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

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Lecture - 15
Requirements for Import/ manufacture of new drug/ IND for sale/ distribution

[FL] Welcome you all to the online course on Current Regulatory Requirements For Conducting Clinical Trials In India For investigational New Drug. I will take you through lecture 12 B which is the regulatory requirements for manufacture or import of investigation, for manufacture or import of new drug or investigational new drug. I will now take you through lecture 12 B, the requirements for import manufacture of new drug for sale distribution and also the requirements for manufacture of unapproved new drug for the patients.

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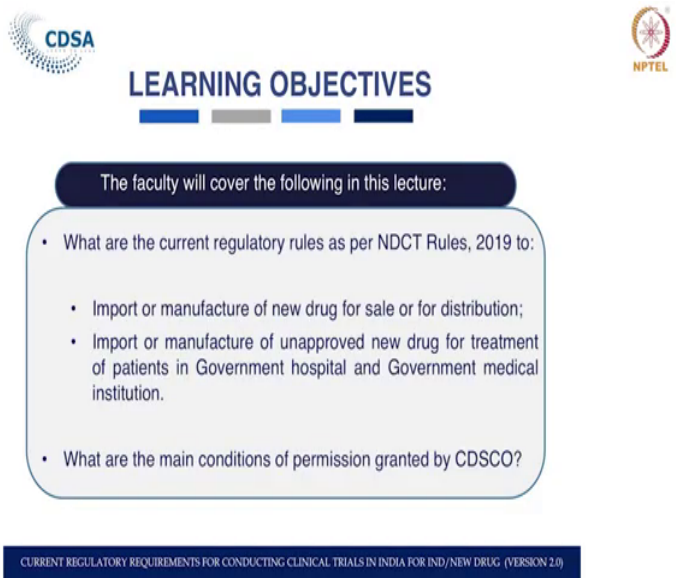

In this lecture what we are going to cover is that; what are the current regulatory rules governing the import or manufacture of new drug for sale or for distribution in the country and also the rules for the import or manufacture of unapproved new drug for the treatment of patients in government hospital and government medical institution. What are the main conditions of permissions granted by CLA Central Drug Standard Control Organization, we which is the Central Licensing Authority?

Before going through the following slides the different slides, I would just like to mention that; in this particular New Drug and Clinical Trial Rules which you may be already aware that there has been a special provisions which has been given in this new rules for the import or manufacture of unapproved new drug. What is unapproved new drug? That means, the drug is not permitted has not been approved and has proved to be qualities of good quality safety and

efficacious drug. The drug has not proved to be safe and efficacious for the treatment of patients in India and has not been approved by the regulatory authority in India.

So, such drugs unapproved new drug which is unapproved in India, but has been approved in other countries as well as drugs which are not approved in India and also not anywhere in the world, but is still under the clinical trial. This new drug and clinical trial rules gives provisions and gives a scope for important manufacture of such unapproved new drug for the treatment of the patients in the government hospital and government medical institution. So, the various conditions or permissions are given in the subsequent slides.

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There are two chapters in this lecture chapter 10 and chapter 11, while the first chapter is the first part the import or manufacture of new drugs for sale or for distribution in the country. The requirements and the regulations for the same and this is chapter 11, which deals with the

import or manufacture of the unapproved drug by the government hospital or institution for the purpose of the patient's treatment.

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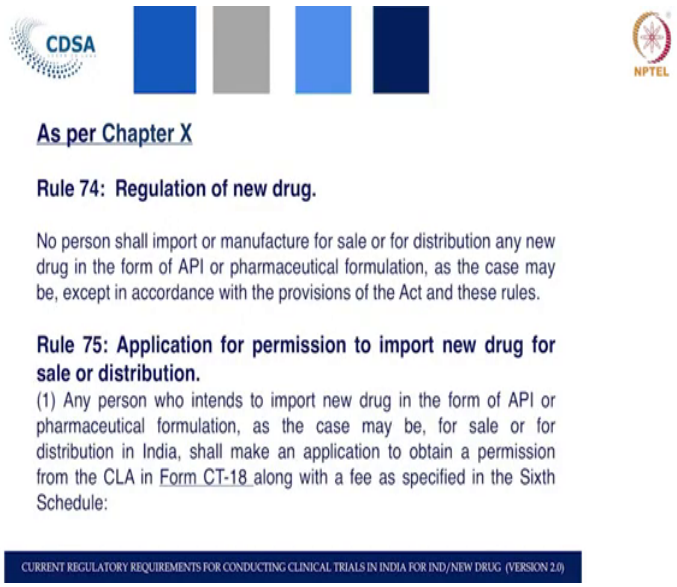

As for this chapter 10, we have two general rules. So, one is the rule 74 and also we have rule 85. And from this rule 75 to 79, we deal with the all the requirements for the import of the drugs for sale and distribution while further firm rules 84 to 80, 80 to 84, we have the rules for the requirements for manufacture of new drug for the purpose of sale or distribution.

And there is also rule 86 to rule 96 which deals with the which is in chapter 11, we have the unapproved drug which is under clinical trial the requirements which is to be fulfilled to import or manufacture such unapproved drug and buy and the and which can be done by the government hospitals and government institution for the purpose of the patient treatment who are suffering from life threatening disease.

So, in all case it is a common requirements in the regulation of the new drug which is stated in rule 74 that neither anybody can import or manufacture any drug for new drug for sale or distribution unless it is under done, under these provisions; that means, unless it is permitted by the central licensing authority and it complies with all the requirements and the conditions which are mentioned in this chapter, starting with rule 75 which is the application for permission to import the new drug.

So, such application should be made in CT form 18, if you go back to the new drug in the clinical trial rules and open this form CT 18, you will see the various requirements are mentioned and it is a very simple and your requirements which have to be filled up and such requirements are actually prescribed and the documents which are to be filled up are as per the second schedule. So, there is a schedule and the new drug and the clinical trial rules, which mentions the different you know there are different tables the tables mentions table 1, table 2, table 3, table 4.

So, as per the type of the drugs which you are going to apply for, whether it is for the purpose of import or if it is o whether it is for the purpose of manufacture. The tables are combined depending on the type of the drug. So, what we mean by that type of the drug? Let us see what we mean by the type of the new drugs. So, and the fees are always all fees for applications are specified in the 6 schedule. So, it goes it varies from the different types and the different stages. So, it is a fee of 5 lakh or 3 lakhs or 2 lakhs, so you can check with the specific 6 schedule for such application.

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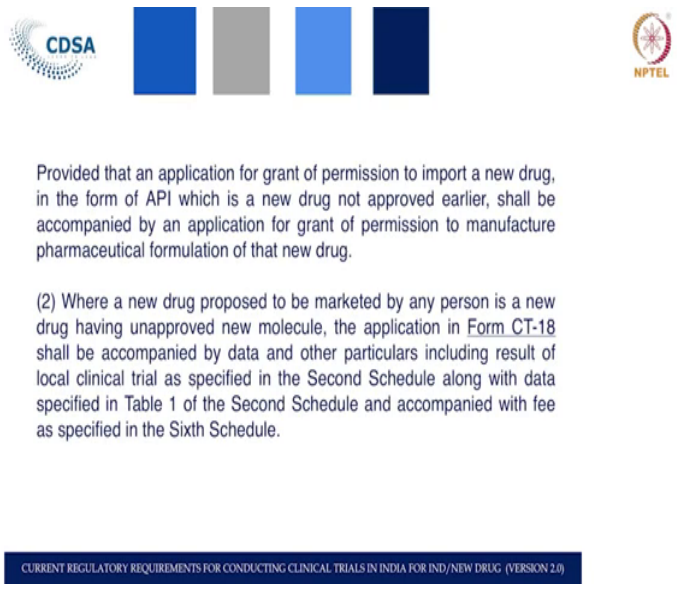

In case the drug is not approved earlier, it is an unapproved active pharmaceutical ingredient and the new drug is made of an unapproved API and it has not been permitted in the country before in such case the applications in CT 18 shall be accompanied with the documentation which is as per table 1 of the second schedule.

So, that entire requirements of the CMC data, the other requirements because there are no they are as per the drugs which is whether it is unapproved, whether it is approved or, but it is still a new drug; that means, it falls under the definition of new drug that it is which like a drug which is manufactured or imported new drug it continues to be a new drug up to 4 years. So, if it falls under that definition. So, in such cases what are the documentation requirements? All are given one after another in this various tables.

Now, when you go to these tables, you see the requirements of the chemistry manufacturing control. What do you mean by this? Whatever are the documentation which are required for you to establish the drug. The characterization of the molecule what is this drug actually, what are the different tests which you have done for the active pharmaceutical ingredient as well as for the finished formulation, your stability study, your process validation data, your different other requirements to characterize that particular drug that this is this drug. And then the various other studies like the toxicological study, animal toxicity study, the pharmacodynamic studies, as well as the clinical trial which you have done.

So, all this comes into this submission requirements in this table 1. So, what are the documents which you have to submit it are clearly specified in this second schedule under the table 1. Now, once, so this is the documentation requirement when you are applying for a drug which is not approved earlier. Coming to the drug which is already approved as a new drug in the country, but it still across the definition of the new drug; that means, it is a it is falls within the 4 year spread in such case the documentations are given in table 2 of the second schedule.

And when it falls to the other definition of the new drug; that means, it is now already permitted for certain claims and now you are proposed to market this drug for another new claim and new indications. So, you have mentioned it for one type of care treatment of one type of cancer and now you are proposing to make this drug use for another type of you claim that drug can be used for treatment of another type of concept.

So, one is the lung cancer, now you propose to use it in the bladder cancer, so whatever it is. So, it is depending on that type of the disease treatment you are proposing it comes into a new claim and new indication or you are proposing it to or it is being proposed to manufacture in a new dosage form what the so? It has been already approved in the country as a tablet, now you are proposing to manufacture it as a capsule or as an injectable form or any other forms and or if it is a new route of administration or it is a new strength.

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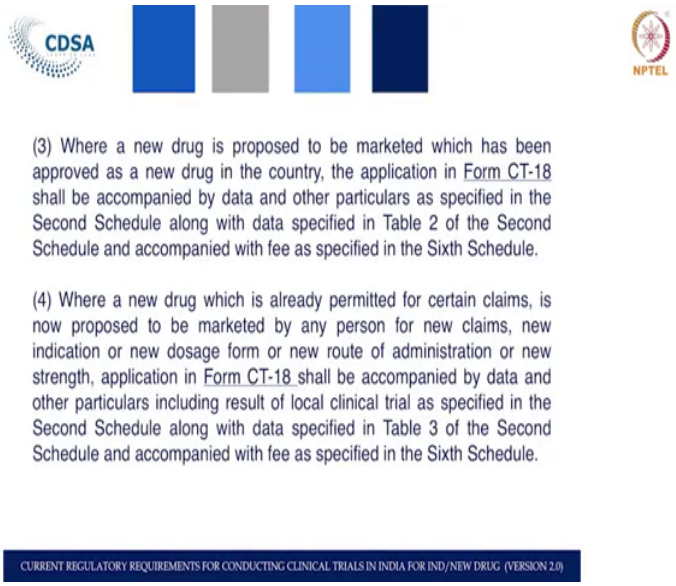

So, you have manufactured 20 mg 30 mg, now proposed to manufacture 50 mg. Whenever you change your strength so it is a new drug and your new route of administration, then in that case also as it across the definition of the new drug. So, if the application will be accompanied by the data and other particulars including the result of the local clinical trial. So, it is all same for the previous also the local clinical trial data has to be specified as well as the other requirements as per the second schedule along with the data which is specified in the table 3 of the second schedule and the fees as per the sixth schedule.

So, for the purpose of all these you have the chemistry manufacturing control data; that means, your manufacturing details, your stability or other requirements of the I have related to the drug and you have the clinical trial data. So, this is your chemistry manufacturing control,

your preclinical data and the clinical data. These are the three things which I have mentioned in this form 18 and in the table various tables as per the type of the drug.

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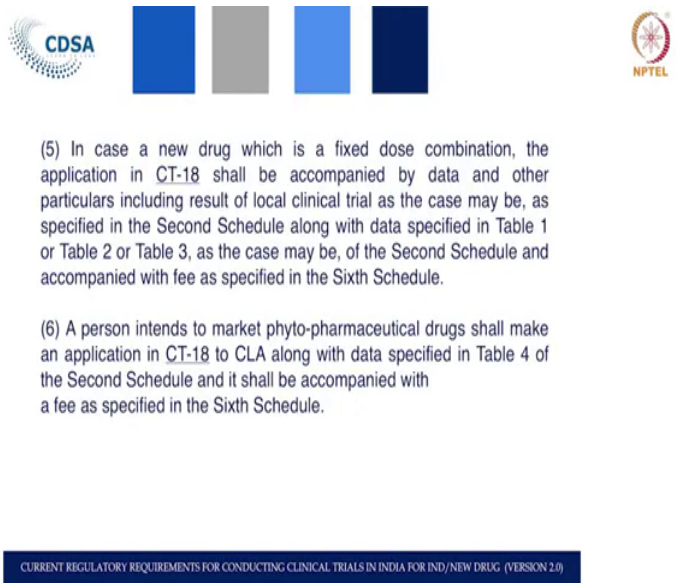

Going to the next, we have the also the drug which is called the fixed dose combinations. You by this time you know what is it through the other lectures, but is fixed dose combinations. Now, when you are combining two drugs and when you are combining for the first time it is also a new drug and then also your data requirement will be same, the application form is always the same and your data will be either table 1 or table 2 or table 3 as per it at (Refer Time: 11:25) source definition.

So, if a fixed dose combination with a new claim. So, it is a table 3, if it is not if it is a like its already being done and it is a subsequent it is table 2, but if one of the fixed dose or if both of them are a new chemical and a new unapproved drug and been combined together either one

of them or both of them then it would be all the data requirements as per table 1. No,w for the phytopharmaceutical drug; it is the same form, but the table becomes table 4 and the fees are all specified in the sixth schedule.

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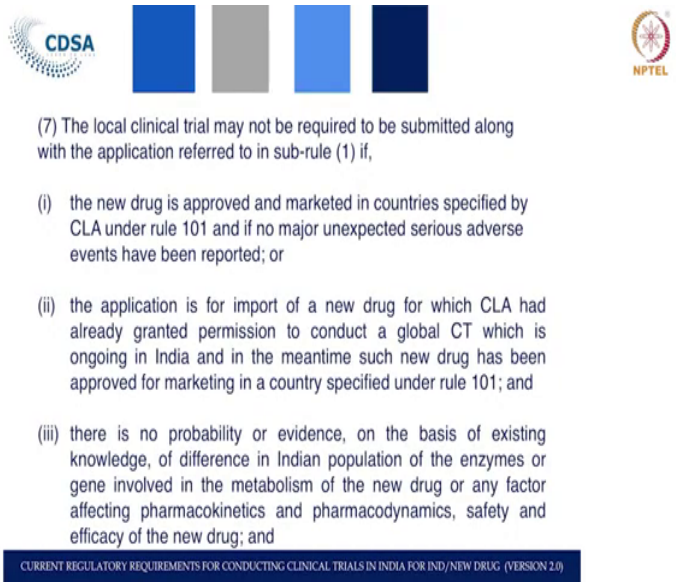

When we say that all this will be accompanied by the local clinical trial data also the new drug and the clinical trial rules keeps up provisions that the local clinical data trial data may not be required. What are the cases? Where the drug has been already approved and marketed in countries which are already specified by CLA. There is a rule under 101, in which there is a CLA specifying that what are the countries where such trials if it has been the local trials have been the trials for that particular drugs have been conducted in such countries. In that case, the requirements of local clinical trials may be waived up subject to various other conditions.

And also that in such cases there should not be any major unexpected serious adverse events being reported for such drug also if such drug is under global clinical trial. So, we the global clinical trial means that the drug is being under clinical trial in different countries of which India is also a part of that trial. In that case also the new drug and also that in the meantime the drug now has been got approved in the countries which is up specified in rule 101.

So, such drug also the locals clinical trials can be kept up. Also that when we find that there is no significant difference in the metabolism of such drug in the Indian population considering the enzymes of the genes involved or any other factors which are affecting the pharmacokinetics or the pharmacodynamic dynamics and the safety efficacy. So, these are some of the conditions as well as, now we go to the next one.

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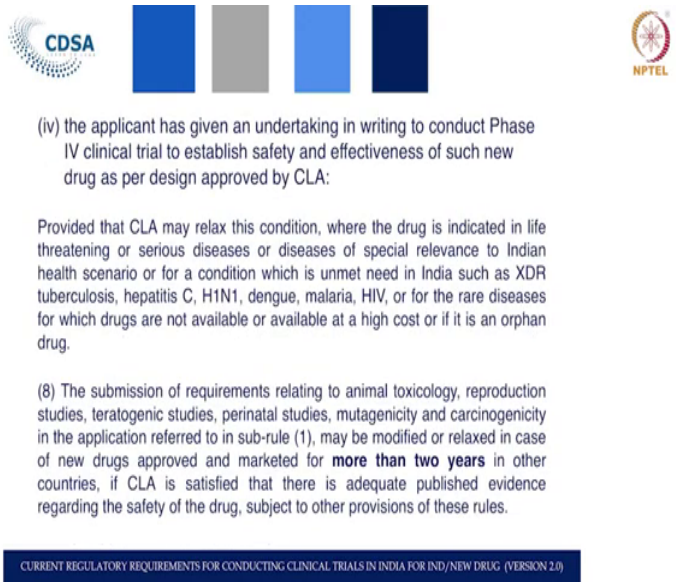

The applicant has given an undertaking to conduct the phase for clinical trial to establish the safety and effectiveness of such drug in as for the clinical trial protocol. So, that means; you have to conduct a phase four clinical trial in the country when there is a local clinical trial waived. Now, such conditions also can be relaxed in case the drug is injected for a very serious disease indicated in a life threatening or serious diseases or diseases of special relevance to the or health it for the Indian population or it is an unmet medical need; that means, this is not such drugs are not available for the treatment of such disease.

For example, the XDR tuberculosis hepatitis C, H1N1, dengue, malaria, HIV or for very rare diseases for which drugs are not available or may be available at a very high cost or it is an orphan drug; that means, it is being used for treatment of patients which are less than 5 lakh in this country. We have also defined the drug, New Drug And The Clinical Trial Rules has also defined this orphan drug. Please verify and refer the New Drug Clinical Trial Rules for this orphan drug.

Now, coming to this submission requirements also the various submission requirements as there is seeing the toxicology data which is the most important animal toxicology data the preclinical, the reproduction studies, teratogenic studies, the various perinatal studies, mutagenicity, carcinogen, carcinogenicity study. Also such study data requirements which is under the second schedule under the various tables also can be modified if the drug is, it can be relaxed modified abbreviated if the drugs is marketed for more than 2 years in other countries. And also that it is being satisfied that there is no such adverse reaction reported or there is no specific safety issues for such kind of drug.

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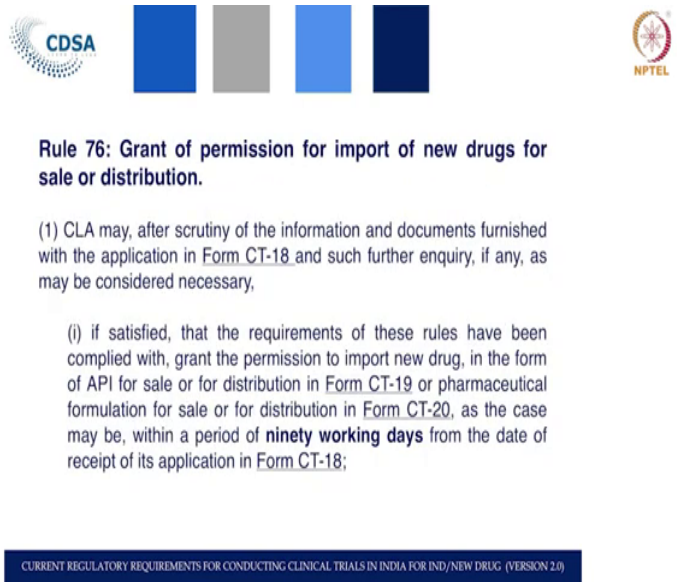

So, the permissions which are being granted under this rule 76 is the grant of permission for import of the new drugs for sale or for distribution. So, when you grant a permission for an import of an active pharmaceutical ingredient; that means, the drug substance the grant is in form CT-19 and for the formulation it is in CT-20. In all cases, there is a time line which is always ninety working days. So, the applications with the conditions of all the rules and all the conditions are full file fulfilled by the applicants, in that case the permission is granted within ninety working days.

And when there are deficiencies, similarly in case of either the if there are deficiencies and the it is during the review it is felt that the deficiencies can be rectified, then the such deficiencies can be issued to the applicant for rectification and in case it is not satisfactory, then the applications can be rejected. Also the applicants can rectify the deficiencies and come back to the CDA CLA within the specified time line and to get a permission for the apply for the new

drug, for the import of the new drug under CT-19 and CT-20 for the formulation or there may be a rejection of the application. So, all this time line for the doing all such activities are ninety days.

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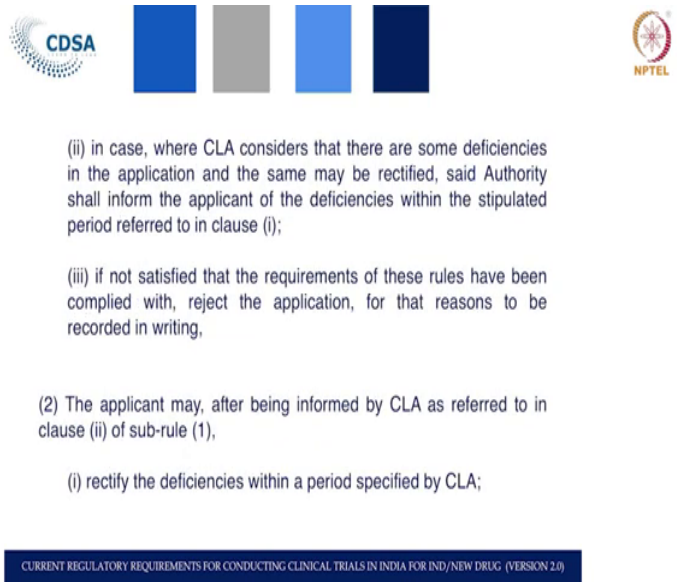

However, in case there is a rejection; as the conditions of the applications are not fulfilled and that there is a rejection. For the rejection always CLA has to write the reasons for the rejection and then only (Refer Time: 17:32) rejection can happen in that case also a reconsideration appeal can be made to CLA for within a period of sixty days.

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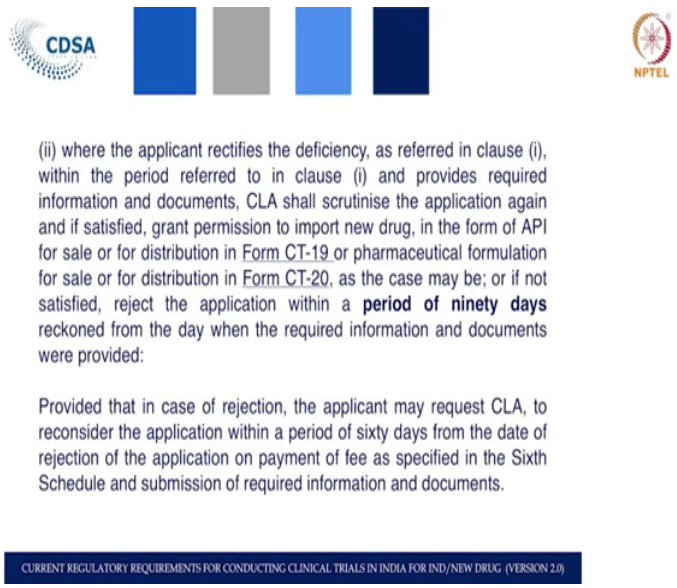

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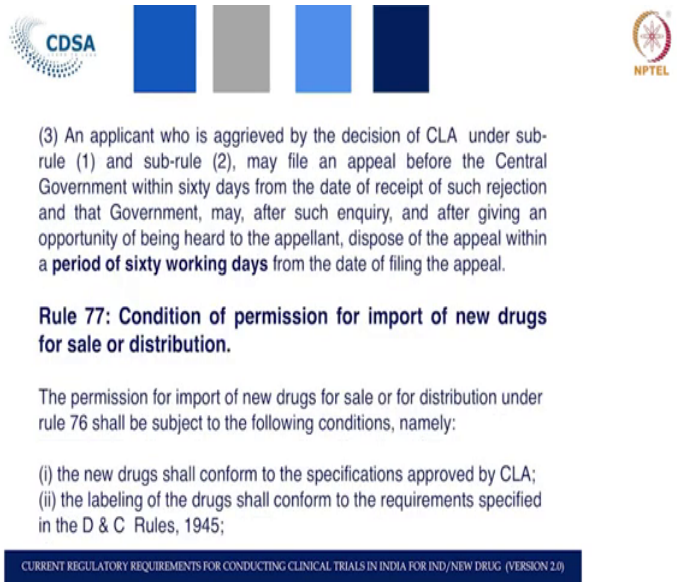

And when they are agreed with the CLAs judgment or with the CLAs decision, then always there is a scope for appeal to the government of India Central Government within sixty days from the date of receipt of such rejection, where the government can take further decision after consideration also within a timeline of sixty working days. Now, what are the conditions for permission for import of the new drugs? This is given under rule 77 that you have to have the drug always confirm to the specifications approved by CLA.

What is the, what is what we mean by the specifications? The specifications of the drug; you know, if you refer to some pharmacopoeia or there can be some drugs which are not in the pharmacopoeia you understand pharmacopoeia the monograph, fare bear our drug standards are written. What are the standards of the drugs? The various parameters the testing parameters, how it looked like, what are the testing which will say that yes it is a drug of good quality.

We can say the potency test, the acid test, the identification taste, the test for loss of water whatever. There are different type of parameters which are given in this monograph and sometimes when there is no monograph then definitely it is the drugs, because normally for a new drug it will not be available in the monograph. You will always find the specifications or the standards which are set by the manufacturer for testing such drug that the for which the drug has to comply with.

So, when they make the chemistry manufacturing control data, they have to fix the specifications of the drug. And that specifications which is tested by CLA before approval of the drug in their own laboratory, the laboratory is specified by CLA. And then it is set that yes the specifications set by the manufacturer and that which has been tested by your laboratory as per the specifications set by the manufacturer are comparable and at same then only such permission is granted. So, they have to always the new drugs once it is given permission has to confirm to the specifications approved by CLA.

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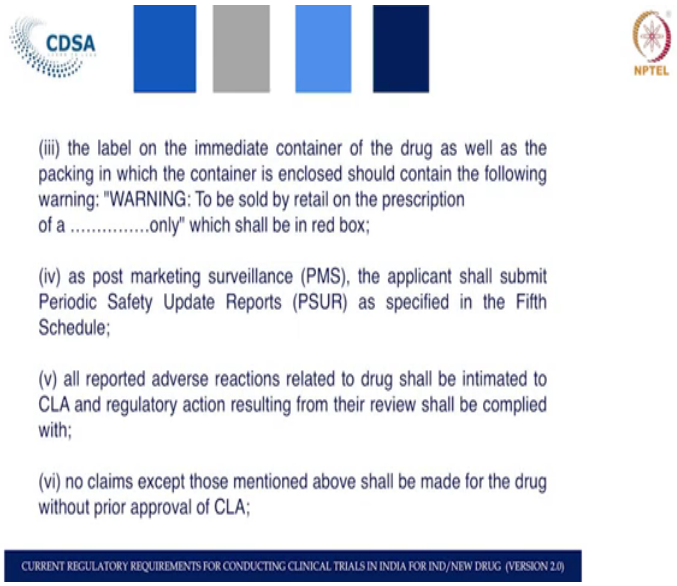

And also they are at the labeling requirements which is in the drugs and cosmetics rules, it is the rule 96 you have to refer to and there are also subsequent rules. And always there has to be a specific warning to be sold by prescription by religious price. So, you have to see the labeling rule which is in the red box.

Now, also there are requirements that as per the post marketing surveillance for all such new drugs there has to be submission of the periodic safety update reports. And this periodic safety update reports what are the content of this periodic safety update reports are specified in the fifth schedule.

Also in case wherever there is an adverse drug reactions reported, it shall be immediately intimated to CLA and regulatory action. What action you have taken when adverse of reaction? It has to be immediately reported and there cannot be any claims made by the

applicant for such drug without the approval of the center. So, whatever claim it has been applied which has been approved by CDSCO, so it can be sold for only that special specific claim.

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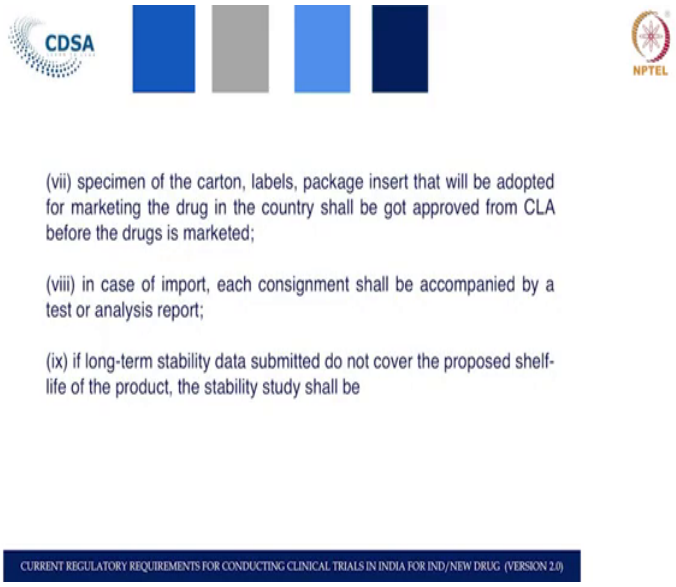

Now, the specimens of the carton labels package inserts all that shall be adopted for marketing shall all be approved by. So, they have to submit the all the specimens, whatever at the packaging way manner packaging container the package inserts the everything has to be submitted to CDSCO, CLA and get approved before they are marketing.

So, we should know that what drug is getting marketed, what is its package. In case of import all consignment shall be accompanied by the test or analysis report. Suppose, the long term stability data you know that stability when, so they have to submit accelerated stability study data as well as a long term stability data. When the accelerated stability study data remain it is

a 6 month study in a accelerator conditions like 40 degree temperature or 75 percent relative humidity as well as there is a long term storage conditions or there can be it depends on what is the storage conditions.

It can be when you say and accelerated conditions of 40 degree and 75 percent, then normally the normal storage conditions the drug the long term storage condition for such drugs could be 30 degree and 75 percent. So, such storage conditions have to be fulfilled, they have to complete that 30 degree 75 percent relative 30degree centigrade temperature and 75 percent relative humidity study for the particular drug for the inter shelf life. And if it is not completed suppose they claim a shelf life; that means expiry of the drug up to 3 years, then they should have the data up to 3 years.

And if it is not in that case, the stability study data will be submitted in the later stage or it can be submitted in a continuous manner once it is completed to the licensing authority, but there has to be a commitment for that and that has to be submitted.

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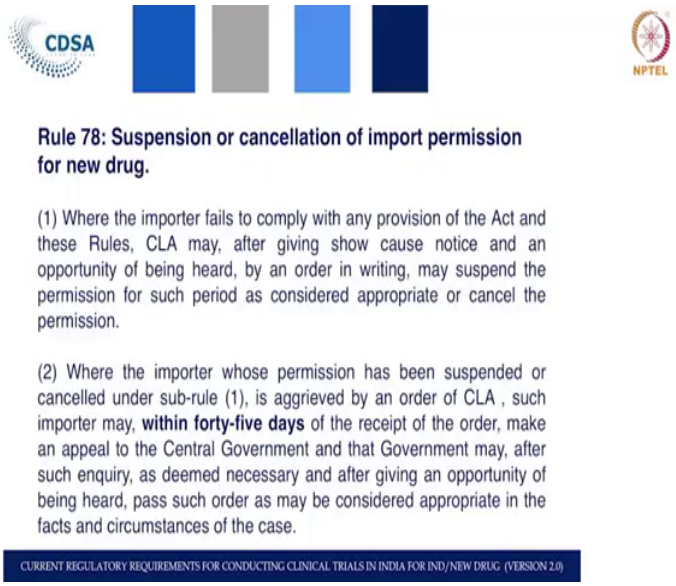

So, there is also the rule that you suspend or cancel the import permission when they do not comply with the conditions which have being mention the lovely condition, the various other conditions. And in such case before a suspension or a cancellation is done by the licensing authority, it is always a show cause notices issued to the applicant and opportunity is given for in writing for giving their justification.

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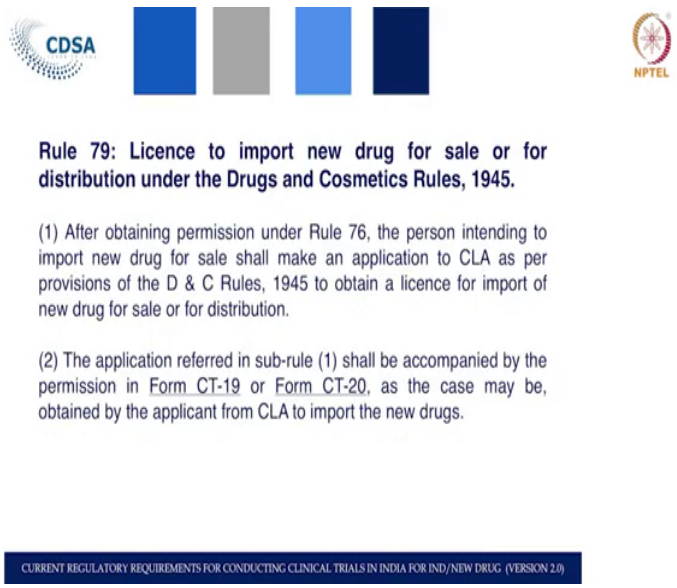

And then in case they are agreed they can go back to the, they can always appeal to the Central Government within 45 days for reconsideration and that can be reconsidered or it may not be reconsidered. In the rule 79, we have the license after the import of the drug. Once you get the import permission of a new drug which is under rule under the CT form 19 and CT form 20, then you have to apply as per the rule under drugs and cosmetics act for the import of such drugs.

So, there are different rules which is in for the import of any drug in the country and which is like the that is the different forms form 40 and form 41 application in form 40 and in license in form 41 and a license to import the various drugs in form 10. So, these are the different licenses which are to be obtained for import of the drugs after you get the permission to import our new drug.

And all cases such applications for a new drug, applications will be always accompanied with the permission in form CT-19 for active pharmaceutical ingredient and for pharmaceutical formation formulation it is form CT-20. In all cases, there is one more in information's; one more thing which is to be noted which is will come in the later stage that an application for import of an active pharmaceutical ingredient will always be accompanied by an application for manufacturing of the pharmaceutical formulation. There cannot be any application of an unapproved drug in the country for import or for manufacture without an application for a pharmaceutical formulation.

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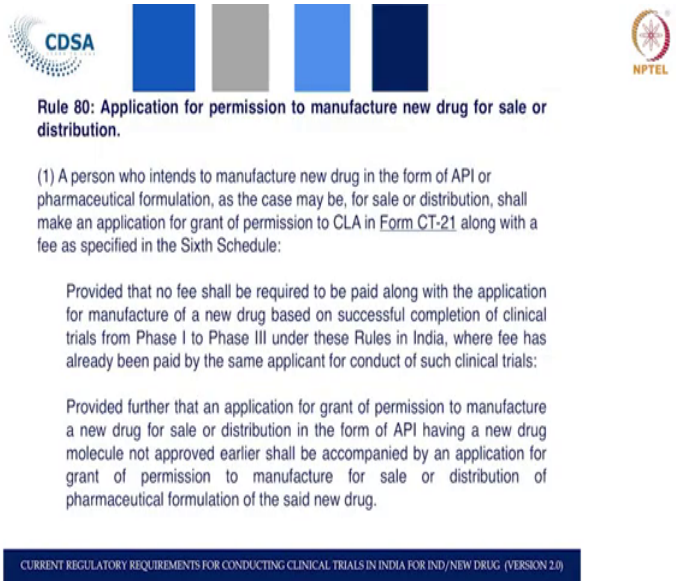

So, no unapproved API is permitted to manufacture or imported in the country without and applications for the manufacture of the formulation. Coming to rule 80 which is the application for permission to manufacture new drug for sale or distribution.

So, in this, once that the application form is CT-21, the fee shall not be required if the in case of manufacture definitely normally a clinical trial local clinical trial has been conducted and fee will be no fee shall be required to be paid in case, there has been successful completion of clinical trial in the country from phase 1 to phase 3 and where the fee has been already made.

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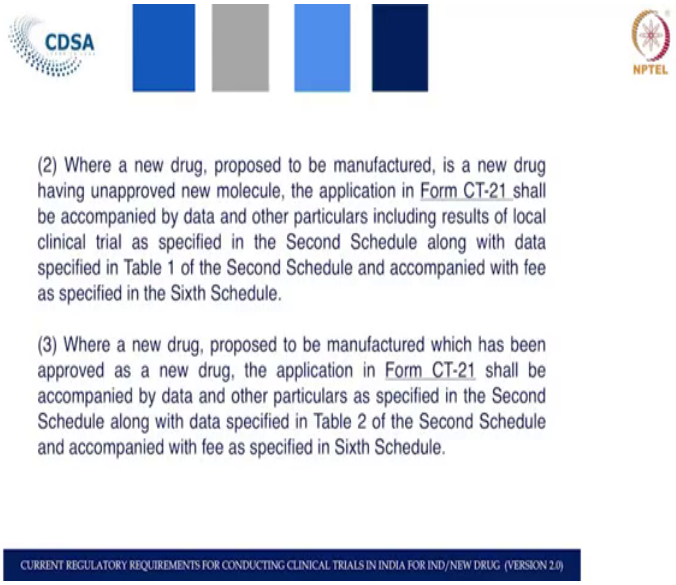

And as I have mentioned that always such application in the form for an application to manufacture a new drug for sale or distribution in form of API, having a new drug molecule which is not approved earlier shall be always accompanied by application for a formulation. And the data requirements are very similar to the import cases, for all cases as per the different type of drugs the that the various tables that is the table 1, table 2, table 3 and the table 4 are to be fulfilled and this after this the also for this the local clinical trial data also.

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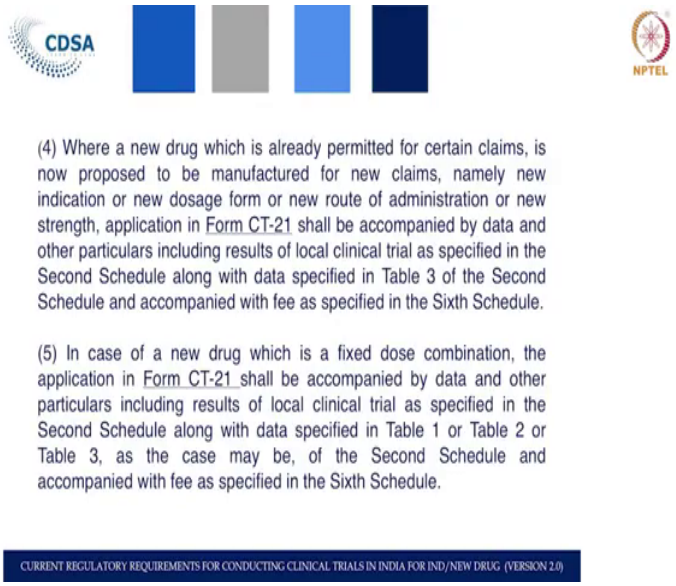

In the same manner may not be required, when there is no report of serious adverse reactions whether it be the drug has been already approved in some other countries, where it has been as specified by central licensing authority under rule 101. And also that there is no specific difference in the Indian population with the population in which the clinical trial has been has taken place.

So, we say that there is no specific differences with respect to the metabolism of the drug with respect to the pharmacokinetics pharmacodynamics parameter with the enzymes or the genes which improve which influence the metabolism of the drug or where it has been there is no such issue of safety and efficacy.

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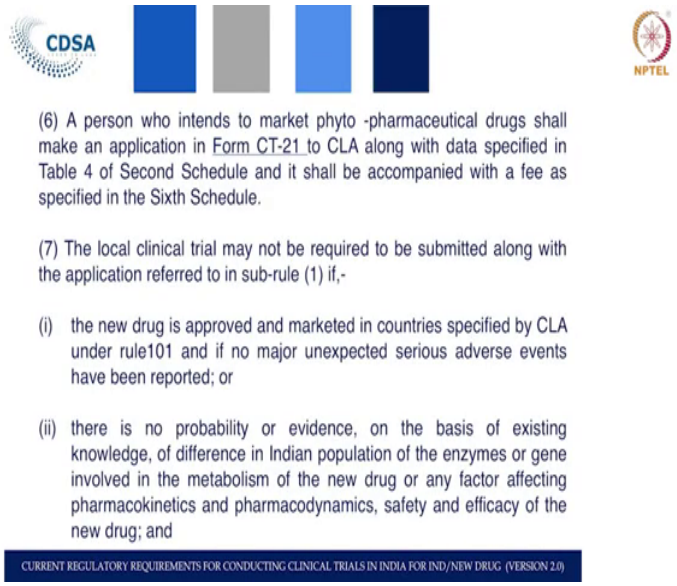

Also in all such cases there has to be an undertaking to conduct a phase for trial. And if such cases such conditions can also be waived up where the drug is indicated for the life threatening disease.

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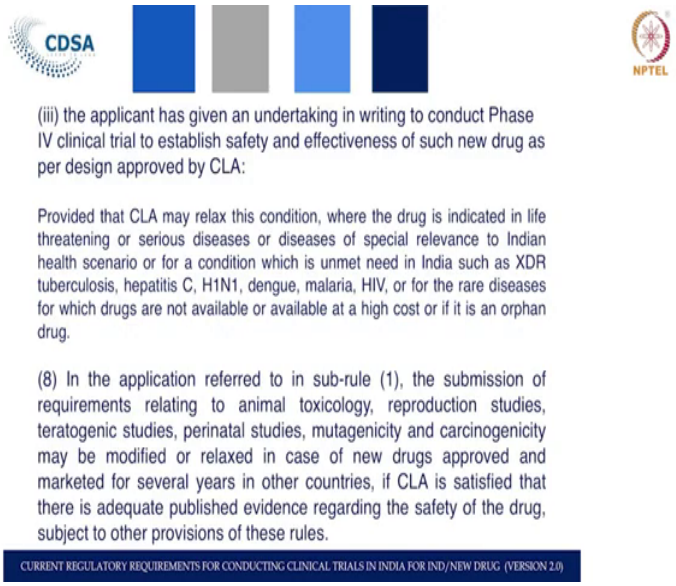

The conditions are same for import and for manufacture, the forms are different for application. Also similar manner the animal toxicological data can be deferred abbreviated or it can be submitted in a abbreviated manner.

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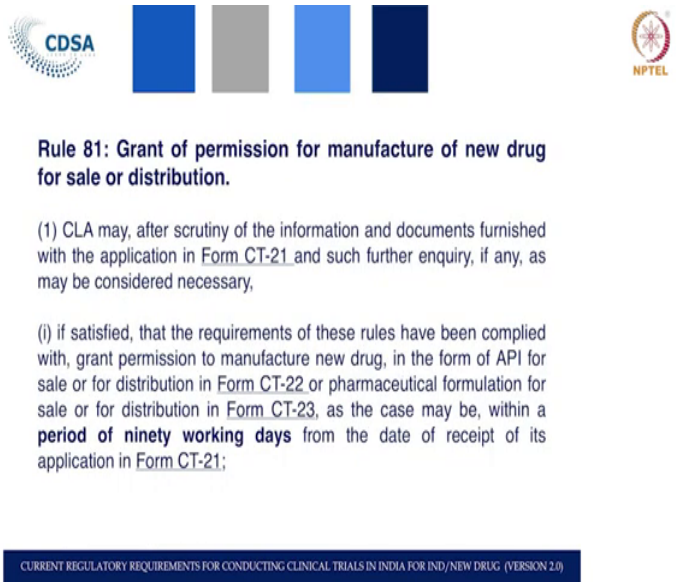

Coming to the grant of permission under rule 81. It said, but once that application is scrutinized the permission is granted. After scrutinization if it is fulfilling, then it is the permission is granted, if there is a query then if there are deficiencies and CLA fills that the deficiencies can be rectified is the same that the deficiencies will be communicated within the specific time line and it has to be responded back within the specific time line and if it is satisfactory license will be granted. So, it is the form CT-22 for API and the form CT-23 for the finish formulation and all the timelines are ninety working days.

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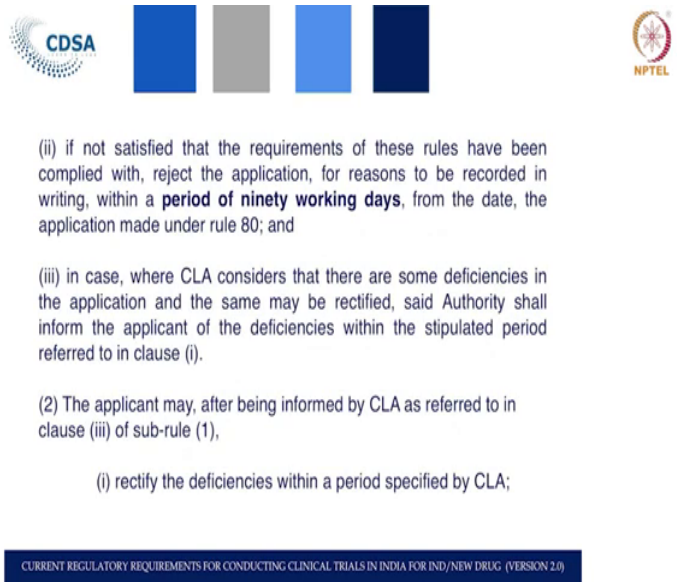

In case where there are deficiencies and this responded permission can be granted or it can be rejected. In case there is a rejection in such cases the same it has to be like there is a; permission with the permission when it is granted is within the ninety working days and in case of rejection if they can the applicant can always appeal to CLA.

So, there is an ample mechanism within sixty working days to reconsider the application and whenever there is an appeal, there is a fee specified for reconsideration and it is a fee of 50000 in all cases.

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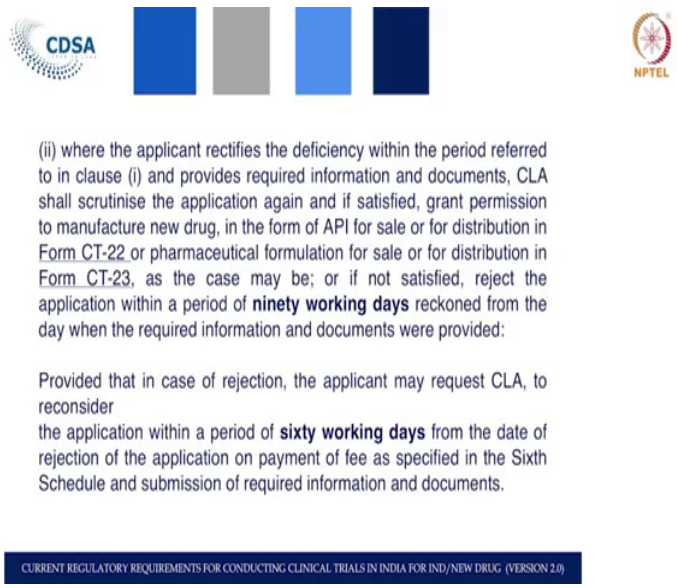

And applicant who is not satisfied with the decision of CLA can go to the Central Government within the period of sixty days and their applications will be reexamined by Central Government for an for either reconsideration or for a final rejection.

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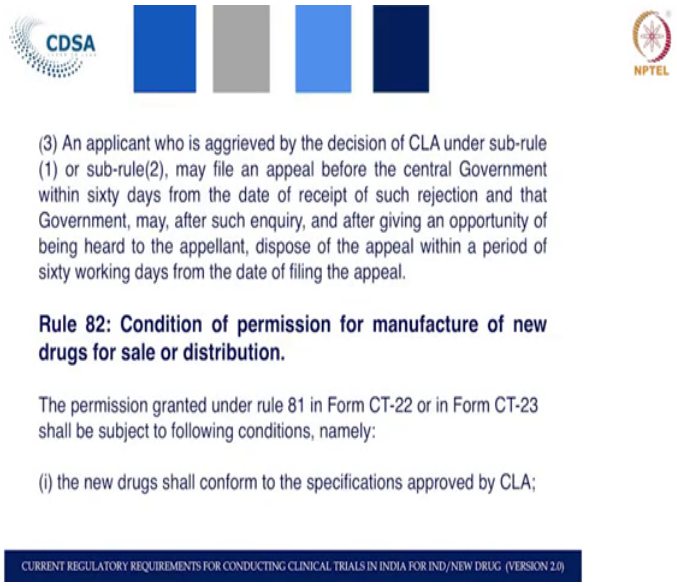

The rule 82, which specifies the conditions is the same that it should conform to the specifications approved by CLA. It should mention that specific warning in the labeling conditions and also post marketing surveillance the PSO and data to be submitted as a post marketing surveillance adverse reaction to be reported no other claims can be claimed except that one which has been approved by the central licensing authority.

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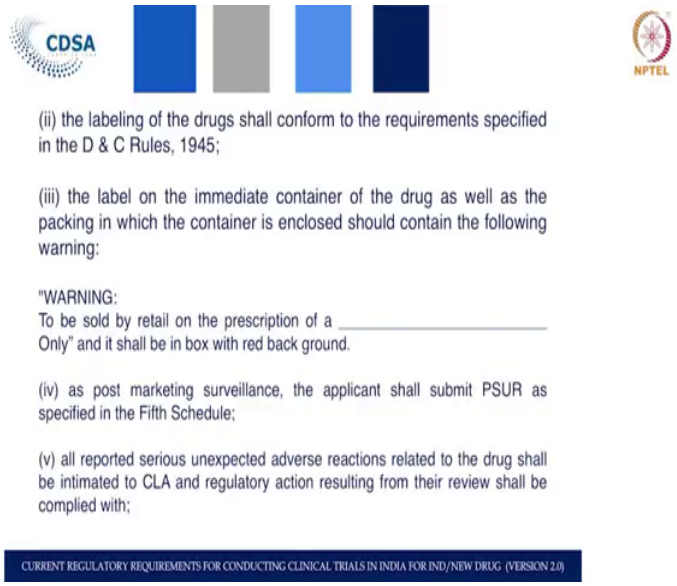

All the specimens of the packagings should be approved by the CLA and long term stability data, if it has not covered the proposed shelf life then that stability data to be continued to be submitted.

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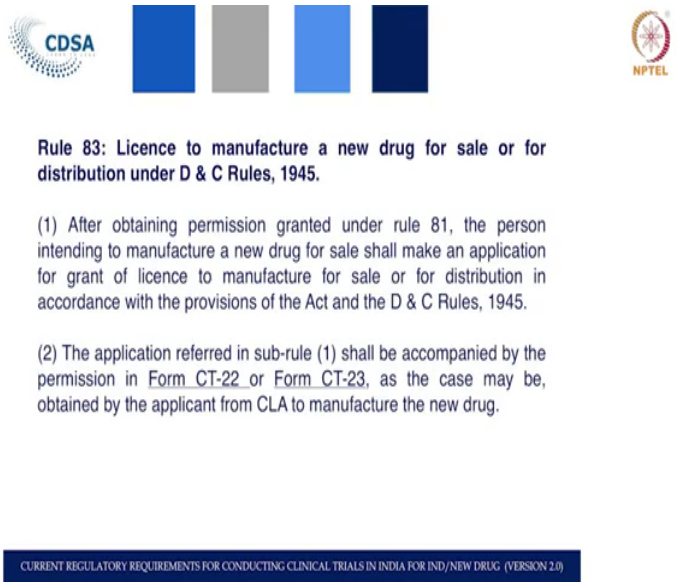

After the permission is obtained in CT-22 and CT-23 the license to manufacture the drug has to be taken under the drugs and cosmetics act. So, there are various licensing forms say 25, 28, 28d. So, they have to go to the respective states licensing authority where the drug is proposed to be manufactured to indicate the permission for manufacturing and in case of the drugs which are biological. So, some of the drugs which are jointly approved which is approved by also a CLA they have to come to both SLA and CLA.

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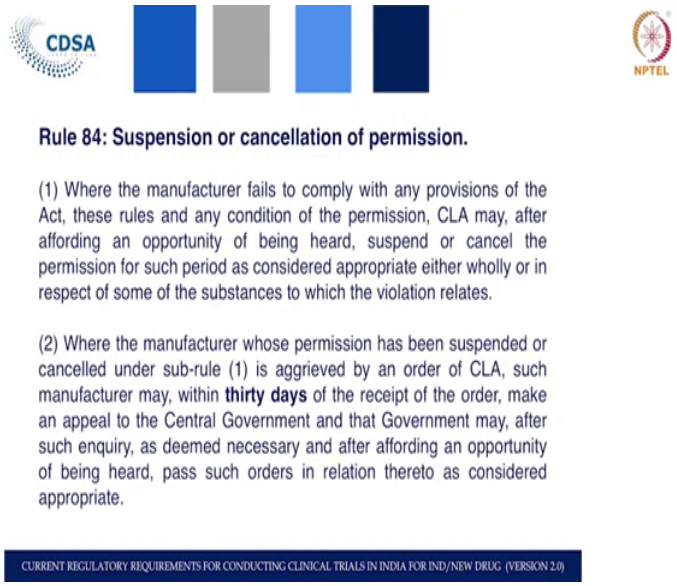

There is also there can be suspension or cancellation of permission, if the conditions of the license are not complied with, but always there is a opportunity for show cause and then giving a after getting the heard and then only such cancellation or suspension happens and where they are aggrieved with the decision, they can always go back to the appeal to the central government. But here the time is less than 30 days they should come back to the Central Government with an appeal within 30 days.

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The rule 85, which says the general responsibility of the importers are the manufacturers in marketing of the new drugs. You cannot approved, you cannot market a new drug and other than the approved indications. The indications in which it has been a approved you can only be manufactured it can be marketed only in that particular dosage form and the indicateon.

The manufacturer or importer of the new drugs were responsible for marketing the new drug there own they can only do the marketing of the new drug in the approved indications that is approved claim in the disease, in which they have claimed to treat and also in the approved dosage form.

And, however; if somebody utilize this drug for some other purposes for other indications and the manufacturer or the importer shall not be punished for the consequences resulting from the

use of the drug for an indication other than for which the drug has been approved, but the manufacture can prove that he has not been involved in doing this.

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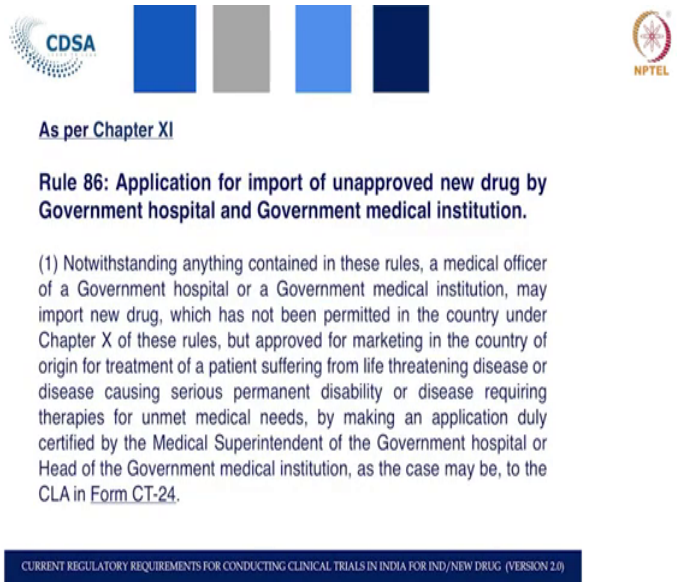

We go to chapter 11 next which is the import or manufacture of unapproved new drug for treatment of patients in government hospitals and government medical institutions which is a very new rule in this new drug and clinical trial rules giving a huge scope and opportunity for the reasons of the patient. It is the it is a very patient centric regulation no.

So, in this what is there? Is that whenever there is an unapproved drug which is not marketed in India and all, but in such cases where the drug has not been approved for marketing in India, but it is already marketed in some other country and it can be imported such drug can be imported. If the drug is not permitted in the country, but approved for marketing in the country of origin for the treatment of the patient suffering from the life threatening diseases or disease causing serious permanent disability or disease requiring therapies for unmet medical needs.

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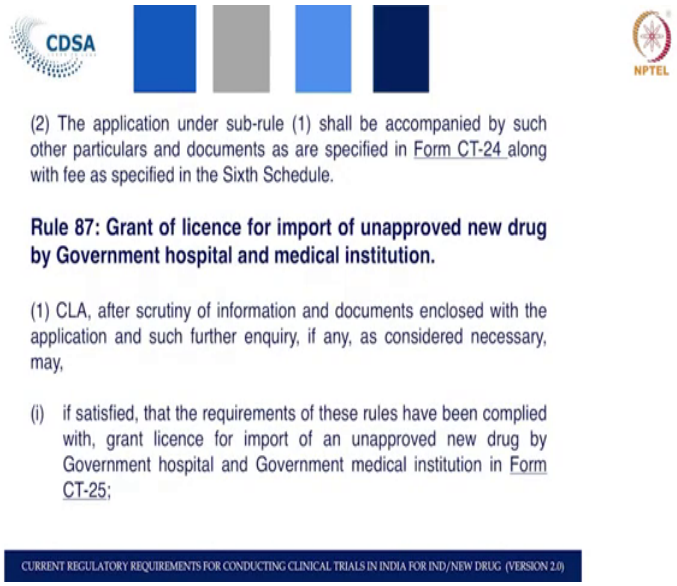

In such case the applications has to be made by the government hospital which is newly certified by the medical superintendent or head of the government medical institution in a particular form which is called CT 24. The applications shall become accompanied by all particulars and documents which is given in the CT 24.

So, when you go through into the CT 24 of all the requirements are specified the name even if such forms will could not only contain the about the drug, but it will also have the content about the patient for whom the permission is given. The details of the patients will be covered in such form. So, the license will be granted in such case in CT 25 after it is satisfied that the documents are all satisfactory documents have been submitted.

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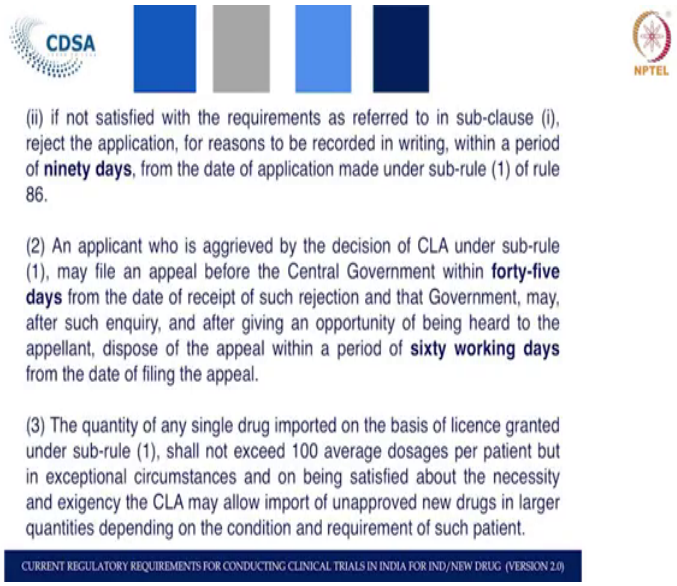

And in case, the there is a rejection in that case there is an appeal to the central government. So, all permissions within ninety days if not, if there is a rejection there is a scope of appeal again to CLA within forty five days and the appeal has to be disposed of and in within a sixty working days.

So, there is a; there is a scope of appeal to the Central Government within forty five days from the, if there is a rejection and the Central Government has to dispose of the appeal within sixty working days. The quantity of the single drug to be imported cannot be more than 100 average doses per patient, but in exceptional circumstances and when it is satisfied that there is a necessity to have more doses such permission of more than 100 doses can be also given for the improve for the import of the unapproved new drugs.

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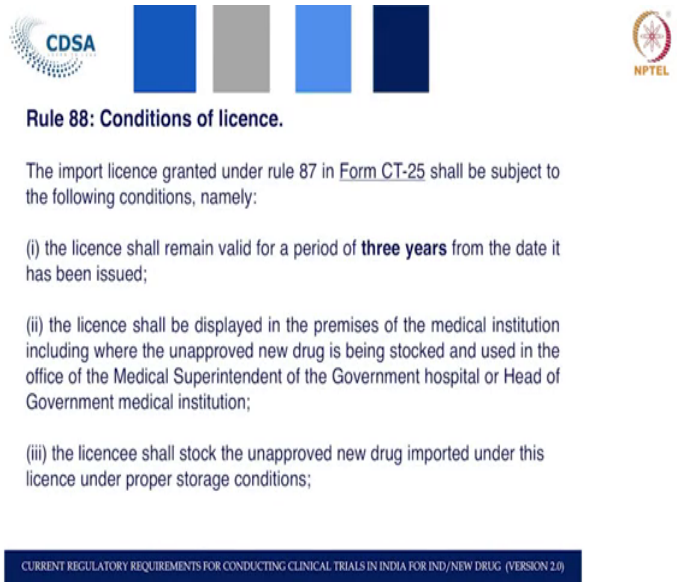

In case of conditions the license are always valid for three years and it has to be displayed. The license shall be displayed these are all conditions of license the stock of such unapproved drug shall be kept and the drug shall be stored in proper storage conditions. And it shall be only used for the treatment of the patients for whom the permission has been taken and it cannot be given to any other persons or any other institution. And the pharmacist of the institution has to maintain the record and all also the these are all to be signed and countersigned by the medical superintendent.

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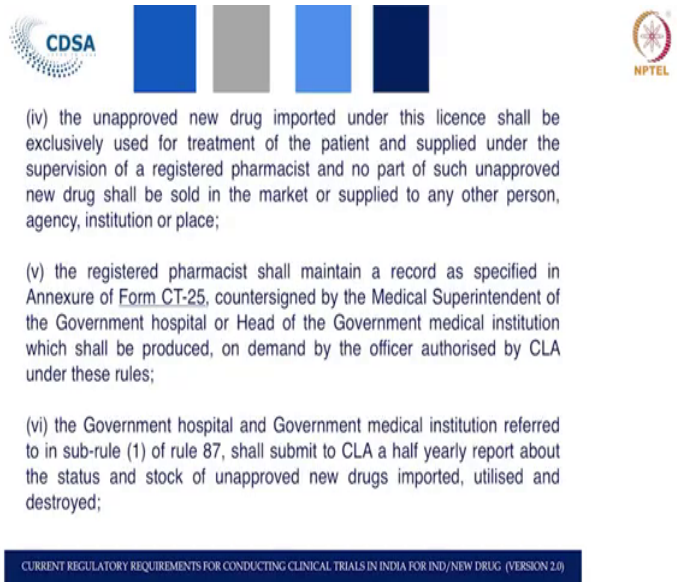

And there has to be a half yearly report to be submitted to the central licensing authority. But the unapproved new drugs there has left over and remain unused then that case also it mean if it is it has expired or it has found to be substandard quality, once it is destroyed the action taken how also has to be recorded. In case there is a rule also there is a rule 89 for the suspension and cancellation of such import license when the conditions are not complied with; when the up when the importer phase to comply with the conditions.

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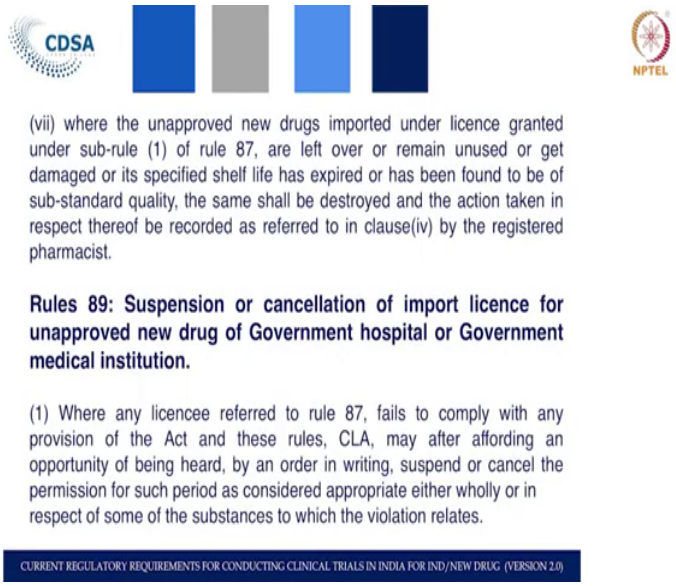

And when such cases of cancellation also there is an appeal mechanism where always they can go to the Central Government within forty five days and for reconsideration. There is rule ninety where there is an inspection provision for all this unapproved new drug which is approved in the which is approved for use by the government hospital or government medical institution and this is also the same manner that is without prior notice such as such as can happen. And then based on the inspection actions are also taken.

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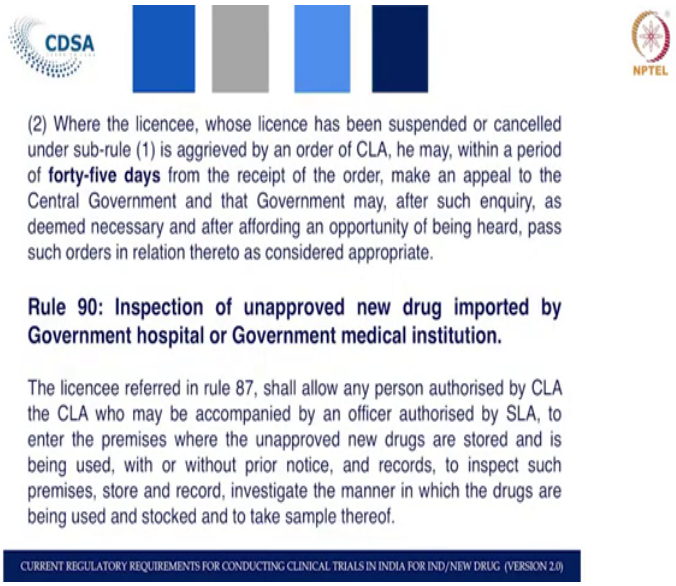

There is also in case of provision for permission to manufacture unapproved new drug in which case it is only when the new drug is under clinical trial. If the new drug is under clinical trial in the country in such case such new drug can be permitted to manufacture for the treatment of the patient of life threatening disease that is that is rule 91.

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But this is a very special rule, but where there are lot of conditions which are to be there are subject to certain conditions. One is that the patient there has to be informed consent from the patient consent of the patient or his legal heirs and also that the government hospital, the person the prescriber is agreeing to treat the patient as well as the ethics committee of the government institution agrees to this.

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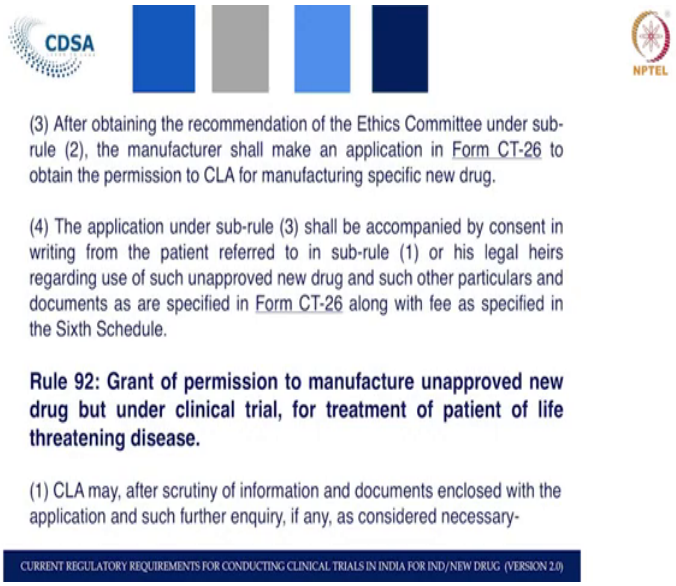

So, when in such cases where the manufacturer they intends to manufacture this drug, they have to come to the she has to take and obtain a writing form from the patient to whom the unapproved new drug has been prescribed. And also has to make an application to the ethics committee of the hospital. So, it all depends on subject to these three permissions.

After obtaining the recommendation of the ethics committee, the consent of the patient or his legal heirs then the application manufacturer can make an application in form CT-26 to obtain the permission for the specific drug, it is which is also quantity specific. The application shall be accompanied by this written consent and also from the patient or from his legal heirs and also the necessary recommendation of the ethics committee and the fees as prescribed in the sixth schedule.

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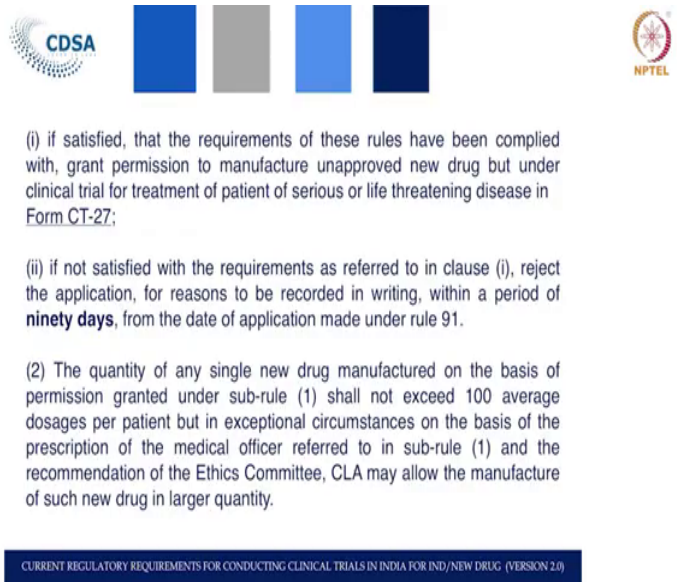

Once the graph transition is granted, it is the permission which is granted in the CT-27, under rule 92. So, if it is satisfied, the same the permission can be granted, if not satisfied; the requirements are not full fulfilled within ninety days, the projection of such application is done and all cases there is scope to go to the Central Government for reconsideration.

Always, the quantity is specified it shall not exceed hundred average doses for patients, but in exceptional circumstances on the basis of the prescription of the medical officer, the and also on the basis of the recommendation of the ethics committee larger quantity can be allowed to manufacture. But if you see the permission under CT-27, the form the CT-27 it specifies the quantity it specifies the patient.

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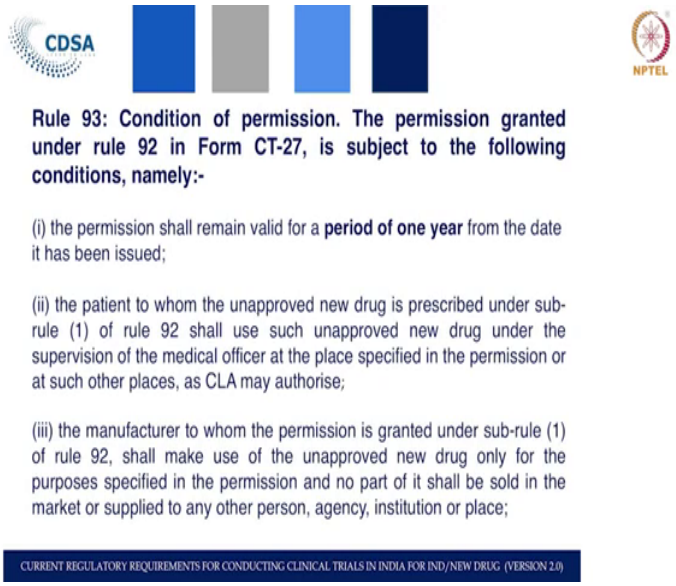

And the permission of such new drug of manufacture shall be which is under clinical trial shall be valid only up to 1 year from the date of the date it has been issued.

And always such new drug shall be used by the patient under the supervision of the medical officer. And always it has to be ensured that such drug cannot be sold in the market or supplied to any other person other than the person for whom it has been prescribed and it is mentioned in this clinical trial permission.

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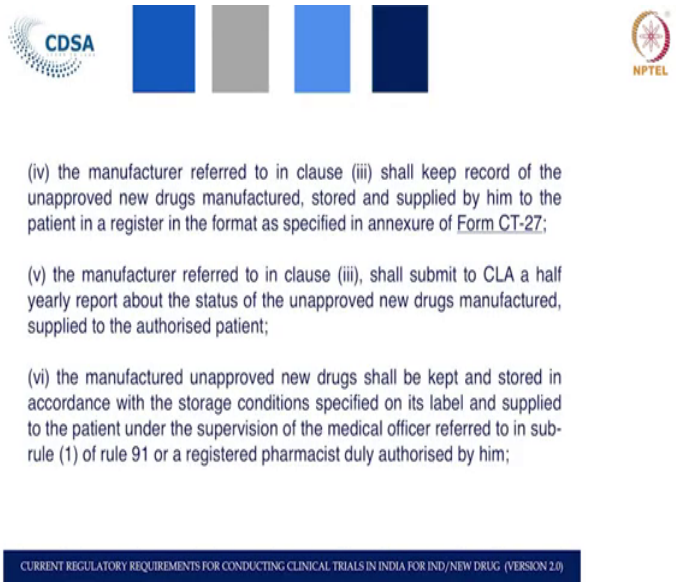

The records to be kept completely by the manufacturer as well as by the pharmacist, the of the government institution and there has to be a half yearly report sent to the CLA who after the of about the status of this unapproved new drugs manufactured supplied. And it has to be stored in the proper conditions as mentioned in the label and also has to be duly supervised and recorded. The registered pharmacist has various things which have to be recorded and which has to be countersigned by the medical superintendent.

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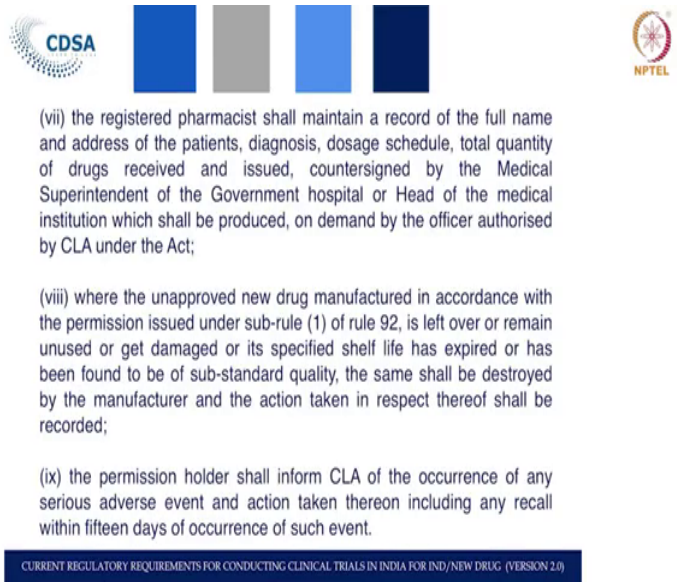

And where it is left over after the use by the patient or where there is a self life has been has expired or there is a substandard quality if and when it is destroyed the records has to be maintained. And also it is very important that in case of any serious adverse event an action taken what has been taken action by the permission holder it has to be informed to the central licensing authority. And in case you in because of the adverse event the drug has been recalled.

And within in the in case of a serious adverse events, there has to be a recall within 15 days and of occurrence ourselves which is such event. So, the it is the this is the most important part is that the permission holder should has to inform to the central licensing authority of the occurrence of any serious adverse event and action taken whenever including, if there is a recall which has been taken because of the serious adverse event within 15 days from the occurrence of such event.

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There is rule 94, which gives the inspection of the unapproved drug for the which is under clinical trial and where the CLA including the person which is authorized by SLA can check it can investigate in such premises for unapproved new drug is been structured store and supply, meet or without prior notice and they expect everything the premises records everything. And in all cases whenever such manufacturing happens it has to be as per the principles of GMP.

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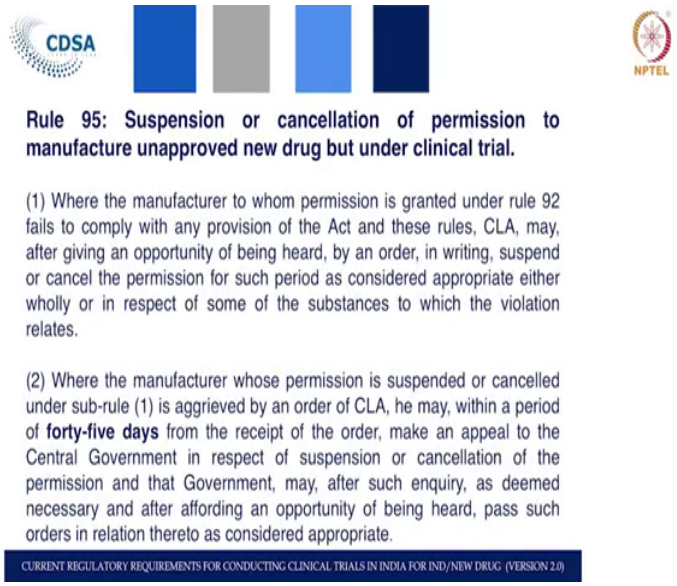

That is can be there is scope of suspension or the rule 95 says about the suspension or cancellation in case of non compliance and in case it is the manufacture it is not is agreed by the order then they can always appeal to the Central Government for reconsideration. And also that applications when it is rejected it has to be rejected within ninety days.

The rule 96, but the it says that the license which is granted under rule 96 after optimal obtaining the permission, the person who is intended to make such drug, they have to comply with the various conditions under the drugs and cosmetics act. And the grant of license they have in that case they have to appeal up now, whenever a permission is obtained for manufacturing in an approved drug the permission to manufacture the drug, the has to be done by the applicant under rule 96 where it will go to the respective state licensing authority and will applied in the specific forms because this is an up drug under clinical trial.

So, again the application has to be under the test license that is the form 30 and the permission will be granted under form 29 to manufacture this drug for.

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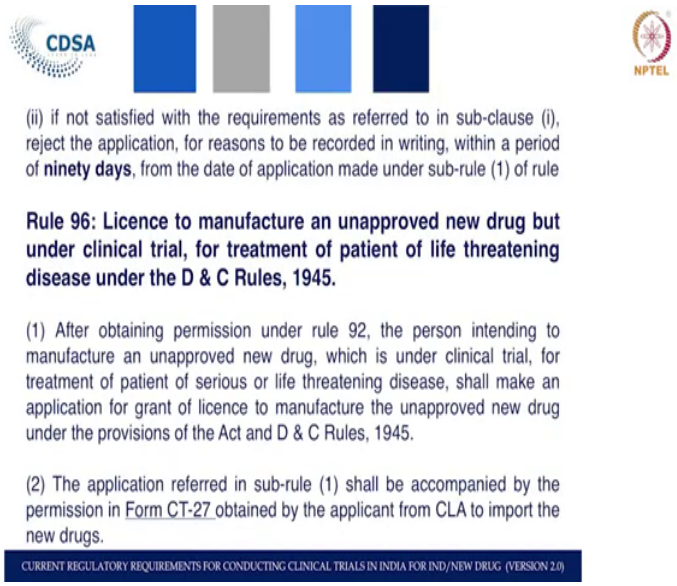

So, this is the license to manufacture after getting the license of the new drug from the CLA. The application shall be accompanied by the permission under CT 27.

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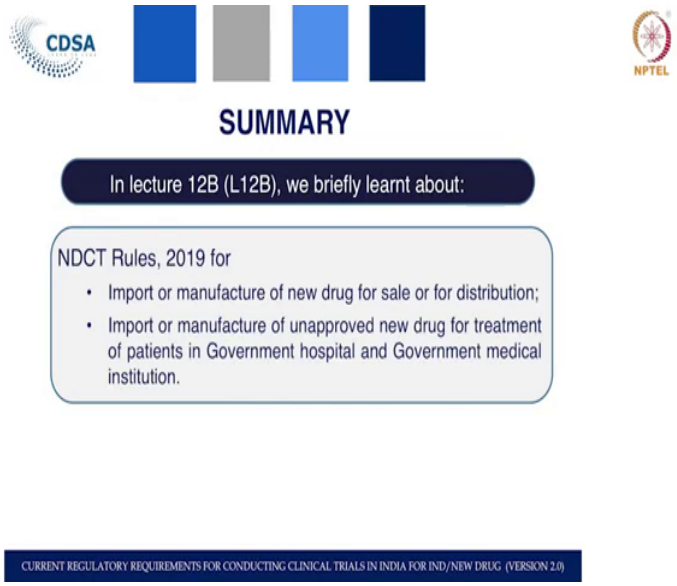

So, finally, what we learnt in this? In these sites that import or manufacture of new drugs for the purpose of sale or distribution and also the special rule, the import or manufacture or of unapproved new drug which is under clinical trial for the treatment of patients in government hospital.

One is the import of the drug of unapproved new drug for treatment of patients in government hospital and government medical institution and another is the manufacture of unapproved new drug which is under clinical trial for the treatment of the patients in the government hospital and government medical institutions provided. It is permitted and it is agreed by the prescriber the patient or his legal heirs and in written consent form and also by the ethics committee. So, let us do a recapitulation of this chapter, chapter 10 and chapter 11.

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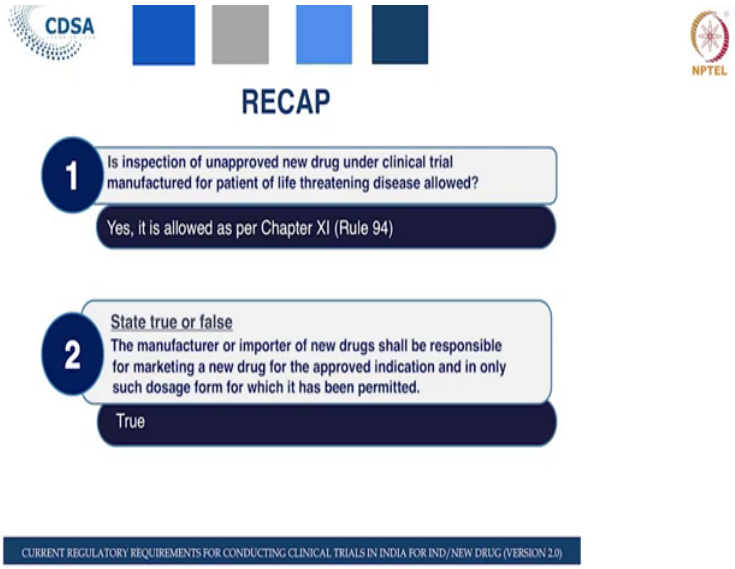

So, is inspection of unapproved new drug, but under clinical trial manufactured for patient for life-threatening disease allowed. What do you think? Yes you are correct probably, always all cases whenever new drugs are permitted for import or manufacture in the country there is inspection which is to be allowed.

And then there is hope that the rules always say what are the details procedure of inspection who are the inspecting authorities. So, it is allowed. Can you say this whether it is true or false? Yes. You can say definitely, the manufacturer or importer of new drugs shall be responsible for marketing a new drug for the approved indication and only such dosage form for which it has been permitted.

I think you know the answer. By this time, you have to know this answer this is a very important question. Yes answer is with you, but before writing the answer, I would like that

you repeat the question or second the manufacturer or importer of new drugs shall be responsible for marketing a new drug for the approved indication and only in such dosage form for which it has been permitted.

So, what is the answer? I think you are right. Yes, it is true. No other, so the other parties you have to understand this false. I hope you have enjoyed this lecture, if you have any comments feedback suggestion, we will be happy to address them.

Thank you and best wishes.