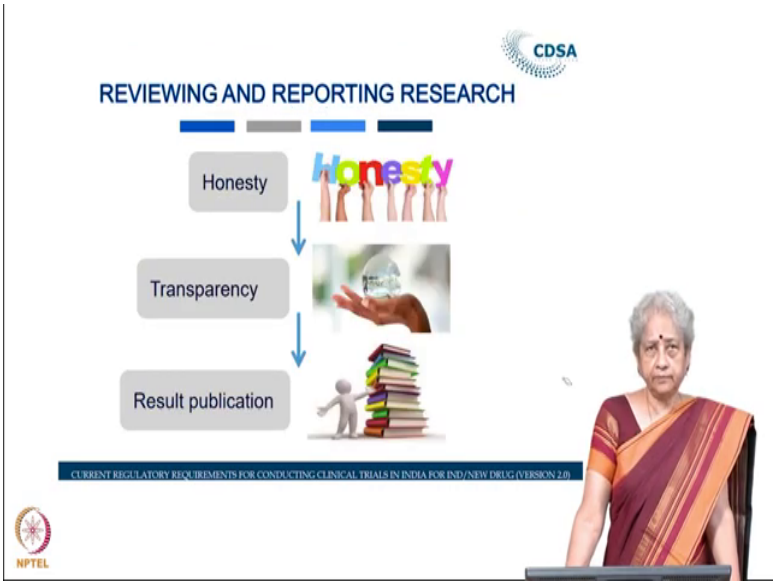
There are these bullet points that you see here are the various topics which have been dealt under this section.

(Refer Slide Time: 12:48)

(Refer Slide Time: 12:59)

Data acquisition whenever we talk about data acquisition we have to actually think about getting permissions, getting authorization from the right parties and how you record this is very important. Who owns the data and who is the custodian of data also has to be decided even before starting the project.

(Refer Slide Time: 13:22)



And when it comes to you have done your research you have conducted it well and now you want to actually report it. So, before that you have the reviewing process. So, all honesty transparency has to be applied when it reaches the position of publication.

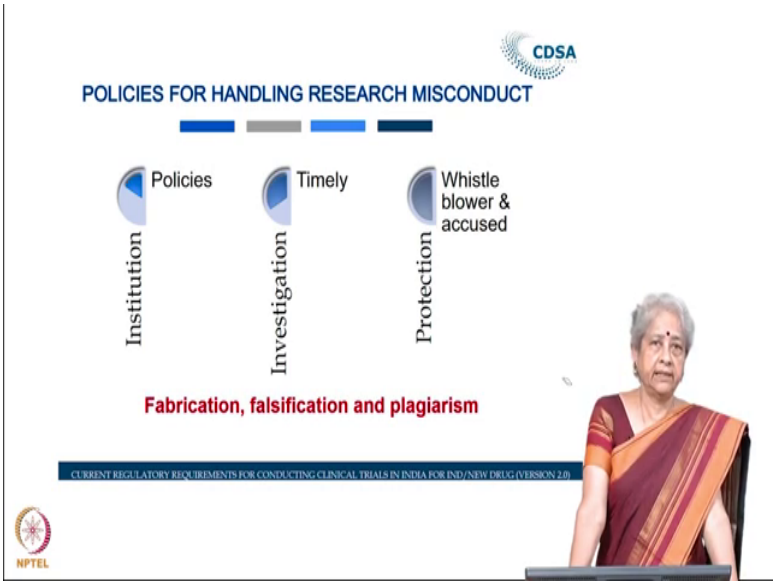
(Refer Slide Time: 13:42)

So, what when we talk about publication, it is the authorship that we talk of which has to be I mean which the guidelines say that one should follow the ICMJE guidelines regarding authorship.

Besides, this is the institutional and department policies also will have to be in place because in certain circumstances this can come in very handling in settling disputes. When it comes to peer review, there are issues regarding that also you know self review and all those issues are dealt with this particular subtopic.

And also emphasis lead that registration of clinical trials have to be there, especially regulated clinical trials have to be mandatorily registered in the clinical trial Registry of India.

(Refer Slide Time: 14:40)



Then there are issues about research misconduct, then the institution should be already prepared with policies to deal with such a situation and the investigation should be held in a timely manner and till that is solved till one reaches the conclusion there should be protection for both whistleblowers as well as the accused because many a times there could be false accusation.

And when we talk of research misconduct the three buzz words are fabrication, falsification and plagiarism. We will not go into detail about these three terms because time will not allow that so you can read this from the guidelines.

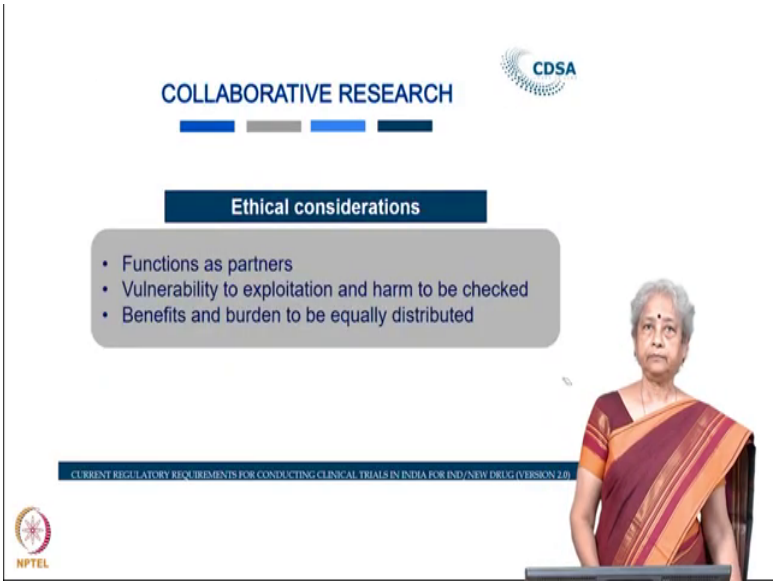
(Refer Slide Time: 15:30)

As I had stated earlier, registration of regulatory clinical trials are mandatory for sorry are mandatory and the others are actually voluntary, but it is always in the interest of the researcher that the trial is or research is registered in the CTRI and a down below that you see the web link for that.

Many a times there are actually complains that there is a lot of delay on the part of the registry to give them the information that their research has been entered into the registry.

There are many things that is asked of the investigator which they actually delay in answering and many a times this is delay is due to that. And you can see from the things that have been outlined there that you have to answer all these things before you can actually say that the whole information has been provided to the clinical trial registry.

(Refer Slide Time: 16:46)



Then we come to the collaborative research. One should understand that whether it is a national collaboration or international collaboration, the partners are always on equal footing should be on equal footing. Vulnerability to exploit and harm the participants under that particular site should be actually always checked and benefits and burden should be actually equally distributed.

(Refer Slide Time: 17:19)

The responsibility of the ethics committee, researcher and institutions in collaborative research is to see what is the social and cultural context. This is very important in order to prevent exploitation.

And then the ECs in between these sites will have their own ECs coming into play and what is the communication between these ethics committees that is important many a times because one particular EC may not culturally agree to the terms that are being dictated for all sites or decided for all.

The researcher expertise and participant protection are very important aspects and they needs to be a participatory designing all are equal partners as I said earlier. So, everybody has an equal say in designing the project.

The safeguarding interest of the participants, researches and institution should be actually decided much before the project is initiated.

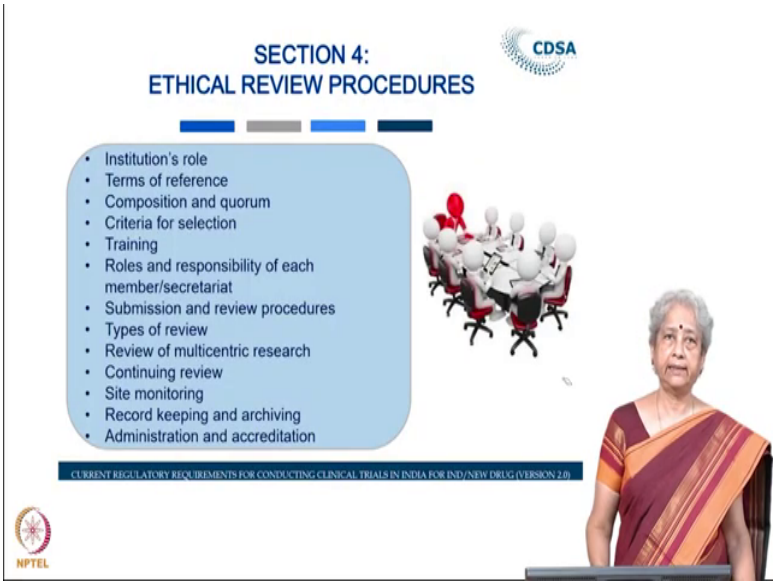
(Refer Slide Time: 18:32)

In the event of international collaboration there are more issues regarding, who owns the sample, what who will actually do the data analysis and how it will be disseminated, publication and IPR issues. In such circumstances, the standard of care actually is the best possible nationally available standard of care which is actually which has been prescribed in the guidelines.

The proposals if they are not done in the country of origin are generally not acceptable and one needs to be complained to the guidelines regulations cultural sensitivities of the countries. Since we have our own guidelines, what exist in a country should be actually respected.

There has to be appropriate MoU and if there is a transfer of biological material there needs to be a material transfer agreement between the parties and this is actually screened by the Health Ministry Screening Committee in order to protect the actually interest of the Indian scientist and also see that sensitive information is not sent abroad for exploitation purposes.

(Refer Slide Time: 20:03)

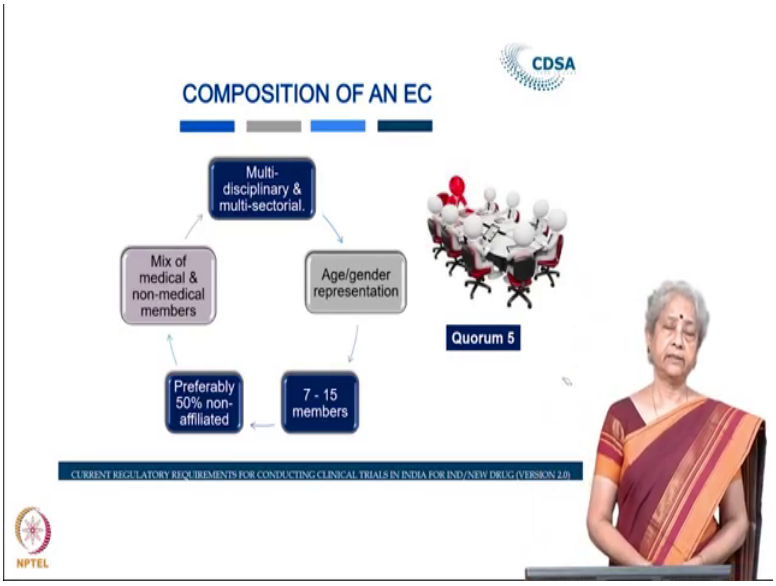


Coming to section 4, which is Ethical Review Procedures: This particular section has been expanded to a great extent and you can see the from the bullet points that there are number of aspects which have been covered under this section.

(Refer Slide Time: 20:11)

What is the structure, what about the competence of the members, how should they function and the independence nature of decision are the points which have been highlighted under this section.

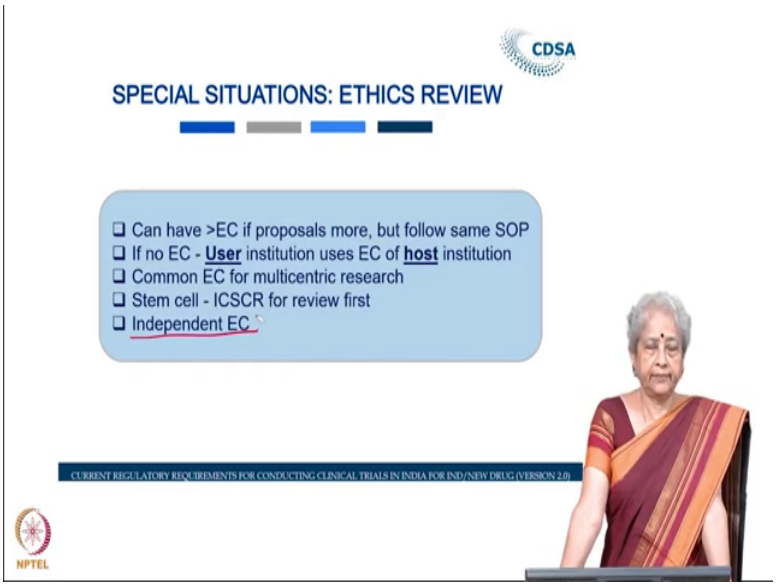
(Refer Slide Time: 20:27)



And the composition of an ethics committee could be multi-disciplinary multi-sectoral there has to be age and gender representation it is not like the ethics committee can have only one member or only one female member or one male member that skews the point of view of ethics committees.

7 to 15 is the number prescribed for membership and preferably 50 percent of these should be non-affiliated. There has to be a mix of medical and nonmedical members because you get the different viewpoints together which gives which enables a better decision making process.

(Refer Slide Time: 21:17)



Now, if an institution handles number of proposals then you can have more than one EC, but they have to follow the same SOP. If an agency or institution is small they do not have ethics committee and they do not have the means to have an ethics committee then they can approach another institution which has somewhat standardized functioning ethics committee. In that case, the institution which they approach becomes the host institute and the one which is asking for the which is requesting that becomes the user institution.

But this is a this will be actually a more use will be effective only if there is MoU between the two institutions highlighting that the host institution can actually have access to the user institutions records for monitoring purposes.

In multicentric research, one could have a common designated ethics committee which will see the proposal in consultation with representatives of the site ethics committees, finalize it and

then the site ethics committees have all the freedom to implement it at their site and also follow it up in a monitoring process.

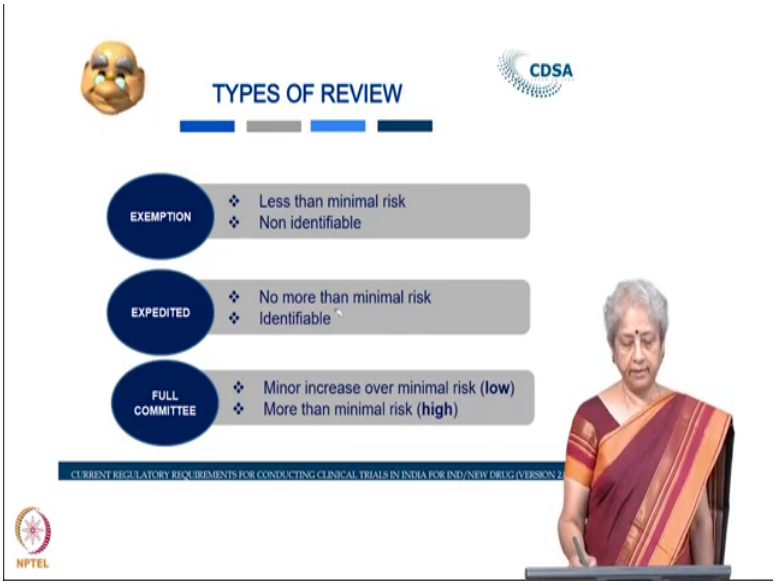
Now, when it comes to stem cells, you have the institutional committee for stem cell research if this would act as the scientific review of that particular project. If you do not have that you can actually go out two specialists; one basic scientist and one clinician into the ethics committee to review such proposals.

Now, when it comes to independent ethics committee initially when the guidelines came out this particular independent ethics committee at that time would handle only the regulatory clinical trials which were bio available and bioequivalence studies. But with the present rule that has come out on 19th march they can handle other regulatory trials, but they have a great responsibility described under the rules.

(Refer Slide Time: 24:15)

So, the role of ethics committee is actually to actually preserve the rights safety and wellbeing of the participants. So, it is one of the pillars which actually protects the welfare of the participants. And it reviews types of biomedical and health research involving human their biological material and data.

(Refer Slide Time: 24:39)



Now, as I told you earlier why we actually divide the risk into various categories is to help the ethics committees to decide whether it goes under exemption from review or is it expedited review or full committee review.

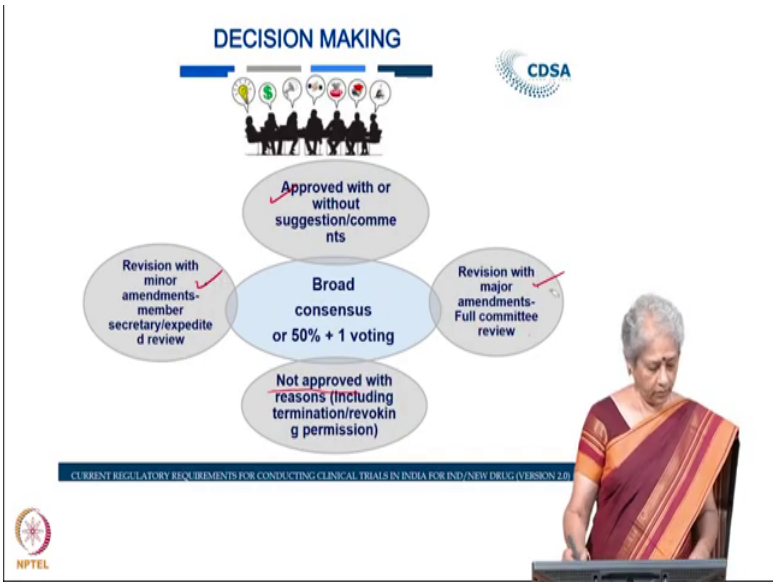
So, less than minimal risk actually goes under exemption and minimal risk goes into expedited review process there are various points highlighted in the ICMR guidelines which can actually be subjected to expedited review.

The point that one has to understand in the process is that exemption actually leads to non identifiable information which you can take it from the website which is in the public domain or the information does not identify any person. But when you say minimal risk it becomes identifiable.

So, you must understand that exemption is non identifiable, expedited is identifiable, full committee is also identifiable, but there you have categorized it into low or high risk of invasion into the body. For example, if you take 5 ml of blood from a healthy individual it will be a low risk, but at the same amount of blood if you take it from a sick neonate child would be high risk.

So, one has to actually decide the invasiveness and classify them, but the review process would be by full committee for both.

(Refer Slide Time: 26:32)

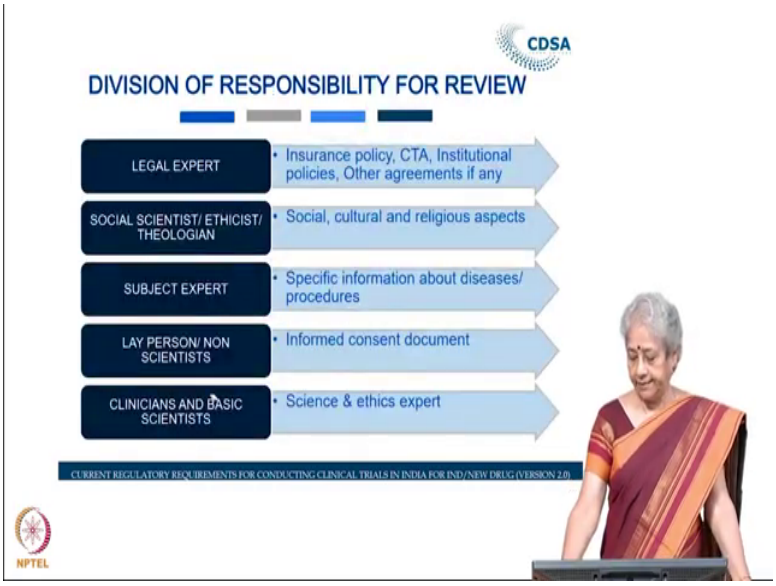


So, now that we have come to decision making, let us see how the ethics committees a decision has to be written. So, we have approved with or without suggestion or comments and if you want revision it has to be a written with minor amendments or with major amendments.

And if does not fit into all this it has to be not approved and that will be actually a better word than saying rejected. And there has to be either a broad consensus or if you prefer voting it has to be 50 percent plus 1.

So, this actually has to be written in the SOP otherwise there is no point actually in making a decision sometimes it is not accepted by some of the international agencies for example, the NIH grants, they want voting to be minuted in the minutes.

(Refer Slide Time: 27:47)



So, So, it is actually a division of labor when we talk about ethics committee review it is always better to divide the task. The nonmedical persons actually bring in the perspectives of the public in a way the legal expert gives you opinion about the insurance policy, the clinical trial agreement, institutional policies and other agreements.

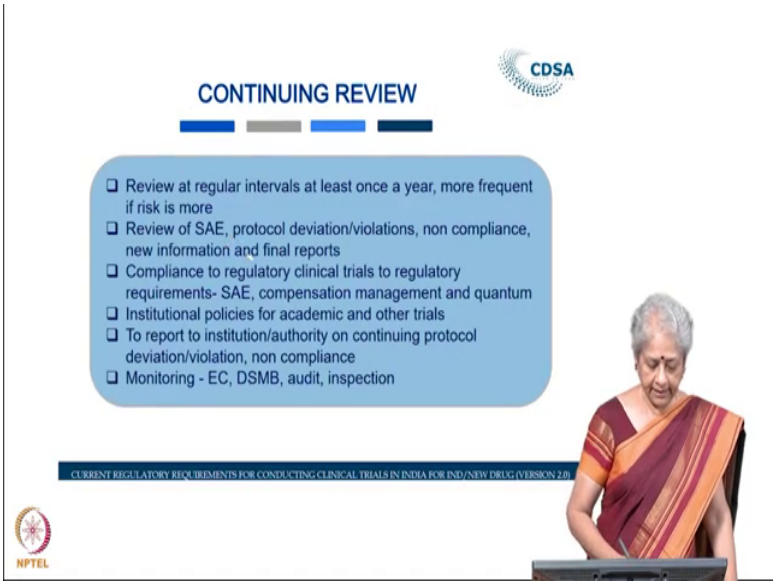
So, the person is expected to bring in the existing laws if required to guide the committee as to what is right and what is wrong.

The social scientist actually brings in the social cultural and religious perspectives to the committee which actually is a softer side of life. And the lay person is the most important person to review the informed consent document. It is believed that if the lay person is able to

understand the language then most of the work is done you expect that the participant also will understand.

But when it comes to the scientific aspects it is the subject expert and the clinician and basic scientists who are actually responsible for providing that perspective. And if the subject expert is not there in the ethics committee they are supposed to provide their comments or come in person, but never have the voting rights.

(Refer Slide Time: 29:19)



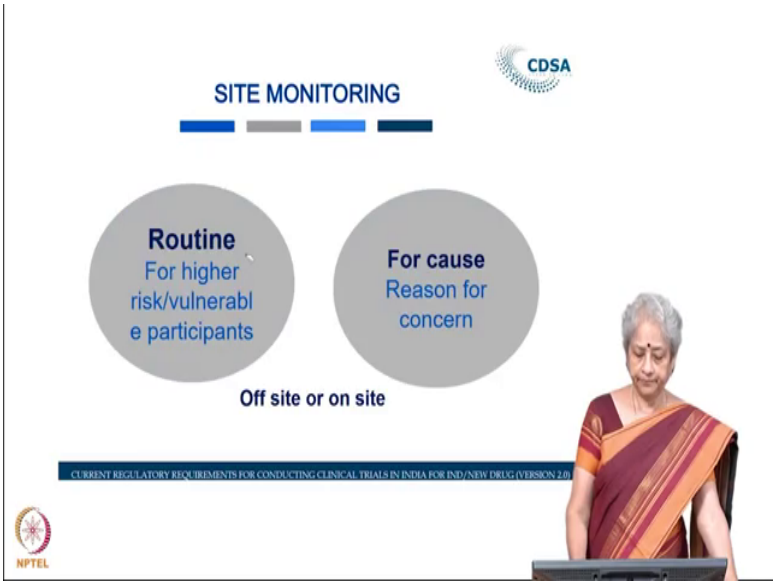
Its not enough actually to think that once you have given approval or opined about minor or major revisions or you have not approved it not approved means the proposals cannot come back again in a revised form. But once you have given approval then it is a continuous process that is why we see continuing review. So, it has to be reviewed at regular intervals at least once a year more frequently if the risk is more like 3 monthly or 6 monthly.

The review of series adverse effects events, protocol deviation, violations non compliance, a new information and final reports all these form the continuing review. This is also to see whether there is compliance to the regulatory clinical trials to regulatory requirements. For example, how do you actually review the series adverse events, what is the compensation mechanism and what would be the quantum of a compensation that would be decided.

Now, institution policies would be there for academic and other trials. So, that has to be considered a against the background. Whenever there is actually continuing a protocol deviation and violation or non compliance this has to be reported to the institution or authority.

Monitoring actually is a process by which you actually keep control of the situation and this could be done by the ethics committee the DSMB and auditor or inspector, inspector of course, is the regulator and that is the last step resorted to.

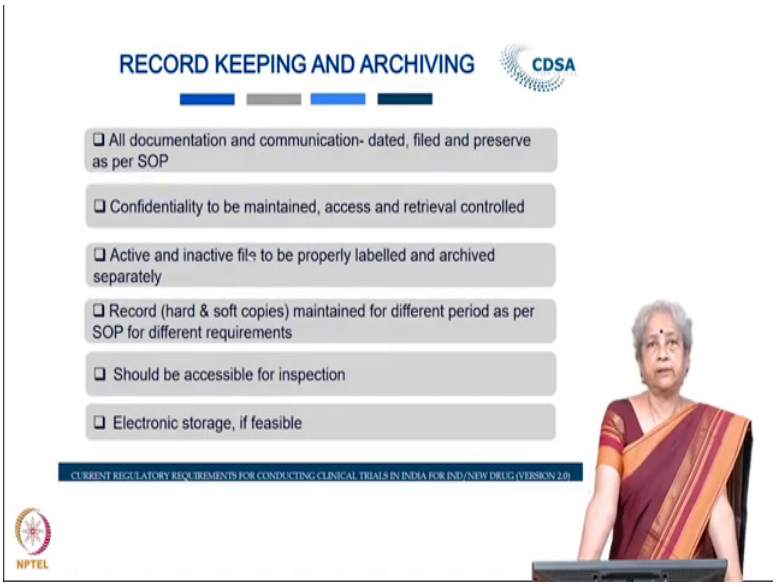
(Refer Slide Time: 31:24)



When you talk of site monitoring it can be offsite or onsite the routine one is for higher risk of vulnerable participants. And for cause there are reasons when certain signals are produced alerts are produced because a particular investigator has not complied despite several requests from the ethics committee is secretariat to provide clarifications or there are number of deviations alarming number of deviations or a protocol violations or somebody has actually complained about what is happening in certain site.

There are many other such reasons which will be actually incorporated in the sov SOP for taking action in such instances and this will be actually onsite part of onsite monitoring.

(Refer Slide Time: 32:22)



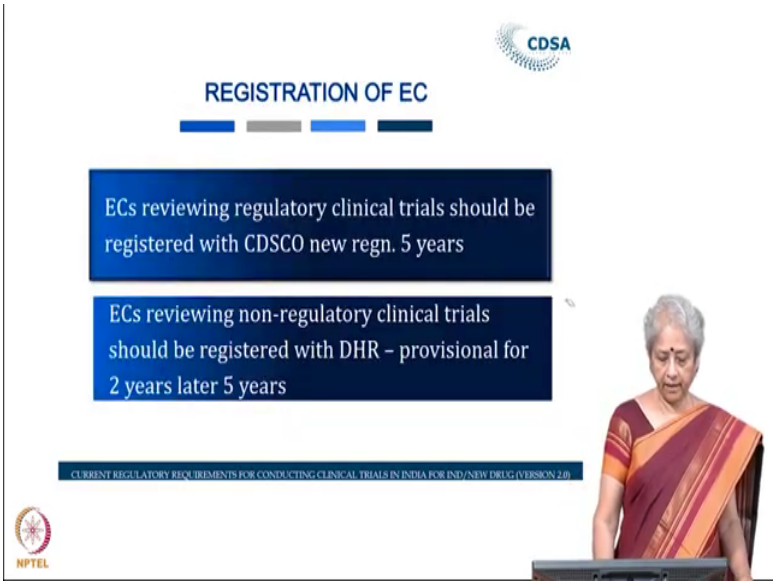
Now, record keeping and archiving is also an important task of the ethics committee secretariat. So, all documentation and communication have to be dated file and preserved as per SOP. So, record keeping and archiving are also important functions of the ethics committee secretariat and member secretary. All documentation and communication have to be filed with date and preserved as per SOP.

Confidentiality has to be maintained there were access to these records have to be controlled and how you retrieve them who retrieves them is also to be controlled.

There could be active and inactive files which have to be properly labeled and archived separately. Record whether it is hard copy or soft copy they have to be maintained for

different periods as per SOP for different requirements. They should be accessible any time for inspection. One could also actually store them electronically if that is feasible.

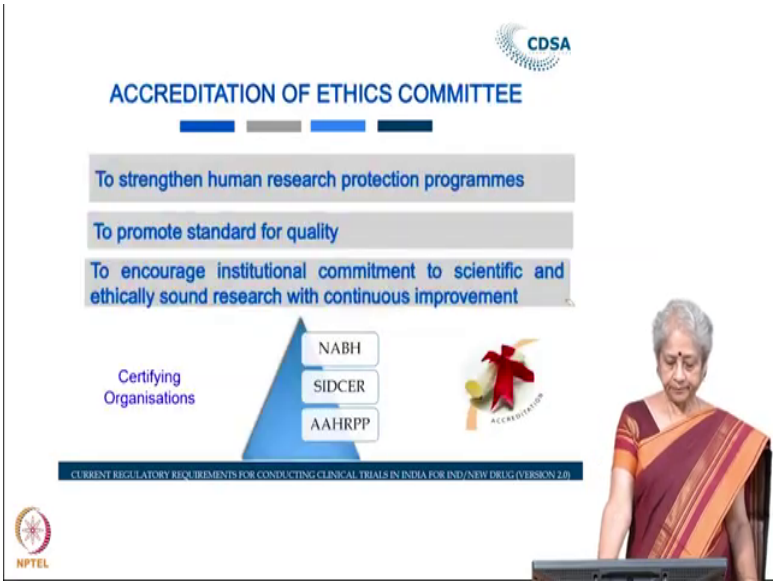
(Refer Slide Time: 33:39)



When it comes to registration ethics committee one will have to now note that earlier it was said that all ECs reviewing regulatory clinical trials should be registered with CDSCO and that was for a period of 3 years.

According to the new drug and clinical trials rule which has a being issued on 19th march 2019 has increased this period to 5 years. Now, all those non regulated clinical trials which are reviewed by ECs were not required to register but from this month if everything is ready one will have to do it with the department of health research and provisionally, the registration will be for a period of 2 years which will be extended to 5 years later.

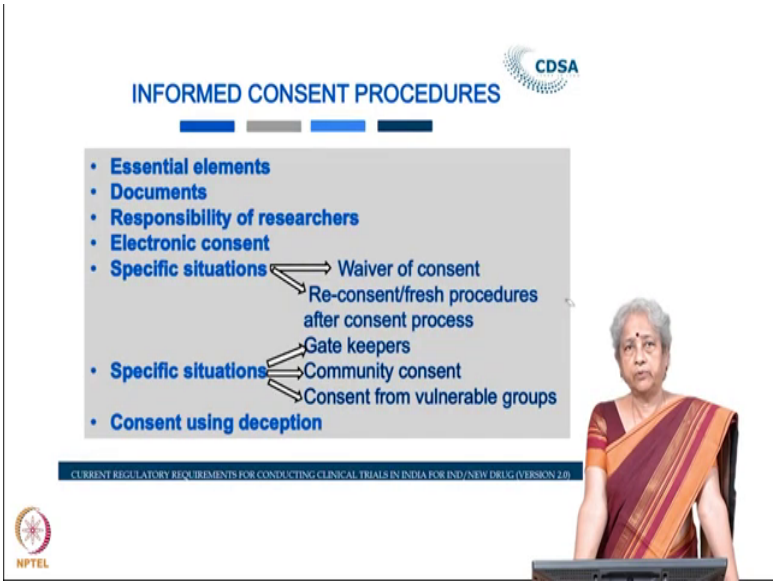
(Refer Slide Time: 34:39)



Accreditation of ethics committee is actually trying to improve quality of a ethics committee functioning and also it strengthens the human protection program and promotes the standard for quality.

The three agencies right now available for such purpose in India are the NABH; which is the national accreditation body and SIDCER which has been actually initiated by WHO earlier and the other one and which sees only the ethics committee and NABH and SIDCER review the NABH for clinical trial ECs is only for ECs SIDCER is also for ECS whereas, AAHRPP is American agency which looks which reviews the whole organization its employees and a small part of ethics committee functioning.

(Refer Slide Time: 35:52)



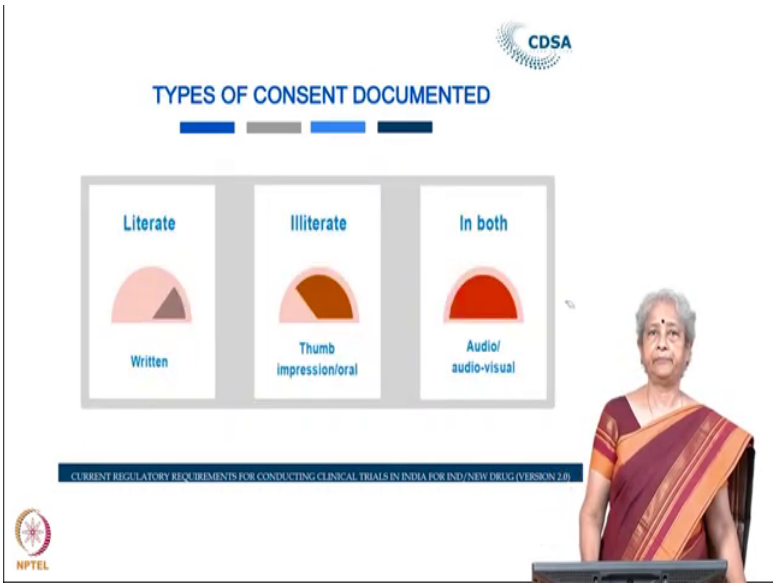
So, coming to section 5 Informed Consent Process on which we had touched earlier. One should understand that all ethics committee all informed consent documents should have the essential elements which have been described on page 50 of the ICMR guidelines and it is a responsibility of the researchers to follow these. There is also the concept of electronic consent wherever applicable especially in pharma trials they do have this mechanism plain.

The other thing that we have to consider is whether we can have waiver of consent and there are situations where you may have to have re-consent or fresh procedures after consent process when you may have to actually take a re-consent.

The special situations where you may have to have another protective mechanism like gatekeepers for example, if you are going to school for a project then you have to take the permission of the and these are called permissions for the principal of the school.

Similarly, if you are drawing people from a particular community you have to get the consent of the community and vulnerable groups again consent from them. There is also a mechanism about consent using deception about which we will talk in a subsequent when we go through the subsequent slide.

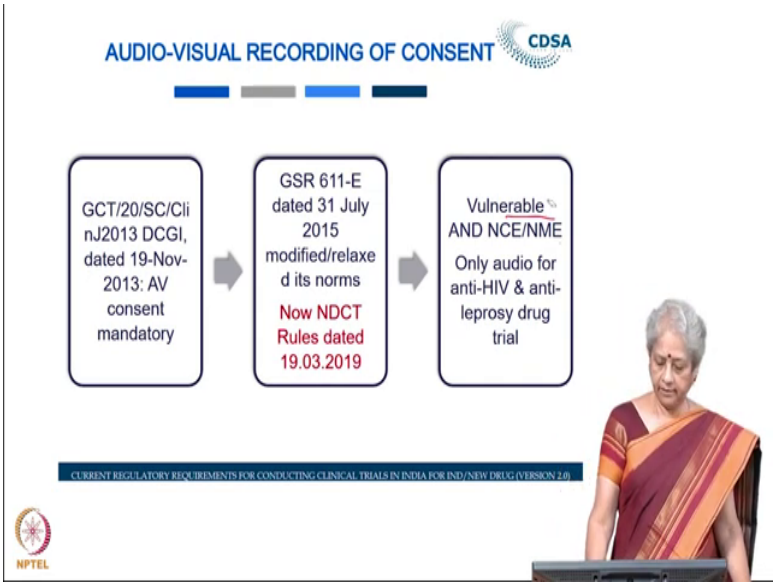
(Refer Slide Time: 37:26)



So, what are the types of consent? How do you document? All types of consent have to be documented. If you are literate then written consent is acceptable but if one is illiterate then thumb impression is taken into account but this has to be corroborated by an impartial witness.

So, any consent process has to be documented if the participant is a literate person then written document written consent signed and dated is accepted. But if the participant is illiterate then it is a thumb impression or suppose you are taking overall consent in that case in these circumstances you need to have an impartial witness at present during the process and whose signature with date is accepted as a documented consent process. In both cases, sometimes you may have to take audio or audiovisual consent depending upon the circumstances.

(Refer Slide Time: 38:35)

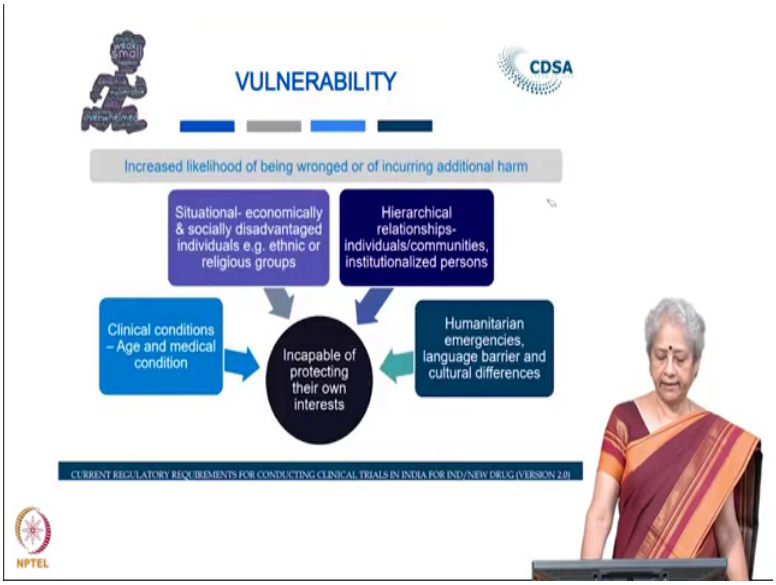


Now, audio visual recording of consent has become mandatory in regulatory clinical trials. Regulations now require that for any regulated clinical trial you need to have audio visual recording and this has been actually repeated although earlier it was GSR 611-E on 31st July 2015.

Now in the new drug and clinical trial rule it has been reemphasized that audio visual recording has to be taken for vulnerable as well as when you are doing clinical trials using new chemical entities or new molecular entities. Only problem is whether these vulnerable populations can be defined into particular types of people because all participants are vulnerable in a in some sense but there is only a relative risk more for certain population than the others.

When one has a clinical trial using anti-HIV and anti-leprosy drug then one need not take audio visual recording one can take only the audio recording in such instances.

(Refer Slide Time: 40:07)

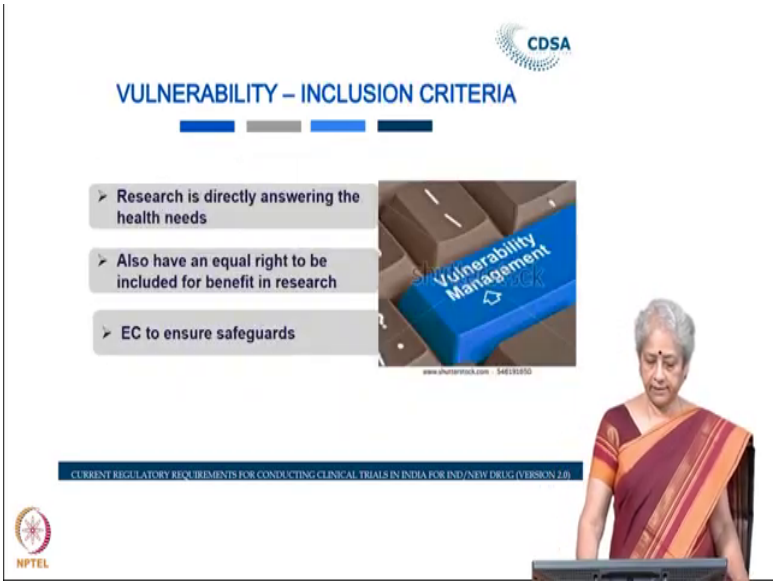


Coming to section 6 about Vulnerable Population, when we say vulnerable population they have this increased likelihood of being wronged or of a incurring additional harm. So, these could be situational or hierarchical or there could be some clinical conditions age related or

medical conditions where there is a total failure of the existing treatment modalities or it could be a humanitarian emergencies, language barrier and cultural differences.

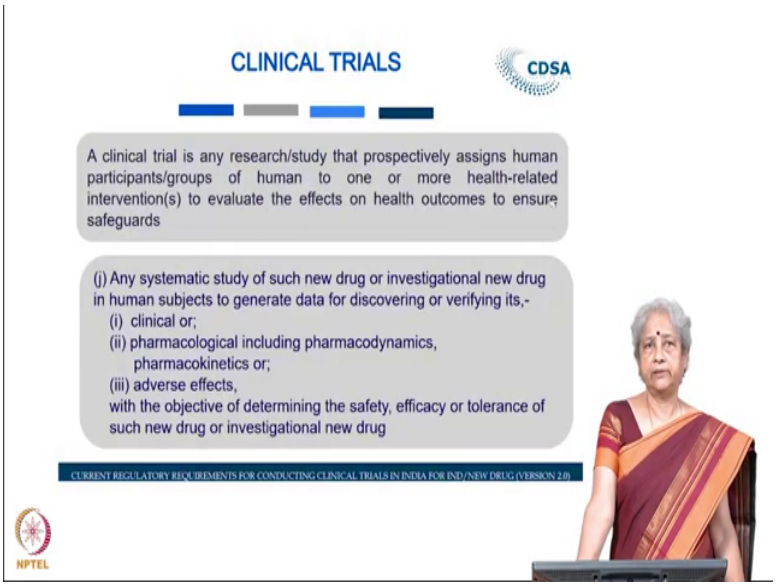
In all these cases, there is some sort of in capability in giving a true informed consent while enrolling in a clinical research. So, the point is that, because of this incapacity when the ethics committee has additional role of seeing, what are the safeguards which can actually protect their own interest.

(Refer Slide Time: 41:04)



One should always remember that the research should be directly answering the or addressing the health needs of this population and one should also consider that they always have an equal right to be included for the benefit that they can get in through research the ethics committee needless to say should actually ensure safeguards.

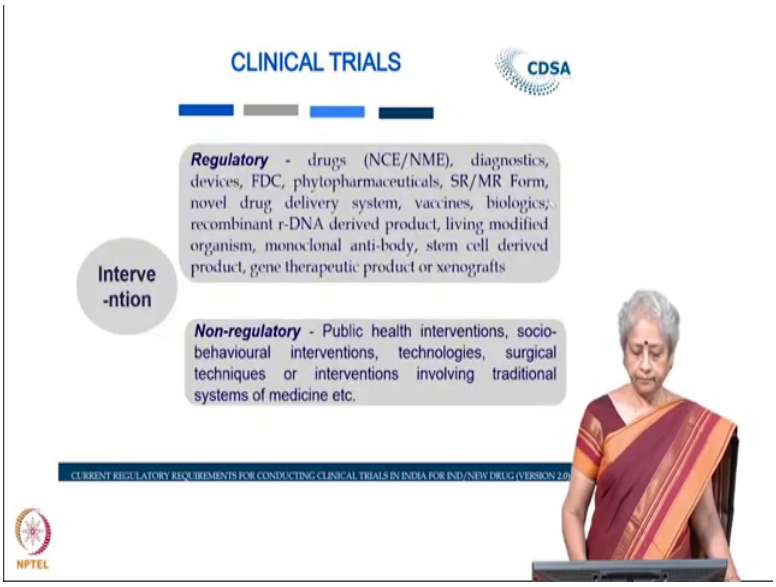
(Refer Slide Time: 41:36)



Coming to section 7 on Clinical Trials for Drugs and other Intervention, it is a huge section and the definition given here is actually a general definition that a clinical trial is any research or study that prospectively assigns human participants of groups of human to one or more health related interventions to actually evaluate the effects on health outcome to ensure safeguards.

Now, this is a general condition and what we have in the new drug and clinical trials rules is what is given below that any systematic study of such new drug or investigational new drug in human subjects to generate data for discovering or verifying its clinical or pharmacological including pharmacodynamics, pharmacokinetics or adverse effects with the objective of determining the safety efficacy or tolerance of such new drug or investigational new drug. So, the language differs a little which is strictly pertaining to definition of new drug.

(Refer Slide Time: 42:50)

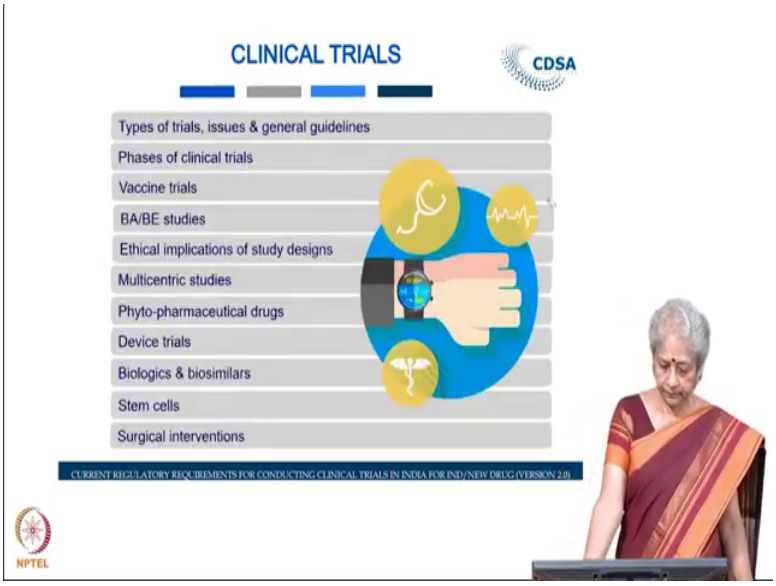


So, when we talk regulatory clinical trials then all these elements that are described under regulatory section are the various terms that have been actually highlighted in the in this square that you have here.

The non regulatory also has clinical trials pertaining to public health interventions, socio-behavioral interventions, technologies, surgical techniques or interventions involving traditional systems of medicine. Now there is a distinction between traditional systems of medicine and phytopharmaceutical.

Phytopharmaceutical has been described in the new drug and clinical trial rules whereas, and it has certain requirements for being included as a phytopharmaceutical whereas traditional systems of medicine is different from that.

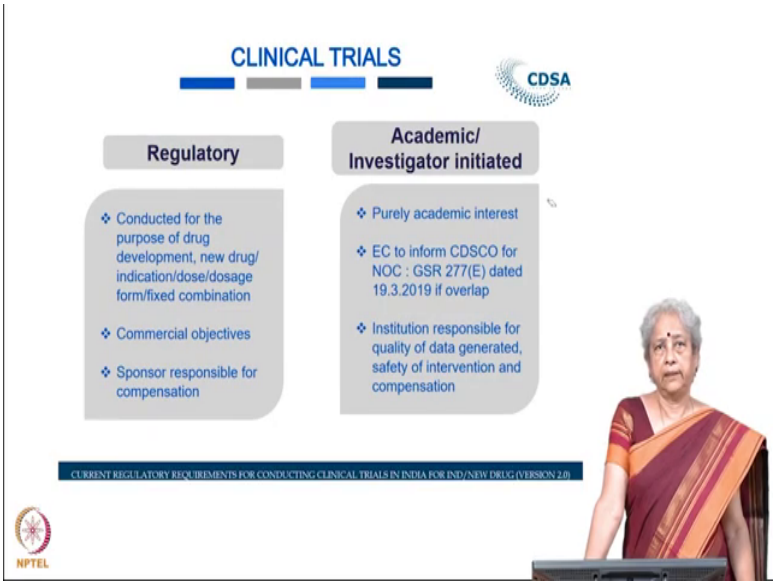
(Refer Slide Time: 43:55)



Now, as you can see there are various topics under this heading we will not go into details about this.

(Refer Slide Time: 44:04)

(Refer Slide Time: 44:08)



And it is most important to understand that there is a difference between regulatory academic or investigator initiated research. Now when you say a regulatory it means that whatever comes under the under the definition of new drug is included under this including devices which is also separately stated new drug, new indication, new dose, new dosage form or fixed combination are included under this. And it has a commercial purpose behind that and when it comes to compensation for injury it is the sponsor who is responsible to do that.

Whereas the regulators have actually separated this out from academic clinical trials there is a purpose behind that and investigator initiated research or what we may now call as biomedical and health research in short form BHR are those which are purely academic in nature.

But whenever an overlap is actually expected so what you see here GSR 277 its nothing but the new drug and clinical trials rule. If the ethics committee expect there is a slight overlap between this academic nature of the project and regulatory requirement.

So, then it has to actually it can approve it, but it has to inform the CDSCO about it wait for the reply for 30 days and then it would be considered if there is no reply from them that it is approved for the purpose that EC had given the decision for.

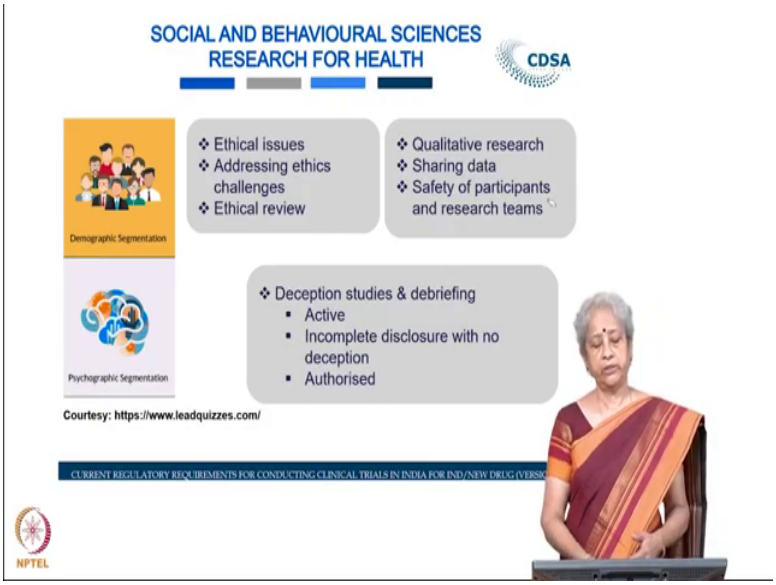
Now institution is responsible here for the data that is generated and the safety of the intervention as well as compensation.

(Refer Slide Time: 46:24)

Coming to section 8 on Public Health Research, there are number of topics in this. One should understand that there is a very thin line between public health service and research. So, the

ethics committee will have to give its decision accordingly and understand the situation as to what is service and what is research.

(Refer Slide Time: 46:52)

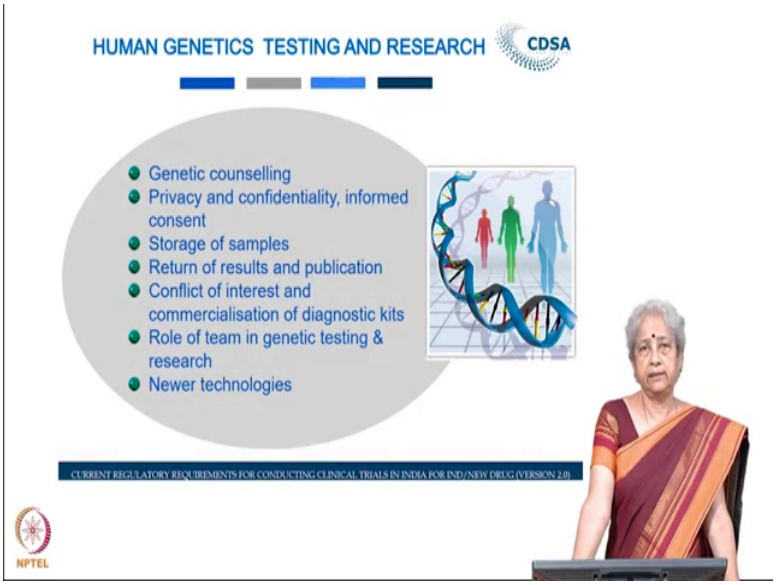


Section 9 pertains to Social and Behavioral Sciences Research for Health and here is where we need to be extra cautious about the ethical issues and also see that it addresses the ethical challenges because of the cultural and religious differences between various sects of population within that geographical area.

In qualitative research sharing data safety of participants all these are very important but one should also remember that. The research teams are also you know they are in unsafe positions actually when they conduct research in their own area. Therefore, for the safety of the resource team interviewer in certain circumstances people from neighboring area are actually employed to do the interview.

Here is where the controversy about deception studies come in. So, it could be active in complete disclosure with no deception and authorized, authorized means the participants are giving authorization to the researcher to not give the whole picture as it is and these are actually sometimes required whenever there are sensitive issues involved and in such cases it is also the duty of the researcher to debrief them the participants about the results and it is only the aggregate data which is actually given out.

(Refer Slide Time: 48:31)



Now, section 10 deals with the Human Genetics Testing and Research here again there is a very little very thin line between service and research one important aspect is genetic counseling is very important whether it is service or research prior to taking the biological material for diagnosis and even after that. Privacy and confidentiality are very important

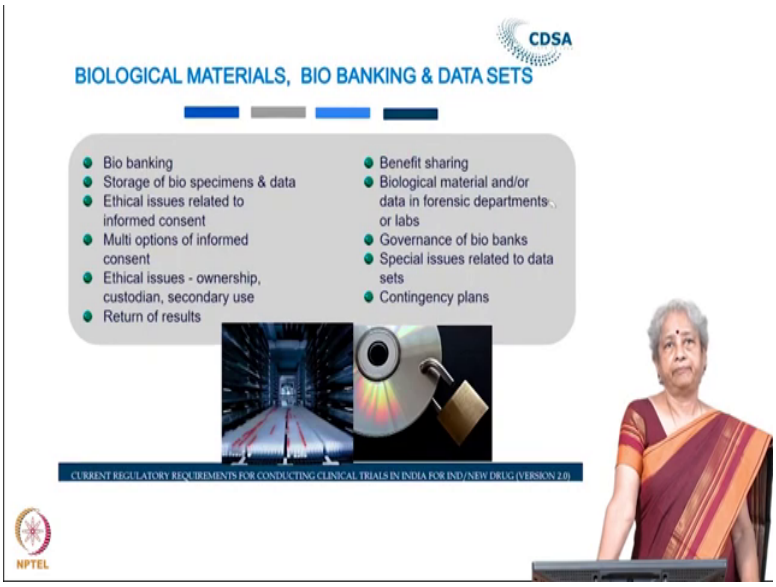
aspects because whenever we talk of genetics it is not one individual who is involved but also the whole family perhaps.

The storage of samples are very important in such instances and when you get results if it is to be of benefit to the participant it is the obligation of the researcher to inform that and when you publish these results also one has to be very careful that there is no stigmatization involved.

Conflict of interest and commercialization of diagnostic kits are important aspects which will also cover in the next section. So, the role of team in genetic testing and research is very important because you are actually you would be branding a particular person having positive disease. So, that revelation could be quite damaging there could be psychosocial trauma related to that.

And we also know about the newer technologies the danger is poses everybody knows about CRISPR technologies, how it is being watched, they have been fraud committed in recent times about it. So these are all aspects where ethics is a very important and ethical policies are very important to be developed and discussed.

(Refer Slide Time: 50:25)



Section 11 deals with Biological Materials, Bio Banking and Data Sets. Now, when you talk about bio banking, it is actually a repository of bio specimens and data. Now ethical issues could be related to informed consent, there could be multiple options given for informed consent and one should always remember that the person who gives the sample is the donor and is the owner that is why we say that the donor has the ownership.

Whereas the researcher as well as the institution is the custodian, they can never say that we own those samples and if it is to be used if these samples have to be used for secondary use and there are certain requirements how you allow that and ethics committee plays an important role in such instances.

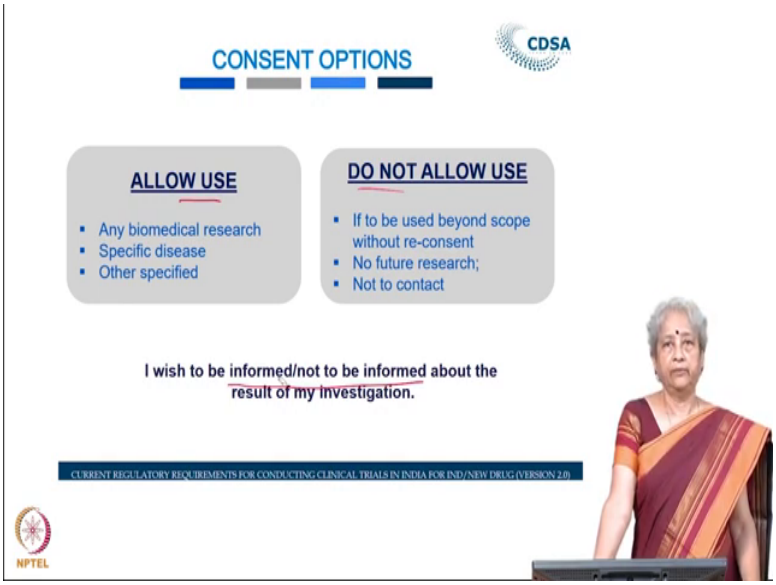
Again here we are emphasizing the importance of return of results and the obligation of the researcher to inform the participants if there is any positive outcome coming out of that

project. Benefit sharing comes into play when this commercialization involved using the biological materials from the bank.

Now, when there is also a section on biological materials or data which are there in the forensic departments or labs how they can be utilized. Governance of bio banks is also important and there are special issues related to data sets where you can use software's because now you all talk about the data being in the cloud. So, prevention of hacking, prevention of stolen data all those aspects come into play.

One should also remember that a bio bank cannot actually just handover or close down at it is will because there are so many samples collected there. So, it has to have a contingency plan to hand over these samples to another party when they mean to close down their facility.

(Refer Slide Time: 52:42)



Consent options in such instances you have to give an option in the informed consent document where you would actually require the person to state whether they want to allow use of this samples or not. Many a times it is written as any biomedical research or it may be for a specific disease or any other specified reason.

So, the person may say that if it is to be used beyond the scope of this particular project you cannot use it again without taking consent from me. So re-consent would be required in such instances. And if there is no future research then the problem does not arise but they may say that, if you are going to use the statement that your sample would be used for any future research then they may say that no, it need not be used for any future research. And once you get the results they may also say that do not contact us to inform us the results.

So, the option of I wish to be informed or not to be informed should also be provided in the informed consent document. So, you have one thing is: allow or do not allow and the other one is: informed or not to be informed. These two options should be there in the informed consent document and if they have actually negatively marked it you cannot use that sample for any secondary use.

(Refer Slide Time: 54:28)

Coming to the last section Research during Humanitarian Emergencies and Disasters, many a times, now this could be manmade or it could be a natural disaster when you have natural disasters cyclically happening you expect that this will happen again in a certain period.

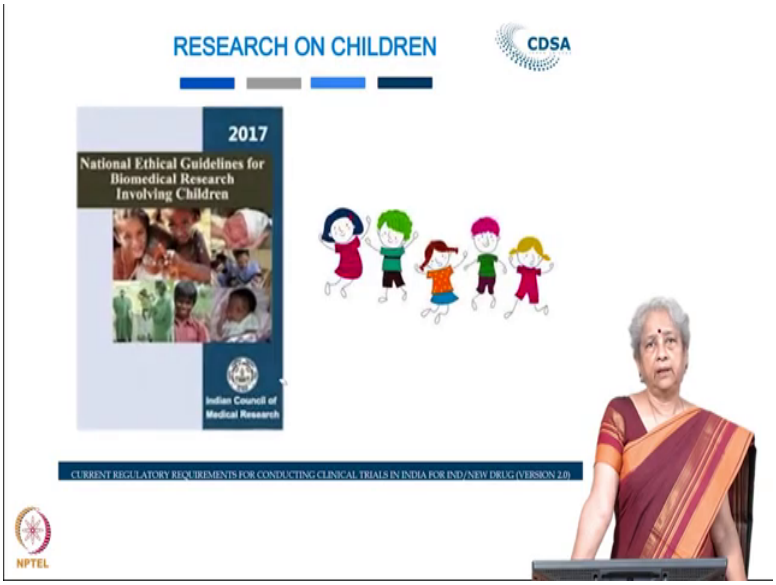
So, at that time you can already prepare you can have preemptive research preparation by keeping the proposals ready with ethics committee approval and when the time comes they can implement it.

There are informed consent requirements which are very specific in such situations as you can see in the floods there, the bombing and the Ebola outbreak how it created situations which was so difficult to handle. So, in this particular section we have tried to address how to go about taking in consent keeping the privacy confidentiality how should ethics review procedures be conducted sometimes they may be total shutdown of the infrastructure then

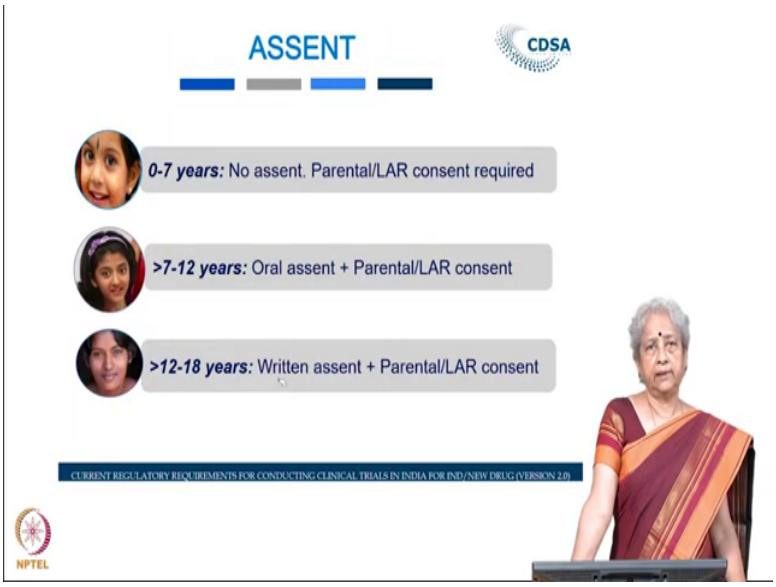
how do you approach the approval process all these have been actually described in this section and also a part about international participation.

Because this is a time when international researchers are already interested in studying the situations so, on what grounds and how this should be done should be very clearly discussed and decided.

(Refer Slide Time: 56:07)



(Refer Slide Time: 56:11)



Now, research on children. So, children of course, are supposed to give assent. So, when you have a child 0 to 7 years there is no assent required only the parental LAR consent is required.

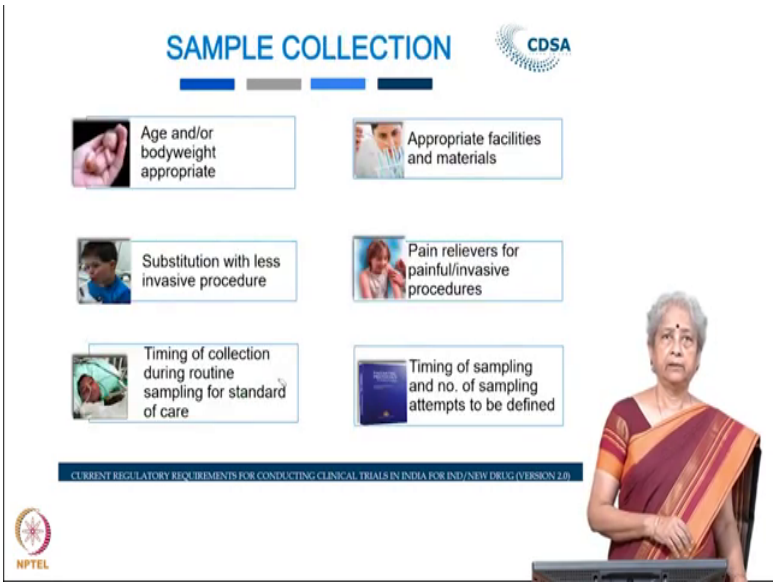
More than 7 to 12 years you can have oral assent so there has to be a very simply worded document describing what you would be actually communicating orally to the child. This also should be filed with the ethics committee and again parental and LAR consent is required.

Whereas for more than 12 to 18 years of age these children are required to give a written assent because it is believed that after around 12 you are actually somewhat cognitively aware of what is happening around you, but here also you require parental and LAR consent.

(Refer Slide Time: 57:09)

Now, if a child refuses that should be respected and that child should not be included in the study. It may not be as acute as you see in this picture, it may be just the body language of the child hiding behind the [FL] of the saree of the mother or behind the father which you have to respect, most of the time the fear is because of injections.

(Refer Slide Time: 57:37)

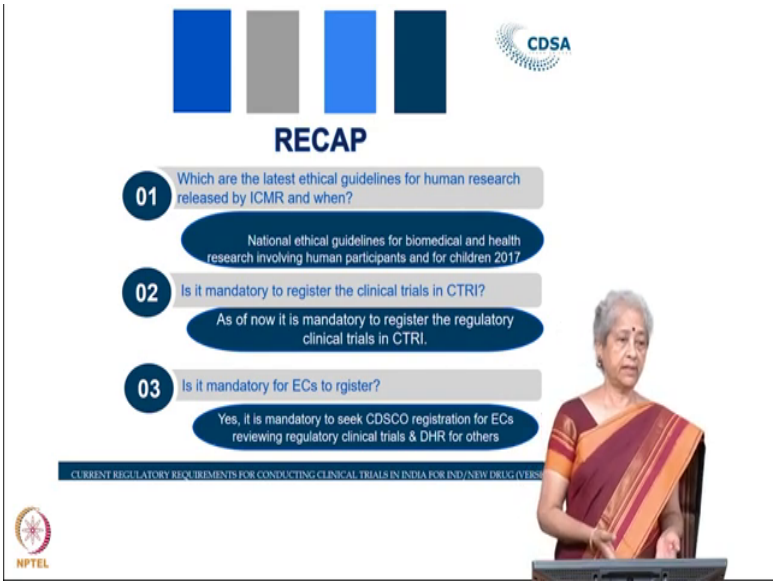


So, how do you collect the samples, there also you have to observe certain things. For example, age and our body weight should be appropriate for your biological sample collection or you can substitute that procedure with less invasive ones, for example, saliva swab instead of taking blood and when should be the timing of collection if the patient is admitted then while you are drawing blood for routine care you can actually draw a little more blood for the research purpose.

Appropriate facilities and materials should be there and if it is pain created as a result of your procedure then you must be able to provide the pain reliever also for such children. The number of times you collect the sample you like blood drawing or spinal tap you have it is a good practice to have a log book as to how many attempts you have made because the more

the number of attempts only denotes that you need further training. So, these are all safeguards to reduce the risk to the children.

(Refer Slide Time: 59:03)

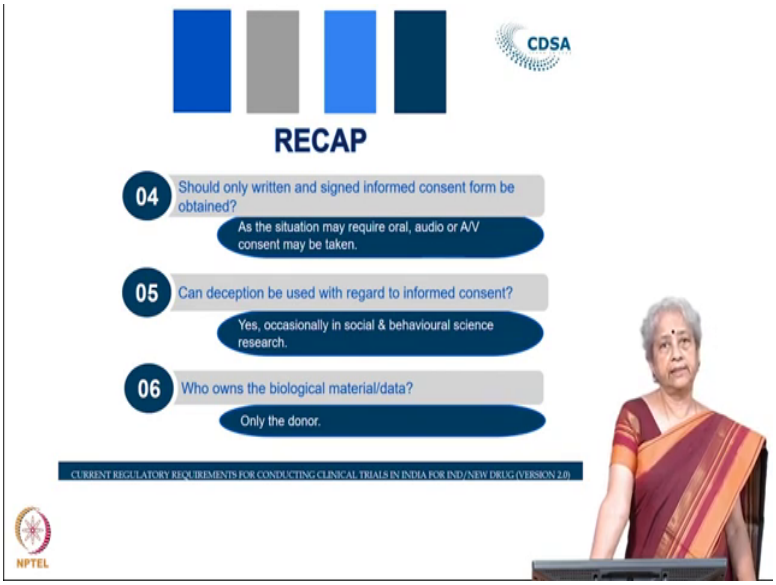


So now, we have come to recap. Which are the latest ethical guidelines for human research released by ICMR and when? There have been a number of our guidelines, but we have concentrated only on two here. So what are they? They are the National Ethical Guidelines for Biomedical and Health Research Involving Human Participants and for Children 2017.

Coming to the 2nd question: Is it mandatory to register the clinical trials in CTRI? Well as of now it is mandatory only for the regulatory clinical trials to register, the others are actually voluntary registration. Third one: Is it mandatory for ECs to register?

Yes, it is mandatory to seek CDSCO registration for ethics committees reviewing regulatory clinical trials and for those not reviewing regulatory clinical trials will have to register in the Department of Health Research from this month onwards once the platform is ready.

(Refer Slide Time: 60:25)

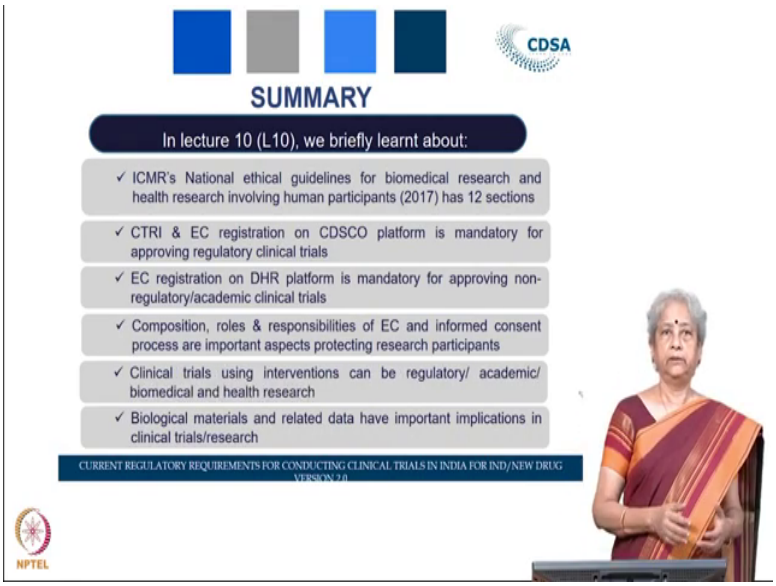


Fourth question is: Should only written and signed informed consent form be obtained? We talked about so much of informed consent process and all that. So, as a situation may require it could be oral, audio, audio visual consent as well.

Fifth question: Can deception be used with regard to informed consent? Generally we all talk about transparency, accountability etcetera. But we also talked about deception. So, when can this be? In social and behavioral science research that to uncertain occasions.

Six: who owns the biological material? By this time you should know that it is only the donor who owns the material and also the data which is related to it.

(Refer Slide Time: 61:31)



So, summarizing in this lecture, ICMR National ethical guidelines for biomedical research and health research involving human participants has 12 sections. CTRI and EC registration on CDSCO platform is mandatory for approving regulatory clinical trials.

EC registration on DHR platform is mandatory for approving non regulatory or academic clinical trials from this month onwards. Composition roles and responsibilities of EC and informed consent process are important aspects protecting research participants. So, the clinical trials using interventions can be we have learned that it can be regulatory academic or biomedical and health research.

Biological material and the related data have important implications in clinical trials or research with that I.

Thank you all for a patient listening.