Current Regulatory Requirements for Conducting Clinical Trials in India for IND/New Drug Version 2.0

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Lecture - 16
Content of Proposed Clinical Trial Protocol

Hello friends, welcome back to the course Version 2.0 Current Regulatory Requirement for Conducting Clinical Trial in India for New Drug and Investigational New Drug.

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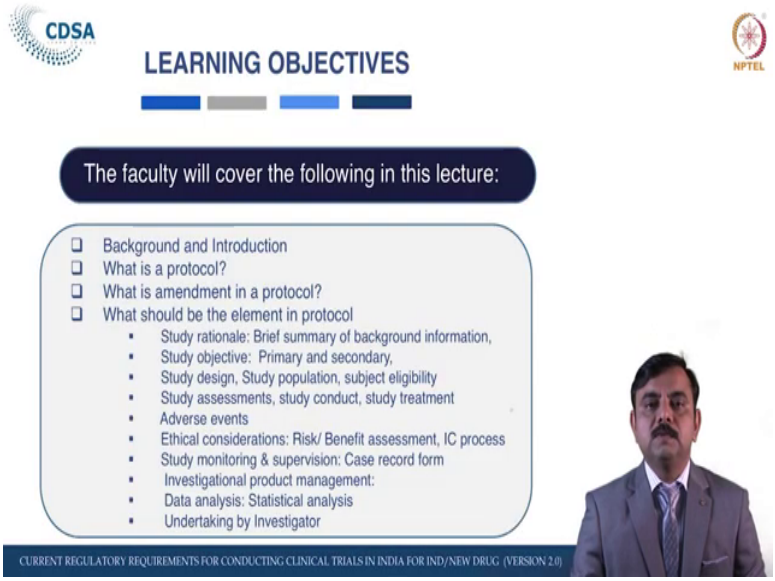

So, this is a lecture 16 and it is related to the Content of Proposed CT protocol. After completion of this lecture, the learners will come to know, what is a protocol? Then what is

mean by amendment in protocol? What should be the element in protocol like, Study rationale Study objective.

The objective may be primary and secondary objective, Study design, Study population subject eligibility study assessment adverse event. Then how to propose this ethical consideration study monitoring and supervision, are related to the investigational product and other things. So, let us start one by one first we will see the objective and rationale of the content of proposed protocol.

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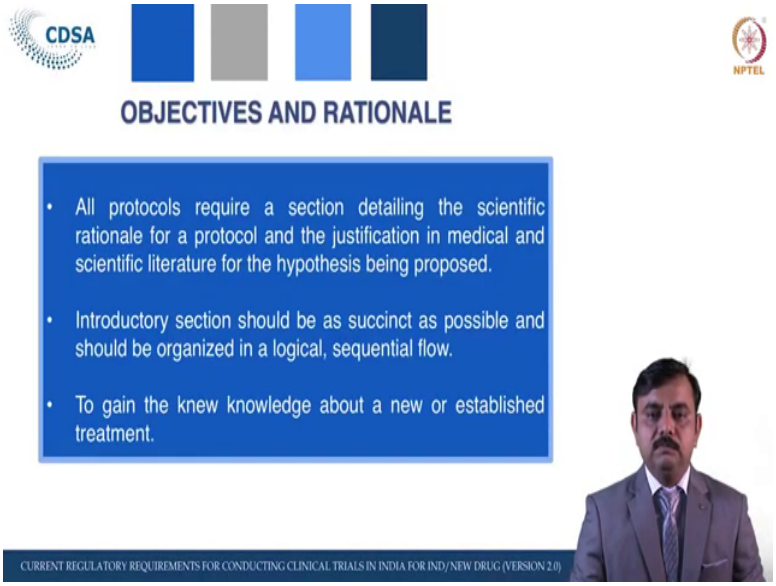

So, the all protocols require a section detailing the scientific rationale for protocol and the justification in medical and scientific literature for the hypothesis being proposed. So, whenever the applicant proposes any clinical trial protocol, there must be some hypothesis and that hypothesis must be scientifically justified.

Then the introductory section which is given in the propose clinical trial protocol should be as succinct as possible and should be organized in a logical sequential flow. So, it should not be inordinate and there should be a logical sequential flow and it is to gain the knowledge about a new or established treatment. So, the objective should be to gain the knowledge about new or established treatment.

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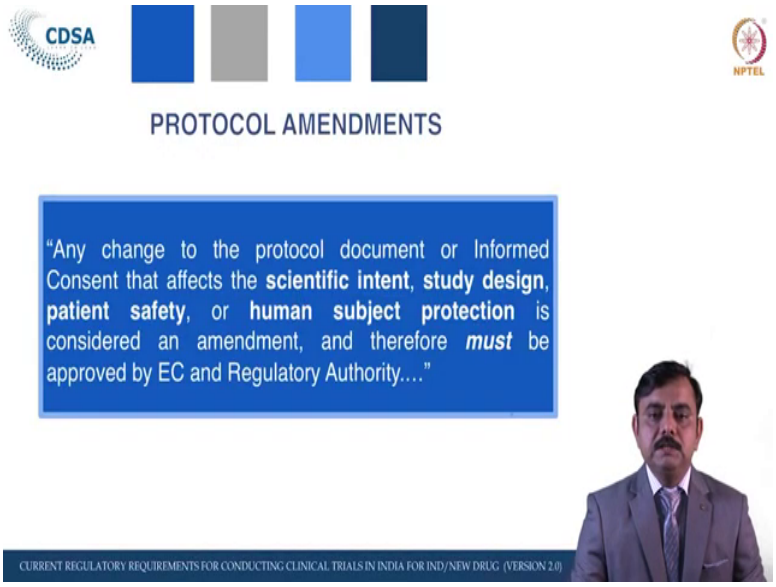

Let us see what is the Protocol Amendment, any change to the protocol document or informed consent that affect the scientific intent, study design patient safety or human subject protection is considered an amendment and therefore, must be approved by ethics committee and Regulatory Authorities. You can see the things which are changed with respect to the scientific intent study design patient safety, which may affect the human subject protection that is required to be approved by the ethics committee and regulatory authority.

We can consider the three types of the protocol amendment, one amendment can be a minor changes which is which may be for the additional safety of the patient, that is required only to notify to the licensing authority. But in case of there are some major and critical changes that need to be taken approval from the licensing authority and ethics committee as well. What is mean by a Protocol?

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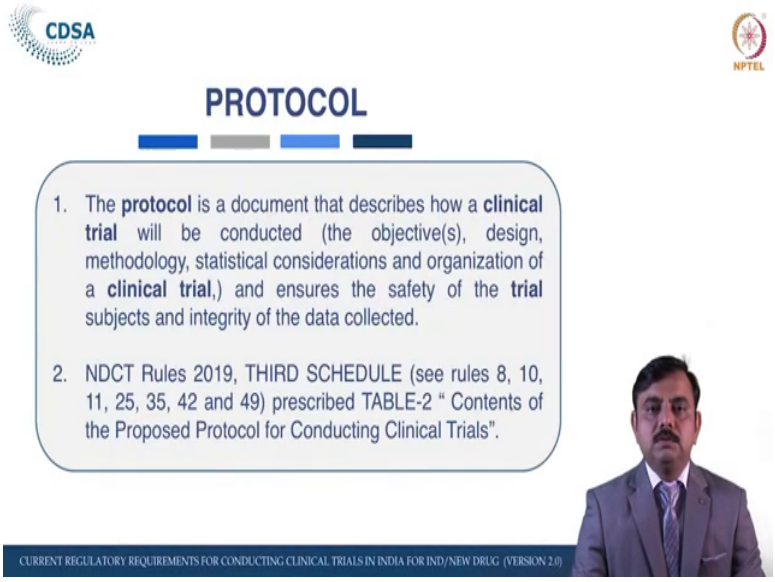

So, the protocol is a document that describes how a clinical trial will be conducted. The objective, design, methodology, statistical consideration and organization of clinical trial and it ensures the safety of trial subject and integrity of the data collected that is called the protocol. Let us see where its position in the rules and regulation. So, we have seen many of the time it is the new drug and clinical trial rule 2019.

So, in this rule in the Third Schedule you can refer the rules, rule 8, 10, 11, 25, 35, 42 and 49 which are related to this schedule and it has been prescribed in TABLE 2. We will be seeing the details in all the table. The content of proposed protocol for conducting clinical trial let us move to the actual content what should be the proposed content of the Clinical Trial protocol.

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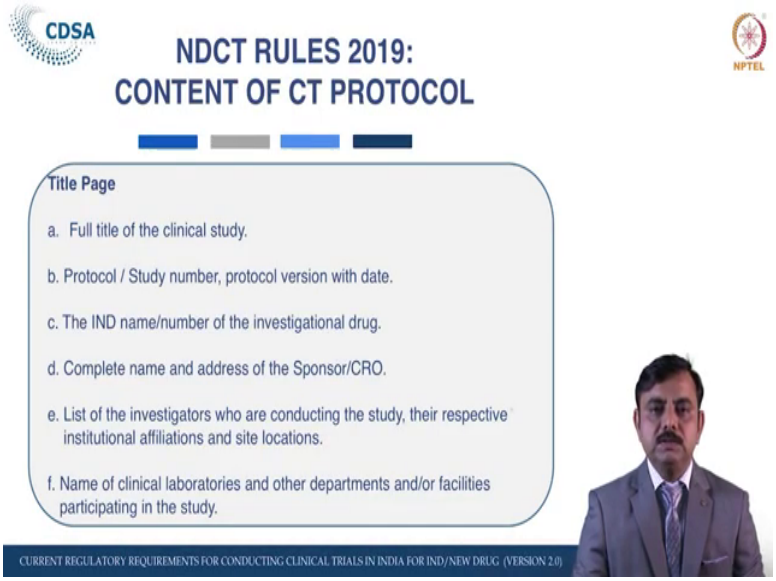

So, first it should have a title page and this title page is a full title of the clinical study that it should from this title it should reflect that which type of study. What type of study design, which population, which phase they are going to cover. Then protocol or study number if it is a version 1 version 0 if it has been amended then which version to be approved and that should be with the date. Then the name of the IND or the NEW drug which is under consideration, then complete name and address of the sponsor CRO who were responsible, then list of the investigator who are conducting the study.

Their respective institutional affiliation and site locations, that should be there in the proposed protocol. Name of clinical laboratories and their department or facilities participating in the study. So, after the trial has been conducted, it required to be the sample required to be analyzed. So, where the samples they are going to analyze and test, the name of that laboratory and detail of the laboratory that is required to be given.

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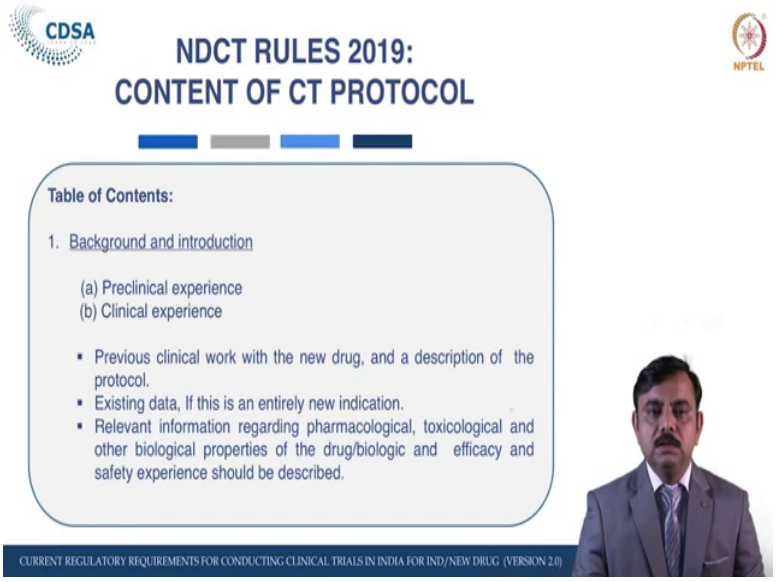

Then under the heading Background and introduction the preclinical and clinical experience has to be given. The previous clinical work with the new drug and description of the protocol, then existing data if this is an entirely new indication. If it is a entirely new indication then the existing data available that is required to be given relevant information regarding pharmacological and toxicological. If it is a biological product then the biological properties of that drug or the product, including it is safety and efficacy experience should be described.

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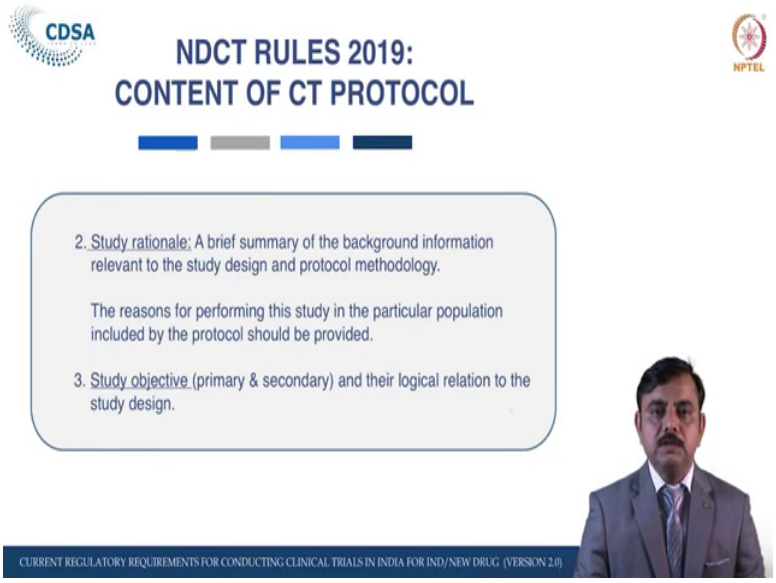

As we have mentioned the study rationale should be there and that study rationale should be in a brief summary of the background information, relative to the study design and the protocol methodology. The reason for performing this study in the particular population included by the protocol should be provided.

Sometimes the study is with a special kind of population, for example sometimes it is with the pediatric or pregnant woman or sometime it is with the patient. So, why they have been included the reason has to be mentioned. This study objective should be clear the primary and secondary objective like to assess the efficacy or to assess the safety. Both the objective primary and secondary and they are logical relation to the study design. Based on that objective how you have constructed the design that logical reason have to be given.

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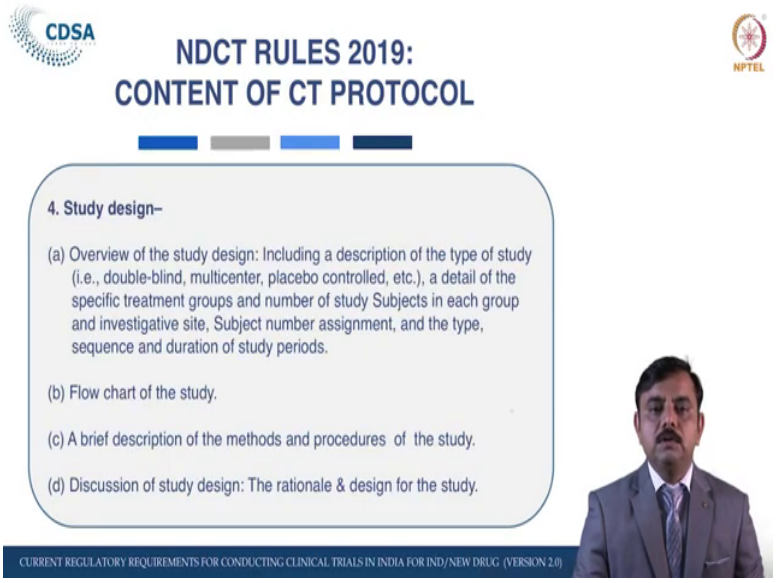

Then study design is the important part, in which in the overview of the study design including a description of the type of study, whether it is a double blind multicenter or placebo control that everything has to be mentioned.

Then a detail of the specific treatment groups and number of study subject in each group and investigative site, subject number assignment and the type sequence duration of the study period. So, that has to be given wherever possible the flow chart of the study how they are going to conduct and the brief description of the methods and procedure of the study required to be submitted. Discussion of the study design, the rationale and design for the study on what basis the study has been designed the discussion has to be given.

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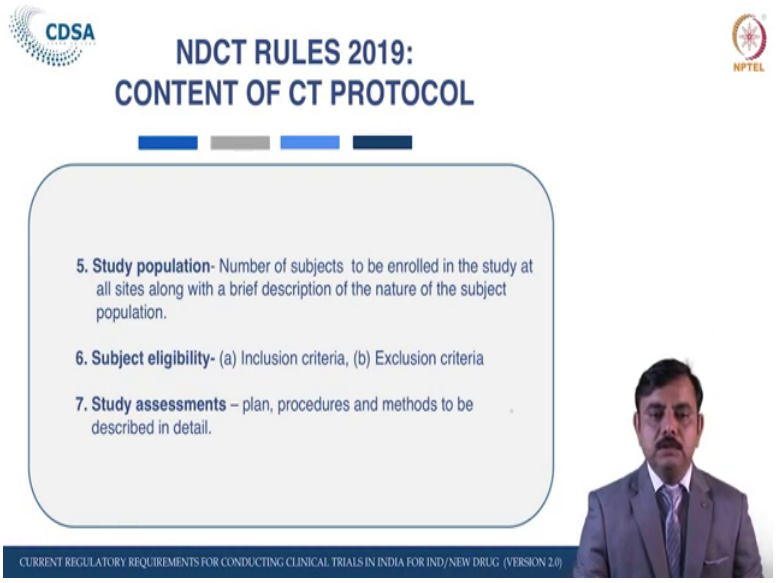

Then study population has to be given and the number of subjects to be enrolled in the study at all site. If it is a multi centric then number of the subjects to be enrolled that has to be mentioned, along with the brief description of the nature of the subject population.

Then subject eligibility criteria has to be given like inclusion criteria exclusion criteria. In the inclusion criteria depending upon the nature of the drug and the phase of the trial it may be healthy subject, it may be a patient or some particular type of population. Exclusion criteria maybe nonsmokers and the alcoholic people they are not allowed. In most of the cases the pregnant woman's and the women's are not suitable for the study. So, that should be mentioned in the exclusion criteria. Then next is the study assessment, regarding the study assessment plan procedure and methods to be described in detail.

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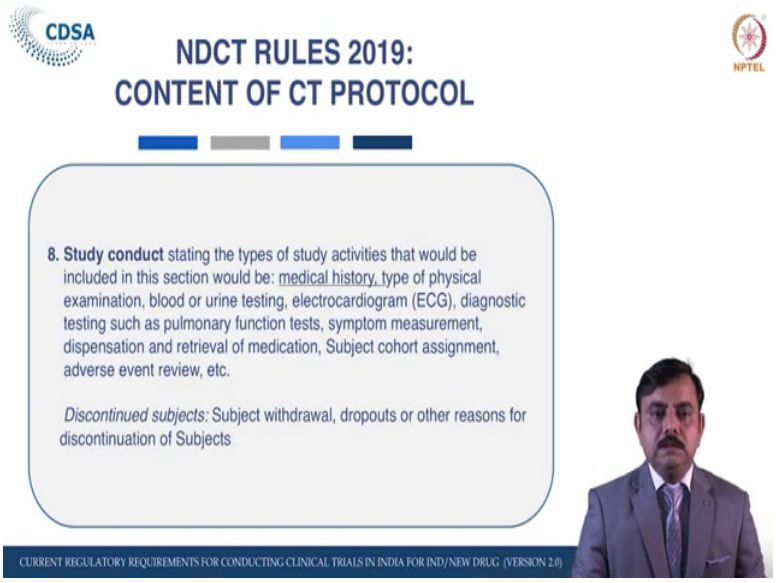

Next is study conduct it is Study conduct, stating the types of study activities that would be included in this section and would be medical history type of a physical examination blood urine testing. Then if it is required the ECG diagnostic testing such as pulmonary function test, then symptom measurement or dispensation and retrieval of medication subject cohort assignment adverse event if any. Then how to review, what is the protocol, what is the procedure for that as to be mentioned.

Then discontinued subject if the subject has been has been discontinued or would be discontinued, then the criteria for that the sop for that subject withdraw or dropout or other reason for discontinuation that has to be mentioned.

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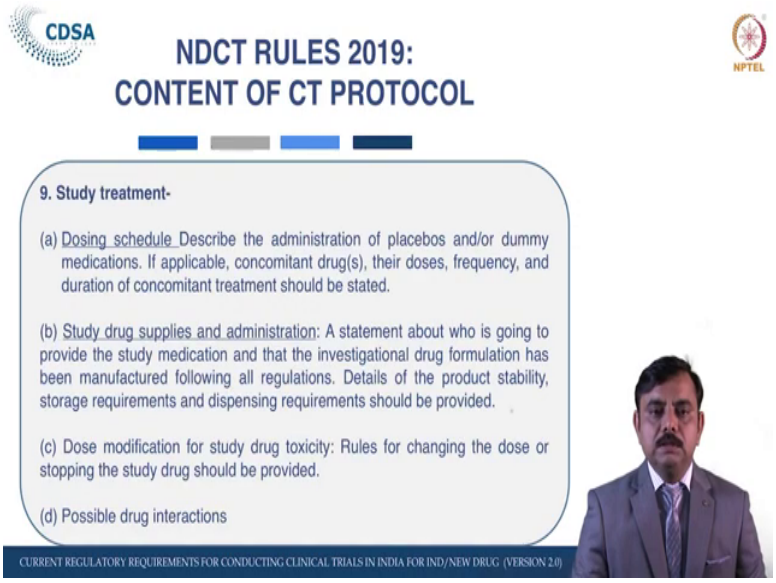

In the study treatment the dosing schedule including the dose the number of doses that is a frequency duration of the experimental treatment and also has to be described the administration of placebo or dummy medication if it is there. And the concomitant drug if applicable then also their doses frequency duration of concomitant treatment should be stated clearly.

Study drug supplies and administration, a statement about who is going to provide the study medication. So, those who are providing the study medication the source should be authenticate and which is the source that required to be mentioned. And that the investigational drug formulation has been manufactured following all the regulation.

Also the statement has to be given that the IP what we have seen the drug to be undergo or the study. Where it has been manufactured and whether they have followed all the norms like

good manufacturing norms and regulation that statement has to be given. Dose medication for studying drug toxicity, in this section the rules for changing the dose or stopping the study drug should be provided. If it is likely to change the dose then that also required to be given. Then possible drug interaction from the published literature or available knowledge, if some drug interactions are there then that has also required to be mention.

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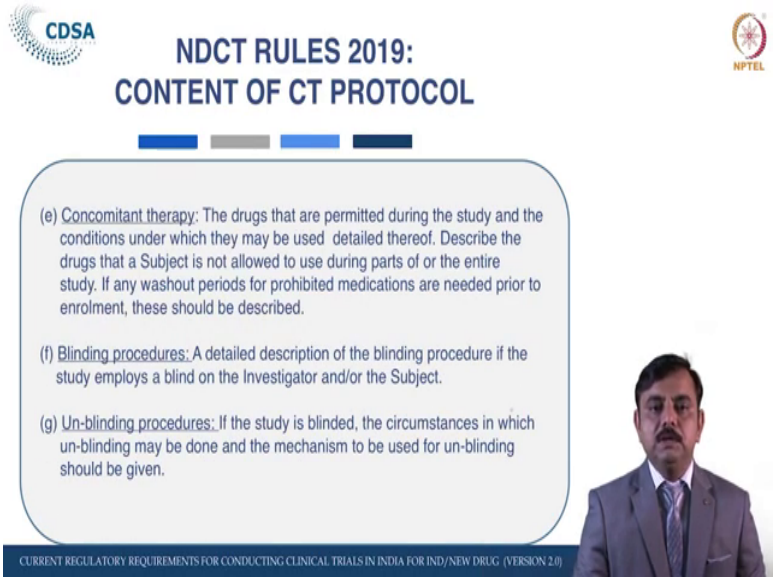

Study treatment we have seen that Concomitant therapy, if concomitant medication is there then the source of that meditation that has to be given and the drug that are permitted during the study and condition under which they may be used the detailed thereof has to be given.

Then if it is a blinding procedure then detailed description of the blinding procedure; if the study implies a blind on the investigator or the subject. The detailed procedure of blinding has to be given. If it is un blinding and the circumstances in which un blinding may be done and the

mechanism to be use for un blinding that should be given. Adverse event in this section the description of expected adverse event should be given then procedure to evaluate.

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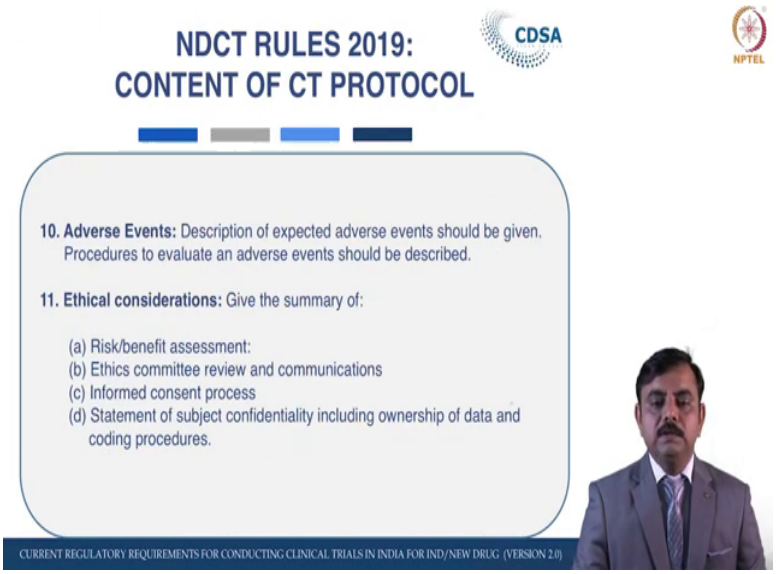

If any SAE is there any injury is there then how to tackle that injury, the procedure to evaluate an adverse event that should be prescribed the next element in this is the ethical consideration. So, regarding the ethical consideration we are having separate lecture. So, in the proposed protocol the summary of the risk benefit assessment has to be given with respect to the ethical consideration.

Then the procedure of ethics committee review and communication procedure for the informed consent process, then what the ethical consideration required to be have the statement of subject confidentiality including ownership of data and coding procedure.

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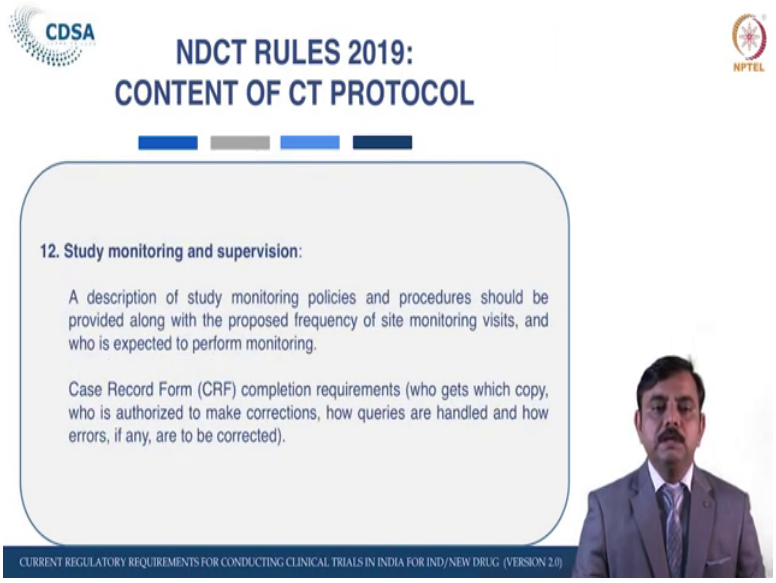

Under the heading Study monitoring and supervision, a description of study monitoring policies and procedure should be provided along with the proposed frequency of site monitoring visit.

So whatever the site monitoring are there, the frequency proposed frequency of the site monitoring visit has to be given and who is expected to perform the monitoring that is also required to be submitted. The case record form completion requirement who gets which copy who is authorized to make correction, how queries are handled, how errors if any that are to be corrected all the SOP should be there and the format of this SOP and copy of the proposed sop should be enclosed.

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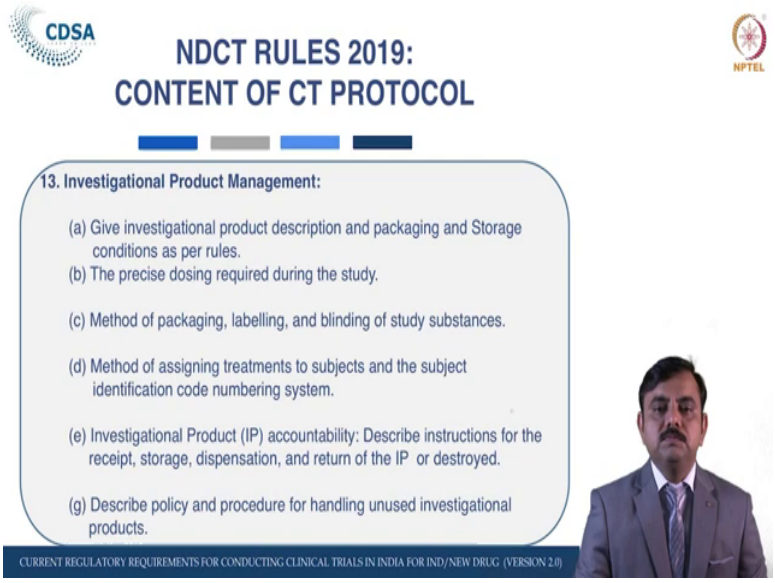

Then with respect to the investigational product and it is management these details have to be given. The product description and packaging and the important thing is the storage condition as per the rules. So, it is mentioned in the rule also that it should be stored properly. So, what would be the storage condition, that also required to be provided. The precise dosing required during the study, method of packing labeling and blinding of study substances the procedure has to be given. Method of assigning treatment to subject and the subject identification code numbering system; in case of if it is a blinding study then the method of assigning treatment to the subject for the control and test that is also required to be given.

The investigational product accountability in this section, the described instruction for the received storage dispensation and return of the IP or destroyed. So, regarding the accountability who would be the accountable person to receive the IP in the clinical trial or bb study program and who will store it how it would be dispensed. And if it is a the quantity has

been leftover then how it is to be destroyed that procedure and SOP should be fixed and given with the proposed protocol. Then along with this the describe the policy and procedure for handling unused IP, the policy and procedure for the unused IP also required to be submitted.

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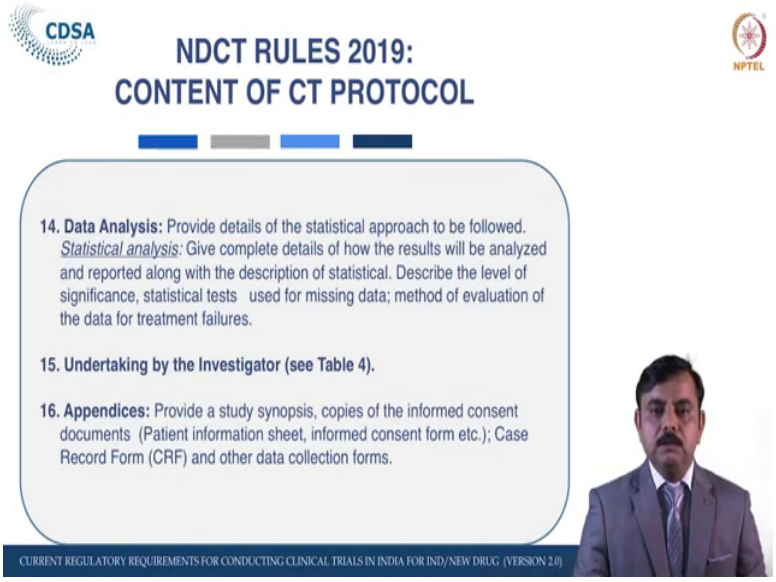

Data analysis under this heading it has to be provided the detail of the statistical approach to be followed including the sample size that is a population. How the sample size was determined including assumptions made in making this determination efficacy and points, primary as well as secondary and the safety endpoint. The statistical analysis in this it has to be the complete details has to be given of how the results will be analyzed and reported along with the description of the statistical.

Then describe the level of significance statistical test used for missing data, method of evaluation of the data for treatment failure that is required to be submitted. Undertaking by the

investigator it is also one of the most important document and we have seen in the tables, the elements to be mentioned in the undertaking by the investigator has been given in the table 4. So, the proposed undertaking by the investigator that has also required to submitted. Then Appendices in this section the applicant has to provide a study synopsis, copies of the informed consent document.

That is a patient information sheet and the informed consent form the copy of this the sample copy, then case record form and other data collection forms that is required to be submitted.

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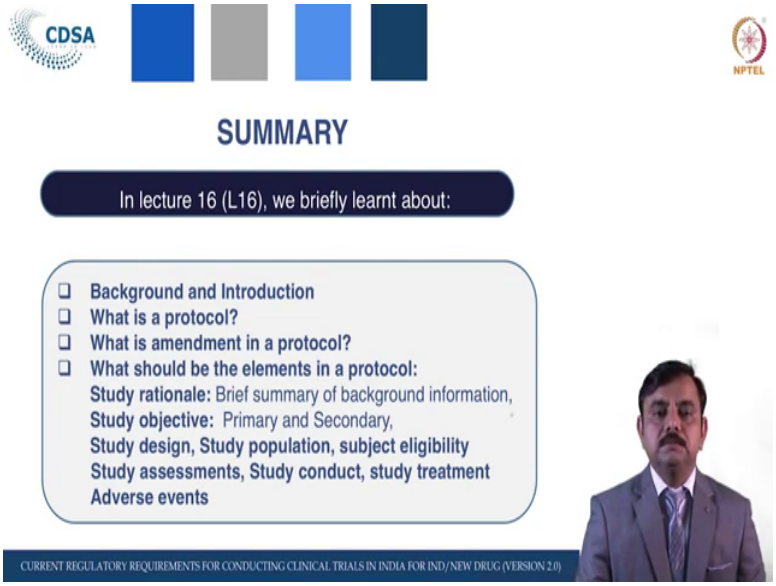

Then we have seen the background introduction. And other thing has to be given. So, this is about the proposed content report. Let us see what we have seen in this lecture. So, in this lecture we have seen background and introduction of the protocol. Then what is means by

protocol, where the amendment is required ah to be notified; where it required approval by the ethics committee and the center licensing authority.

Then what should be the element in the protocol with respect to the study rationale subject population sample size. Then in case of the SEA injury; how do we do the study assessment, study conduct and the reporting of the adverse event regarding the ethical consideration, these things we have seen in this lecture.

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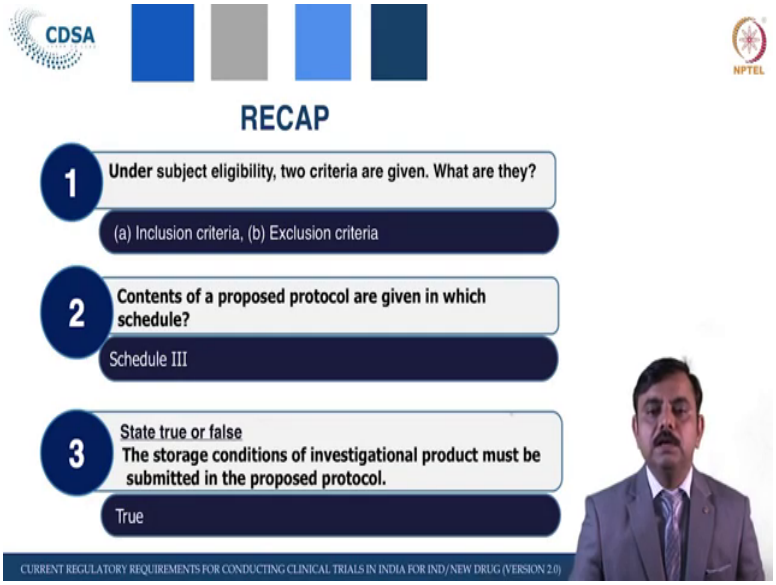

So, let us have the recap of this and the question for you the first question under subject eligibility 2 criteria's are given we have to mention which these two criteria's are there. So, there are mainly 2 criteria Inclusion and Exclusion criteria. The question number two content of proposed protocol given in schedule. So, in which schedule the content of proposed protocol has been given you to mention.

So, it is a schedule 3 in which the content of proposed protocol has been given. The next question you have to answer whether it is true or false, IP storage condition investigational product required to be submitted in a proposed protocol. You have to answer whether it is true or false whether IP storage condition is required or not, yes it is true the IP storage condition required to be submitted in proposed protocol.

So, this is about the proposed content of the protocol, will see in our next lecture what are the how the report has to be submitted. Now we have seen the content of proposed protocol once it is approved, then the applicant has to submit the detailed report and how to submit that report that is also essential and I will be covering that in our next section.

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Till then take care thank you and bye bye.