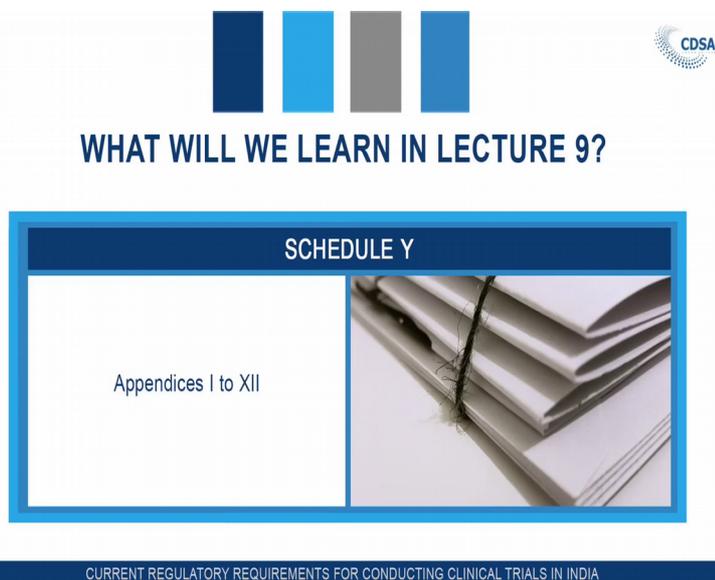


Current Regulatory Requirements for Conducting Clinical Trials in India
Dr. Dhananjay K. Sable
Assistant Drugs Controller (India), CDSCO (HQ),
Ministry of Health and Family Welfare, Government of India

Lecture – L9
Schedule Y – Appendices

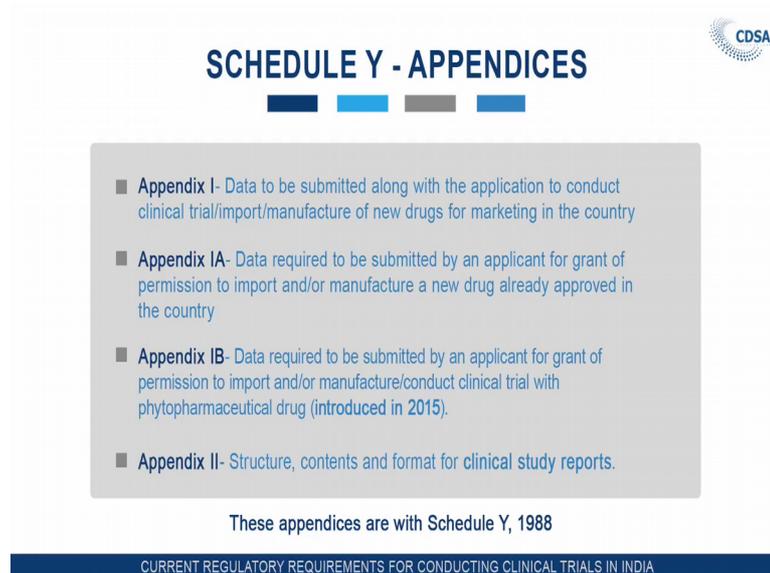
Hello everyone, welcome we will back to the course Current Regulatory Requirement for Conducting Clinical Trial in India. This is lecture 9; hope you have enjoyed earlier lectures. This is lecture regarding schedule Y and its Appendices.

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So, what will we learn in lecture 9? Schedule Y we have already seen so, this will also see here, then appendices from appendix I to appendix XII. So, let us start directly to the appendices of schedule Y. Appendix I is data to be submitted along with application to conduct clinical trial for import manufacture of mineral for marketing in the country.

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SCHEDULE Y - APPENDICES

CDSA

- **Appendix I**- Data to be submitted along with the application to conduct clinical trial/import/manufacture of new drugs for marketing in the country
- **Appendix IA**- Data required to be submitted by an applicant for grant of permission to import and/or manufacture a new drug already approved in the country
- **Appendix IB**- Data required to be submitted by an applicant for grant of permission to import and/or manufacture/conduct clinical trial with phytopharmaceutical drug (introduced in 2015).
- **Appendix II**- Structure, contents and format for clinical study reports.

These appendices are with Schedule Y, 1988

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

So, all these things which is required to be given while submitting the application for clinical trial, for the new drug to be imported or manufactured is given in this schedule. Then appendix I A data required to be submitted by an applicant for grant of permission to import and or manufacture a new drug already approved in the country. This is for the appendix which is for the drug which is already approved.

Then appendix I B is regarding the data required to be submitted by an applicant for grant of permission to import and or manufacture conduct a clinical trial with phyto pharmaceutical drug. This has been introduced in 2015. Appendix II structure content and format for clinical study reports. So, this is for the clinical study report.

(Refer Slide Time: 02:08)

SCHEDULE Y - APPENDICES

- Appendix III- Animal toxicology (non-clinical toxicity studies)
- Appendix IV- Animal pharmacology
- Appendix V- Informed consent
- Appendix VI- Fixed dose combinations (FDCs)

These appendices are with Schedule Y, 1988

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then appendix III animal pharmacology animal toxicology, appendix IV animal pharmacology, appendix V informed consent, appendix VI regarding fixed dosage combination, then appendix VII is undertaking by the investigator.

(Refer Slide Time: 02:26)

SCHEDULE Y(2005) - APPENDICES

- Appendix VIII- Ethics committee
- Appendix IX- Stability testing of new drugs
- Appendix X- Contents of the proposed protocol for conducting clinical trials
- Appendix XI- Data elements for reporting serious adverse events occurring in a clinical trial
- Appendix XII- Compensation in case of injury or death during clinical trial (Rule 122DAB G.S.R. No. 53-E, January 30, 2013)

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

So, these are the appendix from VII to XI that were added after 2005, appendix VIII is related to the ethics committee, appendix IX is stability testing of new drugs. Appendix X is content of the proposed protocol for conducting clinical trial, appendix XI data element for reporting SAE that is Serious Adverse Events occurring in a clinical trial.

And, the last one appendix XII it is related to the compensation in case of death or injury of a clinical trial subject. Rule 122 DAB also added in these 2013 year. So, let us start in detail for the appendix I.

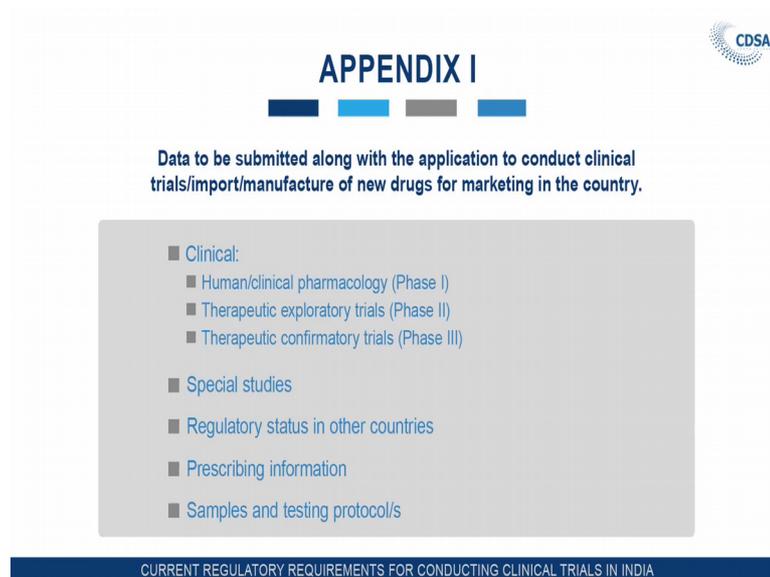
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The slide features the CDSA logo in the top right corner. The title 'APPENDIX I' is centered at the top, with a decorative bar below it consisting of four colored segments: dark blue, light blue, grey, and dark blue. Below the title, the text reads: 'Data to be submitted along with the application to conduct clinical trials/import/manufacture of new drugs for marketing in the country.' A central grey box contains a bulleted list of requirements: 'Introduction', 'Chemical and pharmaceutical information: chemical composition, drug category, stability in the intended container-closure system', and 'Preclinical:' which includes 'Animal pharmacology' and 'Animal toxicology'. At the bottom of the slide, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

So, as we have seen the appendix I is the data to be submitted along with the application to conduct clinical trial for import manufacture of new drugs for marketing in the country. It means if the drug is new drug and somebody would like to import this new drug then they have to conduct clinical trial. Similarly, if it is for the manufacturing of new drug they have to apply for the clinical trial and after the permission they can import or they can manufacture. So, what are the requirement?

So, applicant must have to submit the following, that is introduction then chemical and pharmaceutical information about the drug like its chemical structure, molecular weight, molecular formula, identification then reconnect. All these regarding chemical and pharmaceutical information, then preclinical consist of animal pharmacology that is related to the safety in animal then animal toxicology related to the toxicity, then clinical that is your phase in human being.

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APPENDIX I

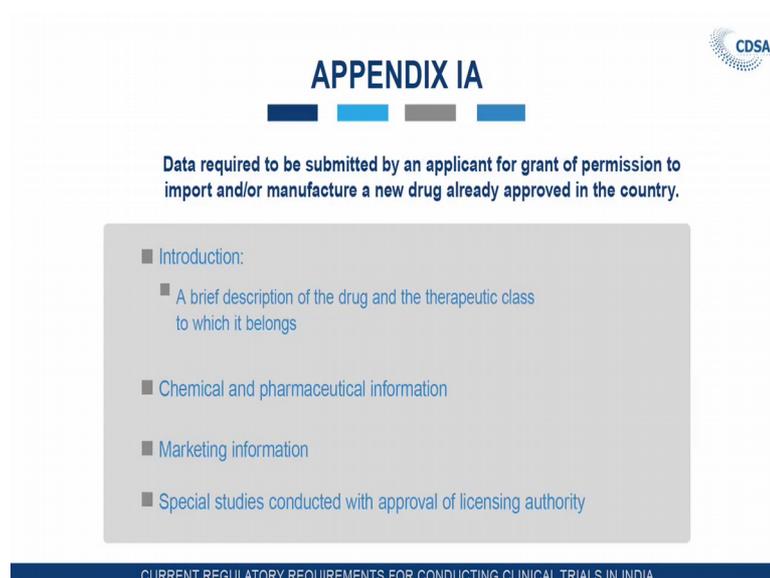
Data to be submitted along with the application to conduct clinical trials/import/manufacture of new drugs for marketing in the country.

- Clinical:
 - Human/clinical pharmacology (Phase I)
 - Therapeutic exploratory trials (Phase II)
 - Therapeutic confirmatory trials (Phase III)
- Special studies
- Regulatory status in other countries
- Prescribing information
- Samples and testing protocol/s

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Human clinical pharmacology that is phase I, then therapeutic exploratory trial phase II, therapeutic confirmatory trial phase III. Then special studies if required like resolution studies, by regulatory studies, by equivalent studies, then regulatory status in other countries whether the drug has been approved in regulatory countries or any other countries whether that has been withdrawn or whether it is prohibited in some countries or it is suspended. Then prescribing information regarding the (Refer Time: 05:21) and indication all these information required to submit, samples and testing protocol this is also required to submit.

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APPENDIX IA

Data required to be submitted by an applicant for grant of permission to import and/or manufacture a new drug already approved in the country.

- Introduction:
 - A brief description of the drug and the therapeutic class to which it belongs
- Chemical and pharmaceutical information
- Marketing information
- Special studies conducted with approval of licensing authority

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Appendix I A it is data required to be submitted by an applicant for grant of permission to import and or manufacture a new drug already approved in the country. It is also same for the import and manufacture of new drug provided that the drug is approved in the country and somebody would like to manufacture this new drug with new dosage form or strength indication. Means is if the drug is already approved and subsequently the applicant has applied same or different then what are the data required to be submitted that is given in the appendix I A.

So, again introduction then brief description of the drug and the therapeutic class to which it belongs. Chemical and pharmaceutical information, then marketing information special studies conducted with the approval of licensing authority. So, in this appendix the preclinical data is not there.

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The slide features the CDSA logo in the top right corner. The main title is 'APPENDIX IB' in bold blue letters, centered above a decorative bar of four colored rectangles (dark blue, light blue, grey, dark blue). Below this, the text reads: 'Data required to be submitted along with application to conduct clinical trial or import and/or manufacture a phytopharmaceutical drug in the country.' A dark blue box contains the sub-heading 'Part I: Data to be submitted'. Below this, a light grey box contains a bulleted list of requirements. At the bottom, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

APPENDIX IB

Data required to be submitted along with application to conduct clinical trial or import and/or manufacture a phytopharmaceutical drug in the country.

Part I: Data to be submitted

- A brief description of phytopharmaceutical drug- botanical name, route of administration, dosage, therapeutic class, indication/claim
- Information on plant/product, published literature, scientific reports, side effects, contraindications mentioned or reported and the manufacturing process
- Human or clinical pharmacology information- published scientific reports and monographs if any

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Now, let us see appendix I B these has been added lately in 2015 and this is regarding the phytopharmaceutical drug. Data required to be submitted along with the application to conduct clinical trial or import and or manufacture of phyto-pharmaceutical drug. Actually these appendix I B it has been divided in two part: part I consist of data to be submitted by the applicant wherein a brief description of phytopharmaceutical drug like its botanical name, route of administration, dosage, therapeutic class, indication claim. Then information on the plant, product, published literature if you have any available,

scientific report then its a side effect, contraindication method of whether any reported manufacturing process all these to be submitted.

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The slide features the CDSA logo in the top right corner. The main title is 'APPENDIX IB' in bold blue text, centered. Below the title is a dark blue box containing the text: 'Data required to be submitted along with application to conduct clinical trial or import and/or manufacture a phytopharmaceutical drug in the country.' Underneath this is another dark blue box labeled 'Part I: Data to be submitted:'. A light grey box below contains a list item: '■ Human or clinical pharmacology information- Published scientific reports and monographs if any'. At the bottom, a dark blue footer bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Then human or clinical pharmacological information published scientific reports monograph if any available.

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The slide features the CDSA logo in the top right corner. The main title is 'APPENDIX IB: PHYTOPHARMACEUTICAL DRUG' in bold blue text, centered. Below the title is a dark blue box containing the text: 'Data required to be submitted along with application to conduct clinical trial or import and/or manufacture a phytopharmaceutical drug in the country.' Underneath this is another dark blue box labeled 'Part II – Data generated by the applicant'. A light grey box below contains a list of five items: '■ Identification, authentication and source of plant used for extraction and fractionation', '■ Process of extraction and subsequent fractionation & purification', '■ Formulation of phytopharmaceutical drug applied for', '■ Manufacturing process of formulation', and '■ Stability data'. At the bottom, a dark blue footer bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Then part II consist of data generated by the applicant, in these also identification of the plant then authentication and source of plant used for extraction and fractionation. Process of extraction and subsequent fractionation and purification, formulation of phyto

pharmaceutical drug applied for, then its manufacturing process of the formula then stability data.

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APPENDIX IB: PHYTOPHARMACEUTICAL DRUG

Data required to be submitted along with application to conduct clinical trial or import and/or manufacture a phytopharmaceutical drug in the country.

Part II – Data generated by the applicant

- Safety and pharmacological information
- Human studies
- Confirmatory clinical trials
- Regulatory status
- Marketing information
- Post marketing surveillance (PMS)

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then safety and pharmacological information, human studies as we have seen in the ah new drug then confirmatory clinical trial, then regulatory status whether it is uploading any other countries or not, then marketing information post marketing surveillance report if any.

(Refer Slide Time: 08:30)

APPENDIX II

Structure, contents and format for clinical study reports

- Title page
- Study synopsis (2 pages)
- Statement of compliance with the guidelines for clinical trials on pharmaceutical products in India
- List of abbreviations and definitions
- Table of contents
- Ethics committee
- Study team
- Introduction
- Study objective
- Investigational plan
- Trial subjects
- Efficacy evaluation
- Safety evaluation
- Discussion & overall conclusion
- List of references
- Appendices

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Now, coming to the next slide that is appendix II it is a structure content and format for clinical study report. So, after completion of the study the report has to be submitted to the licensing authority for its verification and the content and format is given in this appendix II. So, according to this appendix II what should be the content? So, first the title page should be there then study synopsis should be there consist of 1 to 2 pages briefing about the all the studies. Then statement of compliance with the guidelines for clinical trial on pharmaceutical product in India, then whatever the abbreviation for example, BA, BE, Bio Laboratory, Bio Equivalence, CT Clinical Trial.

Whatever the abbreviations used the meaning of that abbreviation and definitions. Table of contents in any list of table of content regarding statistical evaluation and other that also has to be given. Ethics committee; the committee which has reviewed and accorded approval, the name of the ethics committee and detail about the ethics committee; then study team those who are involved in the conduct of the clinical trial detail about them, then introduction study objective. So, primary objective, secondary objective with what purpose the study has been conducted that has to be given.

Then investigational plan trial subject, the number of subject used and their details has to be given, then the procedure applied for the efficacy evaluation, safety evaluation discussion and overall conclusion. So, after completion of the study the discussion conducted by the study team and what is their influence or conclusion that also has to be given. Then list of references which are used during the study and the appendices that has to be given.

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The slide features the CDSA logo in the top right corner. The title 'APPENDIX III' is centered at the top, followed by a decorative bar with four colored segments (dark blue, light blue, grey, dark blue). Below this is a dark blue box containing the text 'Animal toxicology (non-clinical toxicity studies)'. To the left of a central image of a white mouse is a list of 'General principles' in a dark blue box, with each principle in a light grey box: Systemic toxicity studies, Male fertility studies, Female reproduction and developmental toxicity studies, Local toxicity, and Allergenicity/hypersensitivity. At the bottom, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Appendix III is animal toxicology that is a preclinical study nonclinical toxicity studies. So, in this studies the general principles that is systemic toxicity studies, male fertility study, female reproduction and developmental toxicity study, local toxicity, allergenicity hypersensitivity.

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The slide features the CDSA logo in the top right corner. The title 'APPENDIX III' is centered at the top, followed by a decorative bar with four colored segments (dark blue, light blue, grey, dark blue). Below this is a dark blue box containing the text 'Animal toxicology (non-clinical toxicity studies)'. To the left of a central image of a white mouse is a list of 'General principles' in a dark blue box, with each principle in a light grey box: Genotoxicity, Carcinogenicity, Animal toxicity requirements for clinical trials and marketing of a new drug, and Number of animals required for repeated-dose toxicity studies. At the bottom, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Then genotoxicity, carcinogenicity, animal toxicity requirement for clinical trial and marketing of new drug, number of animals required for repeated dose toxicity study. All

this is given here the number of animal the number of animal species so that is also mention here.

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APPENDIX III

Animal toxicology (non-clinical toxicity studies)

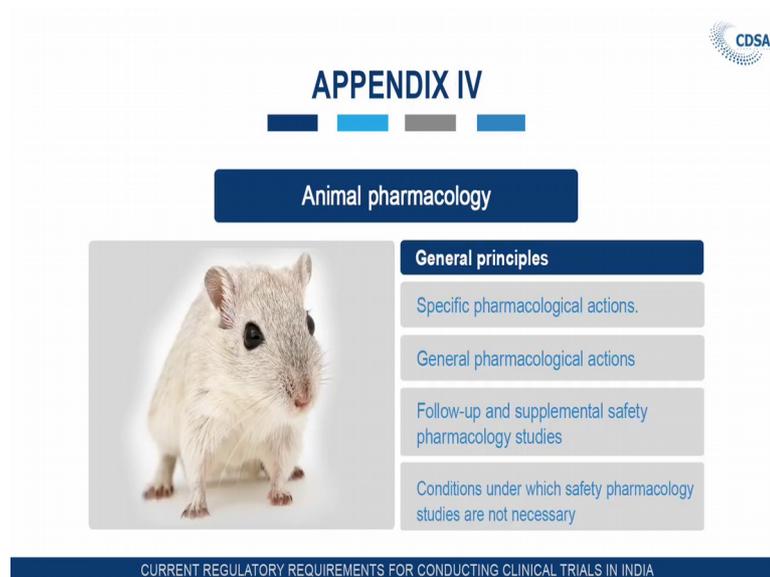
Laboratory parameters to be included in toxicity studies. The animal studies be conducted in an **accredited laboratory**. Where the safety pharmacology studies are part of toxicology studies, these studies should also be conducted in an accredited laboratory.



CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then laboratory parameters to be included in toxicity studies; so, which are the parameter now while conducting preclinical study to be considered that have been also given. The animal studies to be conducted in an accredited laboratory, the animal study we have seen in the history that from the 2005 the GLP made mandatory and again the lab should be accredited. Where the safety pharmacology studies are part of toxicology studying, the study should also be conducted in an accredited laboratory.

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APPENDIX IV

Animal pharmacology



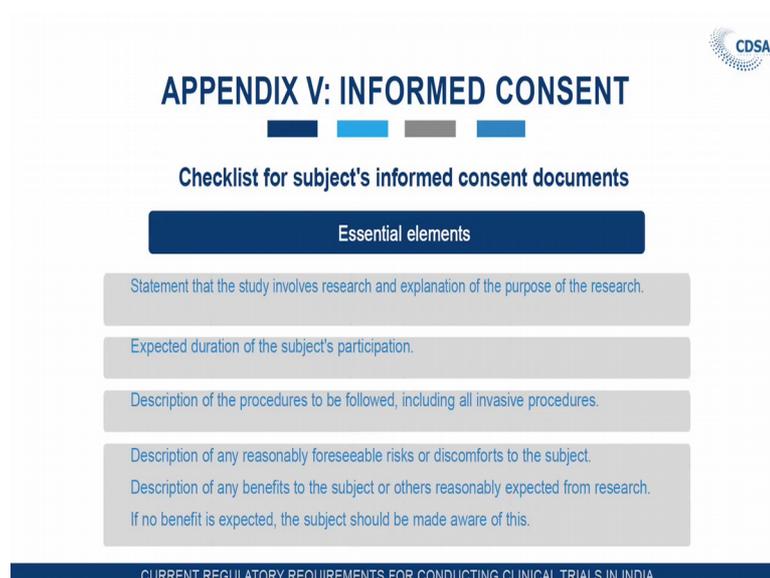
General principles

- Specific pharmacological actions.
- General pharmacological actions
- Follow-up and supplemental safety pharmacology studies
- Conditions under which safety pharmacology studies are not necessary

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Appendix IV is a animal pharmacology. So, this is regarding the safety of the dog; in the general principle is given the specific pharmacological actions, then general pharmacological actions, follow up and supplemental safety pharmacology study. Condition under which safety pharmacology studies are not necessary, timing of safety pharmacology studies in relation to clinical development. Then whether the GLP was there or not application of GLP, the animal studies conducted in accredited laboratory we have seen it; where the safety pharmacology studies are part of toxicology studies the study should also be conducted in an accredited lab.

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APPENDIX V: INFORMED CONSENT

Checklist for subject's informed consent documents

Essential elements

- Statement that the study involves research and explanation of the purpose of the research.
- Expected duration of the subject's participation.
- Description of the procedures to be followed, including all invasive procedures.
- Description of any reasonably foreseeable risks or discomforts to the subject.
- Description of any benefits to the subject or others reasonably expected from research.
- If no benefit is expected, the subject should be made aware of this.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Appendix V is regarding the informed consents, actually this informed consent is also called as informed consent documents. So, first is the patient information sheet, the data to be provided to the patients or subject and next is the information confirmation sheet or consent sheet where the subject has to sign. So, informed consent let us see the checklist for study subjects informed consent document. So, here the essential elements are given the first statement that the study is in research and explanation of the purpose of the research. So, the first and very important thing, that they have to disclose that the study is only for the research purpose and not for any other purpose.

Then expected duration of the subjects participation whatever the time is required for the study for example, 1 week, 1 month that has to be disclosed. Then description of the procedure to be followed including all invasive procedures whatever the description of the procedure what they are going to do whether it is a parental injections or tablet, they are going to give the blood sampling procedure they have to mention. Description of any reasonable foreseeable risk or discomfort to the subject; if any risk is there then that has to be described there. Description of any benefit to the subject or other reasonably expected from research, if no benefit is expected subject should be made aware of this. So, whatever the benefit whatever the risk that has to be disclosed.

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APPENDIX V: INFORMED CONSENT

Checklist for subject's informed consent documents

Essential elements

- Disclosure of specific appropriate alternative procedures or therapies available to the subject.
- Statement describing the extent to which confidentiality of records identifying the subject will be maintained and who will have access to subject's medical records.
- Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomised trials).

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Disclosure of specific appropriate alternative procedure or therapies available to the subject; if this therapy fail then what are the other alternative measures that also has to be

disclosure. Statement describing the extent to which confidentiality of record identifying the subjects will be maintained and who will have assist to the subject medical record. Then trial treatment schedule and probability for random assignment to each statement; if the trial is a randomized trial, then compensation and treatment available to the subject in the event of trial related injury. So, the patient has to be make aware that you will get the compensation in case of any injury or dead during the clinical trial.

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APPENDIX V: INFORMED CONSENT

Checklist for subject's informed consent documents

Essential elements

- Compensation and/or treatment(s) available to the subject in the event of a trial related injury.
- An explanation about whom to contact for trial related queries, rights of subjects and in the event of any injury.
- The anticipated prorated payment, if any, to the subject for participating in the trial.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

And explanation about whom to contact for the trial related queries right of subject and in the event of any injury. So, in case of injury or SAE to whom he has to contact the telephone number, email fax number everything they have to mention. The anticipated prorated payment, if any to the subject for participating in the trial.

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APPENDIX V: INFORMED CONSENT

Checklist for subject's informed consent documents

Essential elements

- Subject's responsibilities on participation in the trial.
- Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the subject is otherwise entitled .
- Any other pertinent information.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Subject's responsibility on participation in the trial; so, what are the responsibilities of that subject that has also mention. Statement that participation is voluntary that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefit to which in the subject is otherwise entitled.

So, the subjects they should have to make clear that the participation is fully voluntary there is no binding and they can we draw at any point in the study. Any other permission or any other pertinent information required to be given to the subject that has to be mentioned.

(Refer Slide Time: 16:31)

APPENDIX V: INFORMED CONSENT

Checklist for subject's informed consent documents

Essential elements

An audio-video recording* of the informed consent process in case of vulnerable subjects in clinical trials of new chemical entity or new molecular entity including procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for records.

* In case of anti-HIV and anti-leprosy studies, only audio recording is required.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then AV recording of the informed consent procedure in case of vulnerable subject in clinical trial for new chemical entity; so, that also has to be mentioned that they are going to have the AV recording. In case of clinical trial of anti-HIV and anti-leprosy only audio recording is required. So, these are some essential elements enlisted here.

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APPENDIX V: INFORMED CONSENT

Essential elements of informed consent

- Purpose of research
- Expected duration
- Foreseeable risk
- Benefits
- Alternative procedures
- Confidentiality
- Compensation
- Contacts
- Voluntary participation and withdrawal
- Subject responsibilities
- Vernacular language

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

The purpose of research then expected duration, foreseeable risk, benefit, alternative procedure, confidentiality, compensation, then to whom to contact; then voluntary participation, subject responsibility and the ICF to be in vernacular language.

(Refer Slide Time: 17:23)

APPENDIX V: INFORMED CONSENT

Checklist for subject's informed consent documents

Additional elements, which may be required

- Statement of foreseeable circumstances under which the subject's participation may be terminated by the investigator without the subject's consent.
- Additional costs to the subject that may result from participation in the study.
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by subject.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Additional element which may be required; so, statement of foreseeable circumstances under which the subjects participation maybe terminated by investigator without the subjects consent. The next is the additional cost of the subject that may result from participation in the study, the consequences of a subject's decision to withdraw from the research and procedure for orderly termination of participation by subject.

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APPENDIX V: INFORMED CONSENT

Checklist for subject's informed consent documents

Additional elements, which may be required

- Statement that the subject or subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the subject's willingness to continue participation will be provided.
- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable.
- Approximate number of subjects enrolled in the study.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

The statement that the subject or is representative will be notified in a timely manner, if significant new findings developed during the course of the research which may affect

the subject willingness to continue participation will be provided. It means if any risk is there or the sponsor or any other (Refer Time: 18:10) they came to know that there is some SAE occur somewhere else then that also has to be informed during the clinical trials. The statement that the particular treatment or procedure may involve risk to the subject; so, the treatment if it is involving the risk that also has to be mentioned, its approximate number of subject enrolled in the study.

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APPENDIX V: FORMAT OF INFORMED CONSENT FORM FOR SUBJECTS PARTICIPATING IN A CLINICAL TRIAL



<p style="text-align: center;">TEMPLATE INFORMED CONSENT FORM FOR SUBJECTS ABLE TO GIVE CONSENT</p> <p>Full Title of Project: _____</p> <p>Name of Principal Investigator: _____ Please Initial box <input style="width: 20px; height: 15px;" type="checkbox"/></p> <p>1. I confirm that I have read and understand the subject information sheet dated _____ version _____ for the above study and have had the opportunity to ask questions which have been answered fully. <input style="float: right;" type="checkbox"/></p> <p>2. I understand that my participation is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. <input style="float: right;" type="checkbox"/></p> <p>3. I understand that sections of any of my medical notes may be looked at by responsible individuals from [company/institution name] or from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to access my records that are relevant to this research. <input style="float: right;" type="checkbox"/></p> <p>4. The compensation arrangements have been discussed with me. <input style="float: right;" type="checkbox"/></p>	<p>5. I agree to take part in the above study. <input style="float: right;" type="checkbox"/></p> <p>Name of Patient/Participant _____ Signature _____ Date _____</p> <p>Name of Person taking consent (if different from Principal Investigator) _____ Signature _____ Date _____</p> <p>Principal Investigator _____ Signature _____ Date _____</p> <p style="font-size: small;">1 copy for patient/participant; 1 copy for Principal Investigator; 1 copy to be kept with hospital notes</p> <p>8.3 Appendix 3: Template Informed Consent Form for Adults without Capacity (For CTIMPS)</p> <p style="text-align: center; font-size: x-small;">(Form to be on departmental headed paper)</p>
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So, this is the format of informed consent form for subject participating in a clinical trial. So, this is a template provided where in the subject has to tick mark that he has read and understood the all the conditions, then he is participating voluntary and for that he is giving this sign in. And, he has to tick mark in the box and he has to give the initials for every elements given here and below you can see the name of participant or then he has to write his name, signature along with the date when he has enrolled. So, all the details he has to fill and give to the PI.

(Refer Slide Time: 19:25)



APPENDIX VI

Fixed dose combinations (FDCs)



Fixed dose combinations refer to products containing one or more active ingredients used for a particular indication.

FDCs can be divided into four groups.

No additional animal or human data are generally required for these FDCs, and marketing permission may be granted if the FDC has an acceptable rationale.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Appendix VI is related to the fixed dose combination. So, what is the fixed dose combination we have already seen; here also it is given the fixed dose combination. It refers to product containing one or more active ingredient used for particular indication. This FDC actually it has been divided into four groups that is when the new individually approved to product or more than two product first time it is combined then it is a FDC in new FDC.

Then if the ratio has been changed the strength has been changed, if the dosage form has been changed indication then also it is considered as a fixed dose combination. As these are already approved in the country no additional animal or human data generally required for this FDCs and marketing permission may be granted FDC has an acceptable rationale.

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APPENDIX VII

Undertaking by the investigator

- Full name, address and title of the principal investigator (or investigator(s) when there is no principal investigator).
- Name and address of the medical college, hospital or other facility where the clinical trial will be conducted: education, training & experience that qualify the investigator for the clinical trial (attach details including medical council registration number, and/or any other statement(s) of qualification(s)).
- Name and address of all clinical laboratory facilities to be used in the study.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Appendix VII head is the most important that is undertaking by the investigator. So, while giving the undertaking by the investigator these are the content the investigator should fill. Full name, address and the title of the PI that is Principal Investigator, if the (Refer Time: 20:38) are more than sometime investigator are also there.

So, if the investigators are there then there is also required to do; name and address of the medical college hospital or other facility where the clinical trial will be conducted. So, wherever these trials are conducting the details about the address of this hospitals or site has to be given. Then education training experience of the PI investigators involved and the other members that details also has to be given. Name and address of all clinical laboratory facilities to be used in the study, what are the laboratories they are using for testing and analysis of the sample the details of this laboratory has to be given.

(Refer Slide Time: 21:25)



APPENDIX VII

Undertaking by the investigator

Name and address of the ethics committee that is responsible for approval and continuing review of the study.

Names of the other members of the research team (co- or sub-investigators) who will be assisting the investigator in the conduct of the investigation(s).

Protocol title and study number (if any) of the clinical trial to be conducted by the investigator.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Name and address of the ethics committee; so, the ethics committee which is responsible for giving the approval detail about that ethics committee whether it is institutional, independent its address, composition quorum all the things regarding ethics committee has to be mentioned. The name of the other members of the research team as already mentioned. Protocol title and study number; so, under the undertaking by investigator again here required to give the protocol title and study number that which study is going to monitor or conduct.

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APPENDIX VII

Undertaking by the investigator

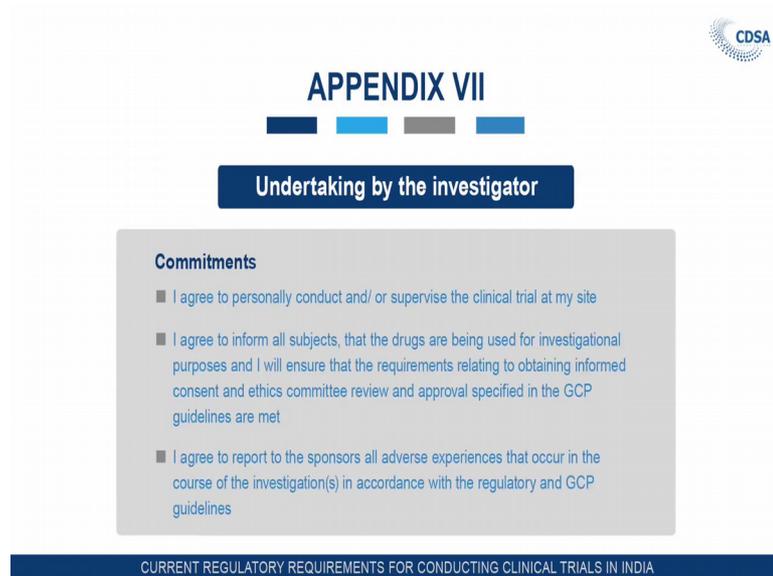
Commitments

- I have reviewed the clinical protocol and agree that it contains all the necessary information to conduct of the study. I will not begin the study until all necessary ethics committee and regulatory approvals have been obtained.
- I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the sponsor and prior review and documented approval/ favourable opinion from the ethics committee of the amendment, except where necessary to eliminate an immediate hazard(s) to the trial subjects or when the change(s) involved are only logistical or administrative in nature.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then some commitments will be given that he has reviewed the clinical protocol and he has agreed that it contains all the necessary information to conduct the study. And, he will not begin the study prior to the approval of ethics committee and the regulatory authority, this commitment has to be signed by the principal investigator and other investigators.

(Refer Slide Time: 22:19)



The slide features the CDSA logo in the top right corner. The main title is 'APPENDIX VII' in blue, with a decorative bar below it. A dark blue box contains the subtitle 'Undertaking by the investigator'. Below this, a light grey box lists three commitments under the heading 'Commitments'. At the bottom, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

APPENDIX VII

Undertaking by the investigator

Commitments

- I agree to personally conduct and/ or supervise the clinical trial at my site
- I agree to inform all subjects, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent and ethics committee review and approval specified in the GCP guidelines are met
- I agree to report to the sponsors all adverse experiences that occur in the course of the investigation(s) in accordance with the regulatory and GCP guidelines

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the sponsor. So, he has to give in the written that he will follow the approved protocol and if any changes are there then he will take the permission from the ethics committee and from the licensing authority.

Then he has to agree to personally conduct and supervise the clinical trial at his site, before that I agree to inform all subject that drugs are being used for investigational purpose. And, I will ensure that the requirement relating to obtaining informed consent and its committee review and approval specified in GCP guidelines are made, that he will follow all the GCP guidelines. And, the research is for the research the trial is for the research purpose that also has to mention. I agree to report to the sponsor all adverse experience that occur in the course of the investigation in accordance with the regulatory and GCP guidelines. This is regarding the adverse experience.

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The slide features the CDSA logo in the top right corner. The main title 'APPENDIX VII' is centered at the top, followed by a decorative bar with four colored segments (dark blue, light blue, grey, dark blue). Below this is a dark blue box with the text 'Undertaking by the investigator' in white. The central content is a light grey box with the heading 'Commitments' and two bullet points. At the bottom, a dark blue footer bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

APPENDIX VII

Undertaking by the investigator

Commitments

- I have read and understood the information in the Investigator's brochure, including the potential risks and side effects of the drug
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their obligations in meeting their commitments in the trial

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

I have read and understood the information in the investigator brochure including the potential risk and side effect of the drug. So, he has to first read all the investigating investigators brochure and if he agree then had to give the agreement. I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are suitably qualified, experience and they have been informed about their obligations in meeting; this agreement also has to be signed.

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The slide features the CDSA logo in the top right corner. The main title 'APPENDIX VII' is centered at the top, followed by a decorative bar with four colored segments (dark blue, light blue, grey, dark blue). Below this is a dark blue box with the text 'Undertaking by the investigator' in white. The central content is a light grey box with the heading 'Commitments' and two bullet points. At the bottom, a dark blue footer bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

APPENDIX VII

Undertaking by the investigator

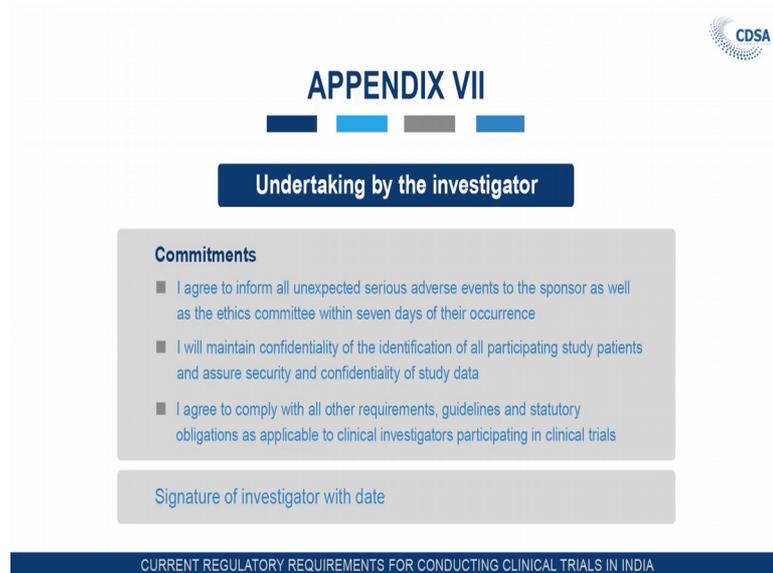
Commitments

- I agree to maintain adequate and accurate records and to make those records available for audit/ inspection by the sponsor, ethics committee, licensing authority or their authorised representatives, in accordance with regulatory and GCP provisions. I will fully cooperate with any study related audit conducted by regulatory officials or authorised representatives of the sponsor
- I agree to promptly report to the ethics committee all changes in the clinical trial activities and all unanticipated problems involving risks to human subjects or others

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then I agree to maintain adequate and accurate record and to make those record available for the audits. So, the PI and the investigator it is their responsibility to maintain all the data and it has to be made available during the audit. Then I agree to promptly report to the ethics committee all changes in clinical trial activities. So, any changes in the clinical trial activities he has to immediately inform to the inform ethics committee.

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The slide features the CDSA logo in the top right corner. The title 'APPENDIX VII' is centered at the top, followed by a decorative bar with four colored segments (dark blue, light blue, grey, dark blue). Below this is a dark blue box with the text 'Undertaking by the investigator'. The main content is a light grey box titled 'Commitments' containing three bullet points. At the bottom of this box is a line for 'Signature of investigator with date'. A dark blue footer bar at the very bottom contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

APPENDIX VII

Undertaking by the investigator

Commitments

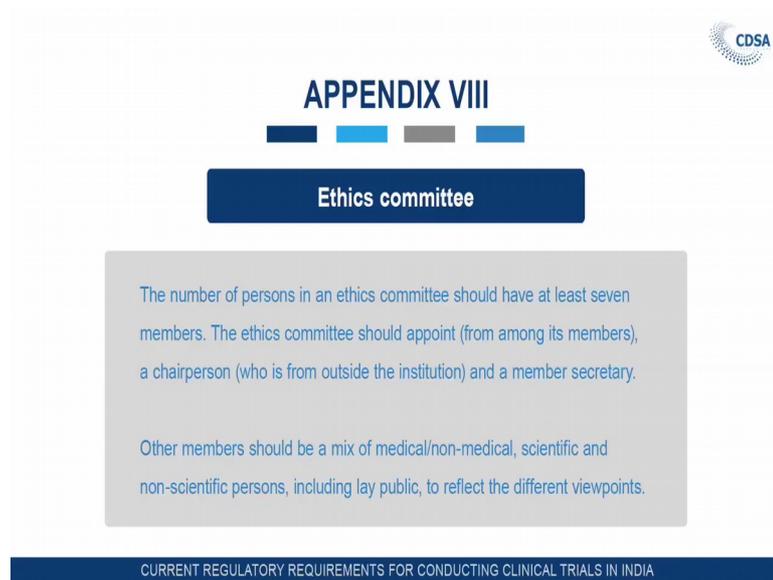
- I agree to inform all unexpected serious adverse events to the sponsor as well as the ethics committee within seven days of their occurrence
- I will maintain confidentiality of the identification of all participating study patients and assure security and confidentiality of study data
- I agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical investigators participating in clinical trials

Signature of investigator with date

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

I agree to inform all unexpected SAE to the sponsor as well as ethics committee within 7 days of their occurrence. I will maintain confidentiality of the identification of all participating study patient and assure security and confidentiality of study data; study data and patients information has to be made it confidentially. Then I agree to comply with all other requirement, guideline and statutory obligation as applicable to clinical investigator participating in clinical trial. Signature of investigator with date; so, all this commitment he has to sign within date.

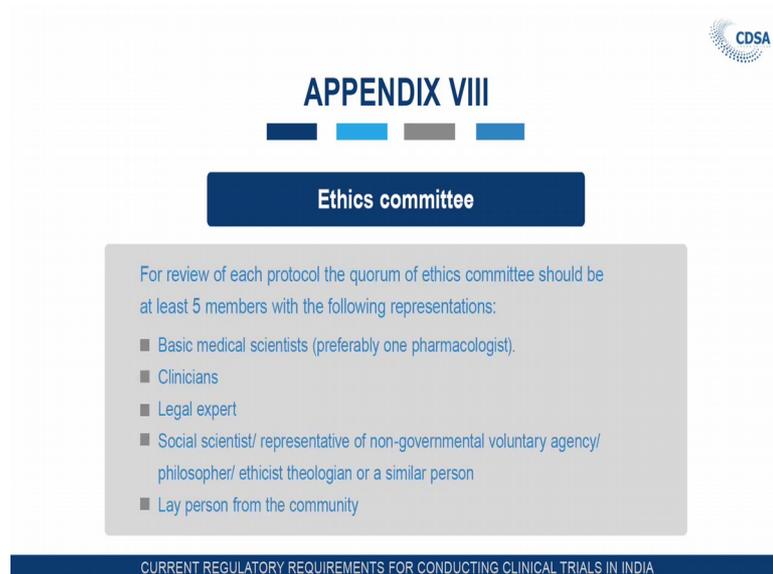
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The slide features the CDSA logo in the top right corner. The title 'APPENDIX VIII' is centered at the top, with a decorative bar below it. A dark blue box contains the text 'Ethics committee'. Below this, a light grey box contains the following text: 'The number of persons in an ethics committee should have at least seven members. The ethics committee should appoint (from among its members), a chairperson (who is from outside the institution) and a member secretary. Other members should be a mix of medical/non-medical, scientific and non-scientific persons, including lay public, to reflect the different viewpoints.' At the bottom, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Coming to the next appendix that is appendix VIII, it is related to the ethics committee. So, we have seen this in detail in our previous lecture. So, we will not go in detail only will have the brief that at least 7 member should be there.

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The slide features the CDSA logo in the top right corner. The title 'APPENDIX VIII' is centered at the top, with a decorative bar below it. A dark blue box contains the text 'Ethics committee'. Below this, a light grey box contains the following text: 'For review of each protocol the quorum of ethics committee should be at least 5 members with the following representations:'. A bulleted list follows: '■ Basic medical scientists (preferably one pharmacologist).', '■ Clinicians', '■ Legal expert', '■ Social scientist/ representative of non-governmental voluntary agency/ philosopher/ ethicist theologian or a similar person', and '■ Lay person from the community'. At the bottom, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Then for the quorum required the 5 members and these members are like this basic medical scientist, clinicians, legal expert and other we have already seen it in detail.

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The slide features a white background with a blue header area. At the top right is the CDSA logo. The main title 'APPENDIX IX' is centered in blue, with a decorative bar of four colored segments (dark blue, light blue, grey, dark blue) below it. A dark blue box contains the subtitle 'Stability testing of new drugs'. Three light grey boxes list the objectives of stability testing. A dark blue footer bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

APPENDIX IX

Stability testing of new drugs

- To provide evidence on how the quality of a drug substance or formulation varies with time under the influence of various environmental factors such as temperature, humidity and light.
- To establish shelf life for the formulation and recommended storage conditions.
- It should include testing of those attributes of the drug substance that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Appendix IX is related to the stability testing of new drug whether the drug is stable or not that has to be proven and the documented proof has to be given. To provide evidence on how the quality of drug substances or formulation varies with time under the influence of various environmental factors such as temperature, humidity and light this stability studies are required. To establish shelf life for the formulation and recommended storage condition; stability studies are also required to establish the shelf life for the formulation and recommended dosage form. It should include testing of the attribute of the drug substance that are susceptible to change during storage and likely to increase quality safety and efficacy.

(Refer Slide Time: 26:58)



APPENDIX IX

Stability testing of new drugs

In case of formulations the testing should cover, as appropriate, the physical, chemical, biological, and microbiological attributes, preservative content (e.g. antioxidant, antimicrobial preservative), and functionality tests (e.g. for a dose delivery system).

Stability testing of new drug substance & formulations:

■ Study conditions for drug substance & formulations intended to be stored under general conditions.

Study	Study conditions	Duration of study
Long-Term	30°C ± 2°C/65% RH ± 5% RH	12 months
Accelerated	40 °C ±2°C/75% RH ± 5% RH	6 months

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

In case of formulation the testing should cover as appropriate, the physical, chemical, biological and microbiological attribute preservative all this has to be mentioned and here it is given. Then the stability testing of new drug substance and formulation, study condition for drug substance and formulation intended to be store under general condition. So, these are the storage conditions and the stability study conditions, stability testing of for the new drug. So, for the general storage condition that is room temperature or 25 degree Celsius; the stability study has to be carried out for the long term and accelerated.

For the long term or also called real time the study condition 30 degree Celsius plus or minus 2 degree Celsius with the relative humidity 65 percent plus or minus 5 percent. The study has to be conducted for the duration of 12 months, for accelerated is 40 degree Celsius plus or minus 2 degree Celsius with the relative humidity 75 percent plus or minus 5 percent for the 6 months. If at any time during 6 months testing under the accelerated storage condition such changes occur that cause the product to fail in complying with the prescribed standard. Aadditional testing under intermediate storage condition should be conducted and evaluated against significant changes criteria.

If the products are required to be stored in refrigerator condition then this following type of the study conditions are and the duration is required. For the long time it is 5 degree Celsius plus or minus 3 degree Celsius, study required to be conducted for 12 months.

And, for the accelerated it is 25 degree Celsius plus or minus 2 degree Celsius with relative humidity 60 percent and duration is 6 months. Now, let us see the product to be stored in the freezer, the study condition for a drug substance formulation intended to be stored in freezer.

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The slide is titled "APPENDIX IX" and "Stability testing of new drugs". It features the CDSA logo in the top right corner. The main content is a grey box with the following text and table:

Stability testing of new drug substance & formulations:

- Study conditions for drug substances and formulations intended to be stored in a freezer.

Study	Study conditions	Duration of study
Study	Study conditions	Duration of study
Long-Term	-20 °C ± 5 °C	12 months

- Drug substances intended for storage below -20°C shall be treated on a case-by-case basis.

At the bottom of the slide, there is a dark blue bar with the text "CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA".

So, these are the conditions, in this case only long term study has to be conducted minus 20 degree Celsius plus or minus 5 degree Celsius for 12 months. Drug substances intended for storage below minus 20 degree Celsius shall be treated on case by case basis.

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APPENDIX IX

Stability testing of new drugs

Stability testing of new drug substance & formulations:

- Stability testing of the formulation after constitution or dilution, if applicable should be conducted to provide information for the labelling on the preparation, storage condition, and in-use period of the constituted or diluted product. This testing should be performed on the constituted or diluted product through the proposed in-use period.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Stability testing of the formulation after constitution of dilution, if applicable should be conducted to provide information for the labelling on the preparation. If the preparation is life preparation and dilution is required then the after dilution how much is the stability shall find that also has to be mentioned. This testing should be performed on the constituted or diluted product through the proposed in hospital.

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APPENDIX X

Contents of the proposed protocol for conducting clinical trials

Title page

- Full title of the clinical study
- Protocol/Study number, and protocol version number with date
- The IND name/number of the investigational drug
- Complete name and address of the sponsor and contract research organisation if any

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Coming to the next slide that is appendix X, it is regarding content of the proposed protocol for conducting clinical trial. So, while applying the form 44 we have seen, that

form 44 is required there for the application of new drug, for manufacture or for import purpose for the clinical trials or marketing in the India. So, these are the contents; first in the title page has been given, full title of the clinical study has to be given.

So, that from the title itself one can understand what type of study is there. Protocol study number and protocol version number with date, if it is the original protocol and protocol number, if it has been revised in the version number or region protocol number. The IND name if in case of the investigational new drug then whatever the name they have given code number that has to be mentioned. Number of the investigational drug, complete name and address of the sponsor and the CRO so, who is the sponsor and where from you getting done the clinical trial that is the CRO that also required to.

(Refer Slide Time: 31:34)

APPENDIX X

Contents of the proposed protocol for conducting clinical trials

Table of contents

- A complete table of contents including a list of all appendices.
- Study rationale

Study objective(s)

- Primary as well as secondary and their logical relation to the study

Study design

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CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Number of investigators involved in the study. So, details about the number of investigator and their name address everything has to be given.

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APPENDIX X

Contents of the proposed protocol for conducting clinical trials

- Table of contents
 - A complete table of contents including a list of all appendices.
 - Study rationale
- Study objective(s) (primary as well as secondary and their logical relation to the study design)
- Study design

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Table of content a complete table of content including list of all appendices, if the appendices are attached than list of all the appendices the table has to be given. Study rationale then study objective all the objective of the study that is primary, secondary whether it is for safety purpose, whether it is for efficacy purpose or to see the adverse reaction that study object has to be given. Then study design like a double blinded study or open label, study randomization is there or not, cross all these sequence treatment period this should be given in the study design.

(Refer Slide Time: 32:35)

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APPENDIX X

Contents of the proposed protocol for conducting clinical trials

Study population:

- The number of subjects required to be enrolled in the study at the investigative site and by all sites along with a brief description of the nature of the subject population required is also mentioned

Subject eligibility

- Inclusion criteria
- Exclusion criteria

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then study population the number of subject required to be enrolling in the study at the investigative site and by all sites along with brief description of nature of subject population required in required to mention. Subject eligibility that is inclusion criteria and exclusion criteria those subjects which are to be included, what should be the criteria for their inclusion and what should be the criteria for the inclusion exclusion that is also has to be given.

(Refer Slide Time: 32:53)

APPENDIX X

Contents of the proposed protocol for conducting clinical trials

Study assessments

- Plan, procedures and methods to be described in detail

Study conduct

- The types of study activities that would be included in this section would be medical history, type of physical examination, blood or urine testing, electrocardiogram (ECG), diagnostic testing such as pulmonary function tests, symptom measurement, dispensation and retrieval of medication, subject cohort assignment, adverse event review, etc.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Study assessment plan procedure and methods to described in detail. Study conducting the type of study activities that would be included in this section would be medical history, type of physical examination, blood or urine testing. Then ECG diagnostic testing such as pulmonary function test, symptoms measurement dispensation and retrieval of medication, subject cohort assignment, AE review etcetera has to be given.

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The slide features the CDSA logo in the top right corner. The main title is 'APPENDIX X' in bold blue letters, centered above a decorative horizontal bar with four colored segments (dark blue, light blue, grey, dark blue). Below this is a dark blue box containing the text 'Contents of the proposed protocol for conducting clinical trials'. The main content area is a light grey box with the following text:

Study treatment

Adverse events (see Appendix XI)

- Description of expected adverse events should be given
- Procedures used to evaluate an adverse event should be described

A dark blue footer bar at the bottom contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Then what are the study treatment that also required to give, then adverse event description of expected adverse event should be given. So, whatever the available knowledge for the adverse event that also has to be mentioned. Procedure used to evaluate an adverse event should be described whatever the procedure; the CRO is following as per the protocol that has to be mentioned. Ethical consideration so, the summary of the ethical consideration required to be give.

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The slide features the CDSA logo in the top right corner. The main title is 'APPENDIX X' in bold blue letters, centered above a decorative horizontal bar with four colored segments (dark blue, light blue, grey, dark blue). Below this is a dark blue box containing the text 'Contents of the proposed protocol for conducting clinical trials'. The main content area is a light grey box with the following text:

Ethical considerations

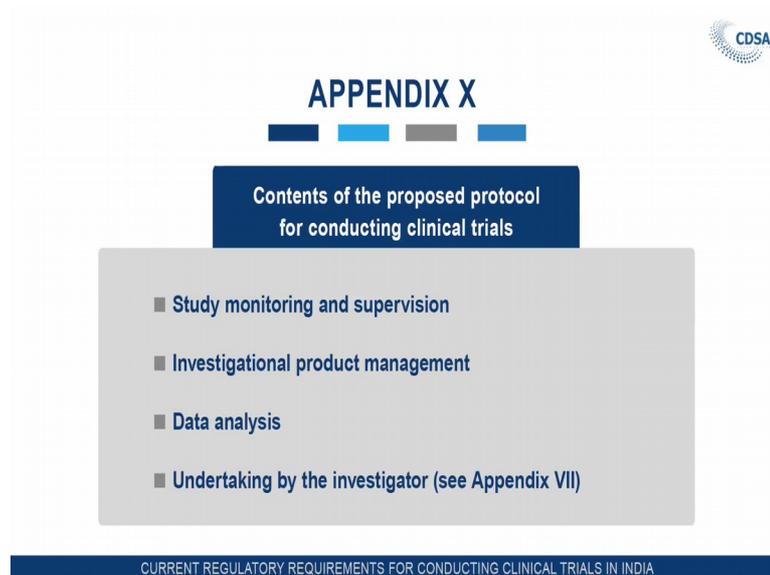
It gives the summary of:

- Risk/benefit assessment
- Ethics committee review and communications
- Informed consent process
- Statement of subject confidentiality including ownership of data and coding procedures

A dark blue footer bar at the bottom contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

Like risk benefit assessment how they have calculated, then it is committee review and communication then informed consent processes how they are the SOP for that. In a statement of subject confidentiality including ownership of data and coding procedure that they will maintain the confidentiality, what is the procedure to maintain the confidentiality that also has to be given.

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Study monitoring and supervision; so, how they are going to monitor the study, who will be the responsible, how they are going to supervise the study the detailed procedure, then investigational product management. So, what are the products they are going to use in the study. So, how they are going to store that product, what is the stability of that product, who is responsible to dispense that product. So, whatever the management is there they have to give; then data analysis undertaking by the investigator we have seen in appendix VII. So, undertaking by the investigator whatever whosever investigator involve, they have to give the sign and the undertaking.

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CDSA

APPENDIX X

Contents of the proposed protocol for conducting clinical trials

Appendices

- Provide a study synopsis, copies of the informed consent documents (patient information sheet, informed consent form etc.), case record form (CRF) and other data collection forms; a summary of relevant pre-clinical safety information and any other documents referenced in the clinical protocol

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then appendices provide a study synopsis, copies of the informed consent document, informed consent document as I have said into part patient information sheet, the information to be converted to the patient and informed consent form that, if you agree then you to sign. CRF and other data case record form and other data collection form; summary of relevant pre-clinical safety information any other document reference in the clinical protocol. So, here it is briefly given the content of this appendix X that is title page table of contents and other things.

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APPENDIX XI

Data elements for reporting serious adverse events occurring in a clinical trial

- Patient details
- Suspected drug(s)
- Other treatment(s) provide the same information for concomitant drugs (including non prescription/OTC drugs) and non-drug therapies, as for the suspected drug(s)
- Details of suspected adverse drug reaction(s)
- Outcome
- Details about the investigator

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Appendix XI is the data element for reporting SAE occurring in clinical trial. So, this is regarding the patient details, suspected drugs other treatment to provide the same information for concomitant drug including non-prescription drug, then details of suspected AE, outcome details about the investigator.

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The slide features the CDSA logo in the top right corner. The title 'APPENDIX XII' is centered at the top, followed by a subtitle 'Compensation in case of injury or death during clinical trial' in a dark blue box. Below this, two light gray boxes contain the following text:

In the case of an injury occurring to the clinical trial subject, he or she shall be given free medical management as long as required.

In case the injury occurring to the trial subject is related to the clinical trial, such subject shall also be entitled for financial compensation as per order of the licensing authority defined under clause (b) of Rule 21 and the financial compensation will be over and above any expenses incurred on the medical management of the subject.

At the bottom of the slide, a dark blue bar contains the text: 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

The next is appendix XII; compensation in case of injury or death during clinical trial. So, this is your related to the compensation in case of the clinical trial. In the case of an injury occurring to the clinical trials subject he or she shall be given free medical management as long as required. In case injury occurring to the trial subject is related to the clinical trial so, subjection also be entitled for financial compensation as per the order of the licensing authority, that is a drug controller general of India; we also called the CLA will be over and above any expense incurred on the medical management of the subject.

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APPENDIX XII

Compensation in case of injury or death during clinical trial

In the case of clinical trial related death of the subject, his/her nominee(s) would be entitled for financial compensation as per the order of the licensing authority defined under clause (b) of Rule 21, and the financial compensation will be over and above any expenses incurred on the medical management of the subject.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

In the case of clinical trial related death of the subject his or her nominee would be entitled for financial compensation as per the order of the licensing authority defined under clause b of rule 21, and the financial compensation will be over and above any expense incurred in the medical management of the subject.

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APPENDIX XII

Compensation in case of injury or death during clinical trial

The financial compensation for clinical trial related injury or death could be in the form of:

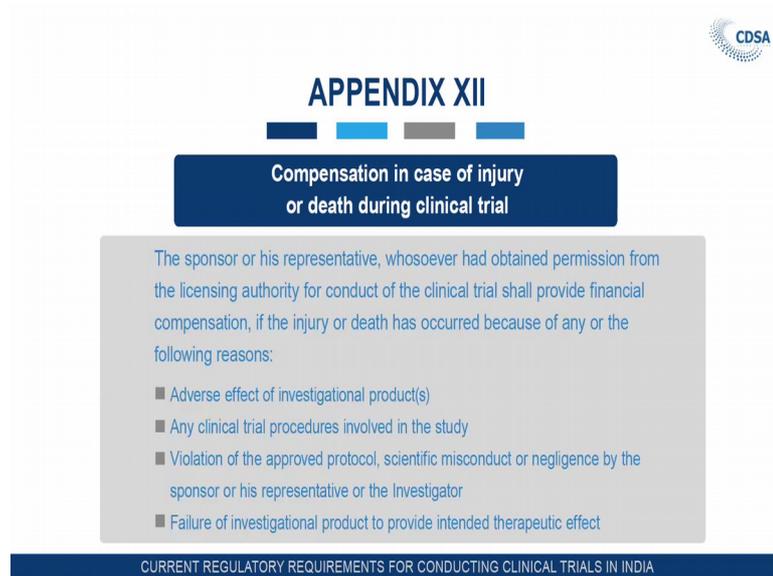
- Payment for medical management
- Financial compensation for trial related injury
- Financial compensation to nominee(s) of the trial subject in case of death
- Financial compensation for the child injured in-utero because of the participation of parent in clinical trial

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

The financial compensation for clinical trial related injury or death could be in the form of payment for medical management, then financial compensation for trial related injury. Financial compensation to nominees of the trial subject in case of death, financial

compensation for the child injured in-utero because of the participation of parent in clinical trial.

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The slide features the CDSA logo in the top right corner. The main title is 'APPENDIX XII' in bold blue letters, followed by a subtitle 'Compensation in case of injury or death during clinical trial' in white text on a dark blue background. Below this, a light gray box contains the text: 'The sponsor or his representative, whosoever had obtained permission from the licensing authority for conduct of the clinical trial shall provide financial compensation, if the injury or death has occurred because of any or the following reasons:'. A bulleted list follows, with four items: 'Adverse effect of investigational product(s)', 'Any clinical trial procedures involved in the study', 'Violation of the approved protocol, scientific misconduct or negligence by the sponsor or his representative or the Investigator', and 'Failure of investigational product to provide intended therapeutic effect'. At the bottom, a dark blue bar contains the text 'CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA'.

APPENDIX XII

Compensation in case of injury or death during clinical trial

The sponsor or his representative, whosoever had obtained permission from the licensing authority for conduct of the clinical trial shall provide financial compensation, if the injury or death has occurred because of any or the following reasons:

- Adverse effect of investigational product(s)
- Any clinical trial procedures involved in the study
- Violation of the approved protocol, scientific misconduct or negligence by the sponsor or his representative or the Investigator
- Failure of investigational product to provide intended therapeutic effect

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

The sponsor or his representative whosoever had obtained permission from the licensing authority for conduct of the clinical trial shall provide financial compensation, if the injury or death has occurred because of any of the following reasons. The reasons are given here below. Adverse effect of investigational product, any clinical trial procedure involved in the study, then if there is a violation of the approved protocol, if the protocol has been approved and the PI has not followed the condition stipulated there in, scientific misconduct of the protocol or any negligency by the sponsor of his representative or the investigator, failure of investigational product to provide intended therapeutic effect.

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APPENDIX XII

Compensation in case of injury or death during clinical trial

The sponsor or his representative, whosoever had obtained permission from the licensing authority for conduct of the clinical trial shall provide financial compensation, if the injury or death has occurred because of any or the following reasons:

- Use of placebo in a placebo controlled trial
- Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol
- Injury to the child in-utero because of the participation of parent in clinical trial

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Use of placebo in placebo controlled trial, if any adverse effect due to the concomitant medication if any other medication has been used and due to which the adverse effect or SAE occur, but this is excluding standard care necessitated as part of approved protocol. Injury to the child in-utero because of the participation of parent in clinical trial, procedure for payment of financial compensation has to be given. So, these are all the appendices is given in the schedule Y we have seen.

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RECAP

- 1** How many appendices are there in Schedule Y?
I to XII (including IA & IB).
- 2** When was phytopharmaceuticals Appendix IB introduced under Schedule Y?
It was introduced vide G.S.R. 918 (E) on November 30, 2015.
- 3** Under which rule and appendix the compensation in case of injury or death during clinical trial is included?
Rule 122DAB and Appendix XII.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Now, let us have quick challenge for you by giving the question as usual. So, have the first question, how many appendices are there in schedule Y? So, there are XII appendices including appendix I A and I B. Then next question, when was phytopharmaceutical drug appendix I B introduced under schedule Y? So, it was introduced vide GSR 918 on 30th November 2015. Next question under which rule and appendix the compensation in case of injury or death during clinical trial is included? So, this is rule 122 DAB and appendix 12 related to the compensation.

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RECAP

4 In which case AV recording should be done for informed consent?
Vulnerable subjects.

5 What is Appendix V?
Informed consent.

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In which case AV recording should be done for informed consent? So, the answer for this is vulnerable subjects, AV recording is required. The last question what is appendix V? This is very important appendix. So, the appendix V is related to the informed consent document.

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SUMMARY

In Lecture 9, we briefly learned about:

- Appendices of Schedule Y.
- We also learned that appendices are the requirements for approval/marketing of new drug, subsequent new drug (includes FDC, biologicals, vaccines, phytopharmaceutical drug).
- We understood that appendices are provided to help the applicant in generating data for regulatory approvals.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Let us summarize and briefly the lecture 9. So, in this lecture 9 we have seen all the appendices that is appendix I to appendix XII including I A and I B. We have also learned that the appendices are the requirement for approval of marketing new drug, subsequent new drug, then FDC, biological, vaccine, phyto-pharmaceutical drug. We understood that appendices are to help applicant to generate data for regulatory approval. So, this is all about the lecture 9 and schedule Y and its appendices. So, we will see again in our next lecture till then bye bye and.

Thank you.