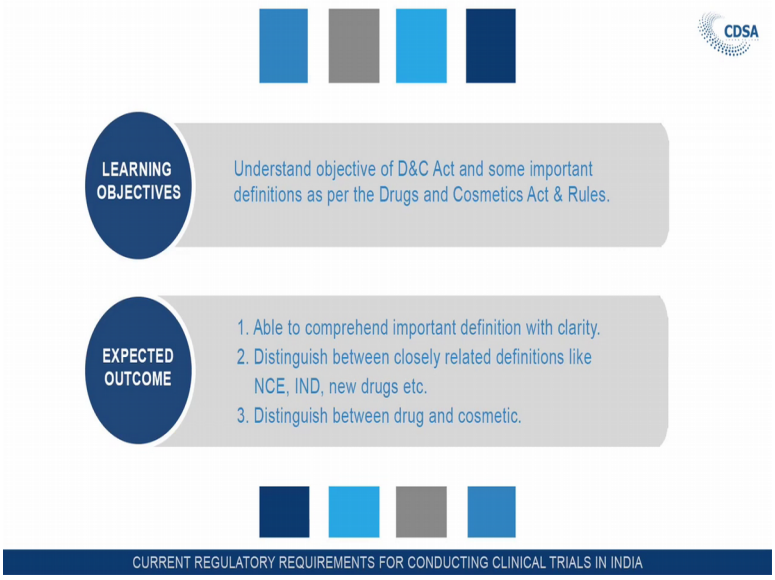
Current regulatory requirements for conducting clinical trials in India

Dr. Dhananjay K. Sable
Assistant Drugs Controller (India), CDSCO (HQ),
Ministry of Health and Family Welfare,
Government of India

Lecture – 02
Definitions

Hello friends, welcome back to lecture 2. The lecture 2 is about objective of Drug and Cosmetic Act and some of the important definitions given in this Drug and Cosmetic Act.

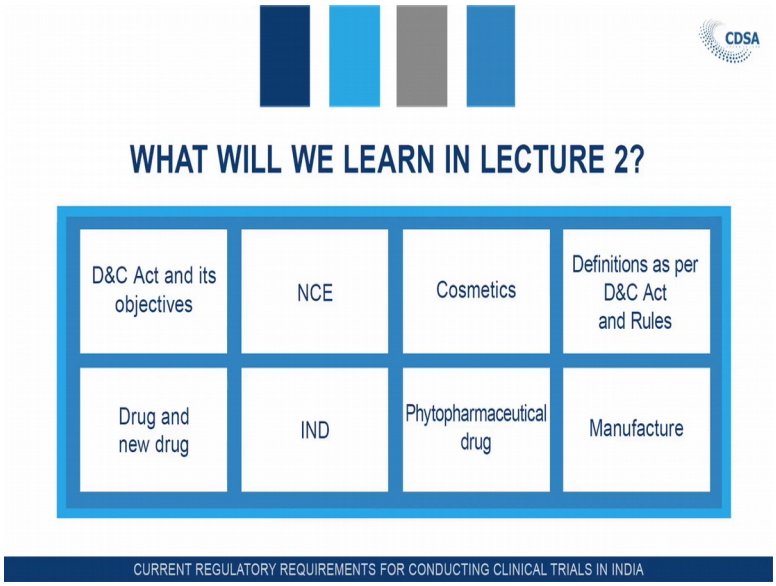
(Refer Slide Time: 00:30)



Learning objectives to understand objective of Drug and Cosmetic Act and to see some important definitions as per Drug and Cosmetic Act and rules their under. The expected outcome you would be able to comprehend important definition with clarity, you will be able to distinguish between closely related definitions like IND, NCE, new drug and other. You would be able to distinguish between drug and cosmetic.

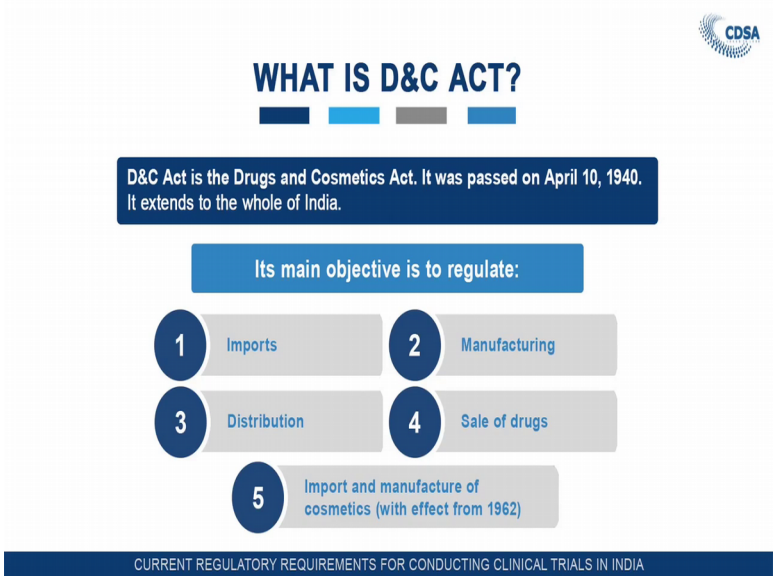
So, what we are going to see exactly in this lecture 2.

(Refer Slide Time: 01:09)



First Drug and Cosmetic Act that is D and C act and its objective, the import what is mean by drug, what is mean by new drug, what is NCE, what is IND, what is NME then what is the difference between Drug and Cosmetic Act, what are the phyto-pharmaceutical drug, what it mean by the manufacture.

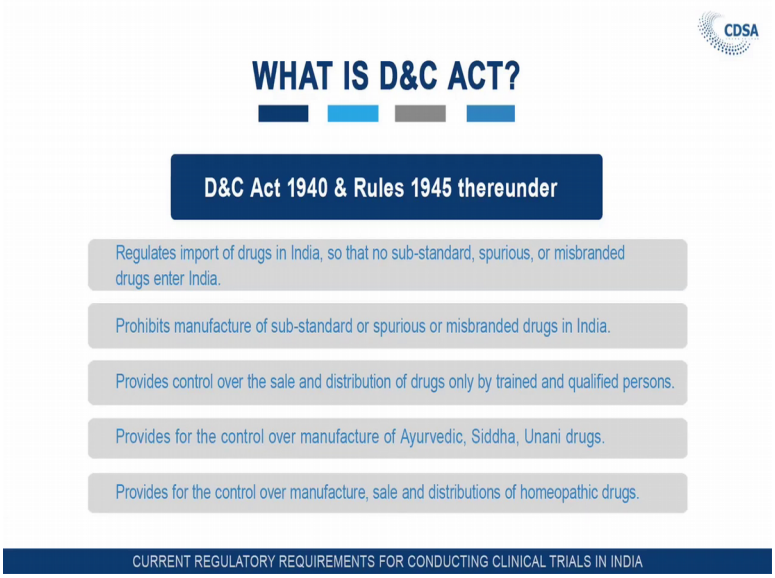
(Refer Slide Time: 01:39)



So, let us start with the Drug and Cosmetic Act. D and C Act is Drug and Cosmetic Act. It was passed by legislature on April 10 1940, with its main objective to regulate import manufacture sale and distribution of drugs and cosmetic.

The word cosmetic has been added later on in 1962 to regulate manufacture sale and distribution of cosmetics. This Act extend to the whole of India including Jammu and Kashmir also. Earlier it was accept Jammu and Kashmir, but since 1972 with the amendment Jammu and Kashmir word has been removed and now it extend to whole of India. Regulation is to ensure safety quality and efficacy of a drug and to prevent any substandard in quality of a drug and to achieve this objective Drug and Cosmetic Act has been provided with certain functions.

(Refer Slide Time: 02:54)

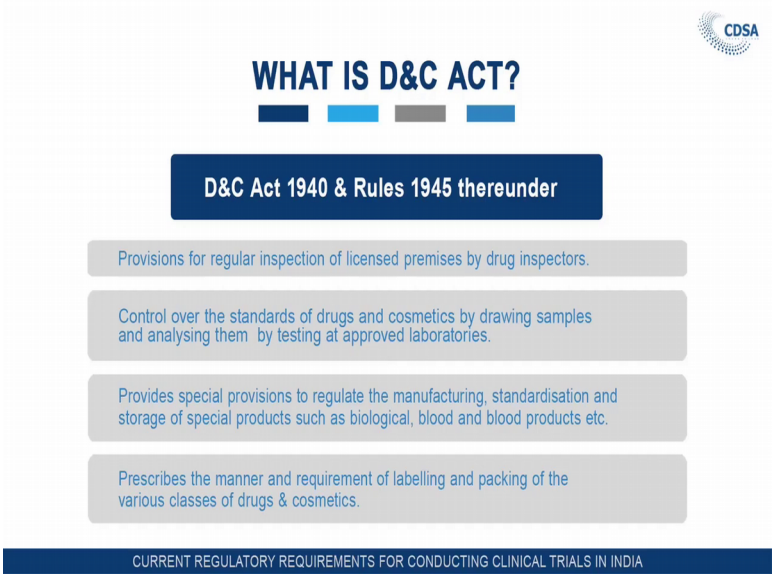


Drug and Cosmetic Act 1940 and rules 1945 there under is to regulate import of drug in India. Import of drug is regulated so, that no substandard spurious or misbranded drugs will enter into India and this can be control and regulated by issuing import license and by issuing the registration certificate. It prohibit manufacture of substandard spurious or misbranded drug in India. Drugs in India available by two ways either by import or either by manufacture and it reaches to the patient by import or by sale. So, with these three things that is import, manufacture sale and distribution required to be control and regulated.

The act and rules prohibit manufacture of substandard or spurious or misbranded drug in India. The sale and distribution of the drug is restricted to registered pharmacist only. The act is also provided for the regulation of Ayurvedic Siddha and Unani medicines. The Act provides for the control over manufacture and sale of homeopathic drug also.

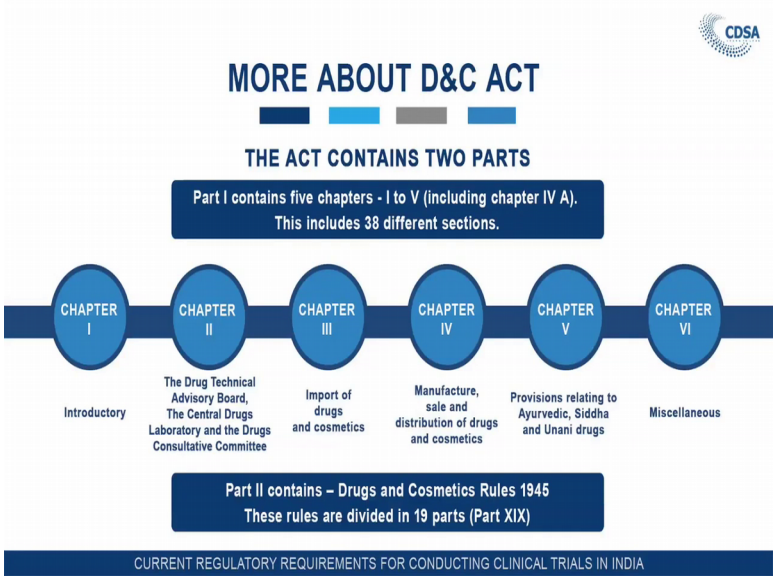
The Act is provided with the provision for regular inspection of licensed premises by drug inspectors.

(Refer Slide Time: 04:25)



It provide control over the standard of drug and cosmetics by drawing the samples. Drug inspectors are empowered to draw the samples available in the market and they are supposed to send the sample for testing and analysis to approved laboratories. The act provides special provision to regulate the manufacturing standardization and storage of some special products such as biological products, blood product and other. The Act also prescribes the manner and requirement of labelling and packing of the various classes of drug and cosmetic.

(Refer Slide Time: 05:20)



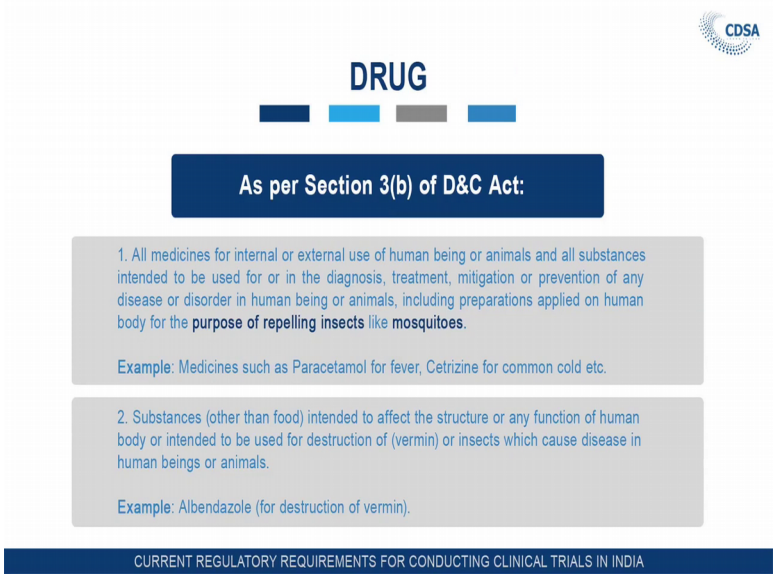
Let us see the Act and rules. We can see we can divide the act and rule in two parts as such there is no dividation or no two parts. But part one contain the Act which contain five chapters, actually there are VI chapter including chapter IV A, but it is up to V hence we call there are five chapters.

Chapter I is introductory chapter where in all these definitions are given chapter II is related to the DTAB and DCC committee. The DTAB is Drug Technical Advisory Board and DCC is the Drug Consultative Committee. Chapter III is import of drug and cosmetics, chapter IV is related to the manufacture sale and distribution of drug and cosmetics, chapter IV a is a provision relating to Ayurvedic Siddha and Unani drug, chapter IV is miscellaneous chapter some of the provision given in this chapter which are not cover under the previous four chapters.

(Refer Slide Time: 06:40)

Part II contains the rules drug and cosmetic rules. These rules are further divided into 19 parts, part 10 a is particularly for import of manufacture of new drug for clinical trial or marketing. There are currently more than 172 rules followed by schedules. The schedules are given from schedule A to schedule Y. Schedule Y is specifically for the clinical trials. Schedule Y is requirement and guideline for permission to import and or manufacture of new drug for sale or to undertake clinical trial schedule Y we will see in our next lecture in detail let us see the definitions given in the act.

(Refer Slide Time: 07:27)



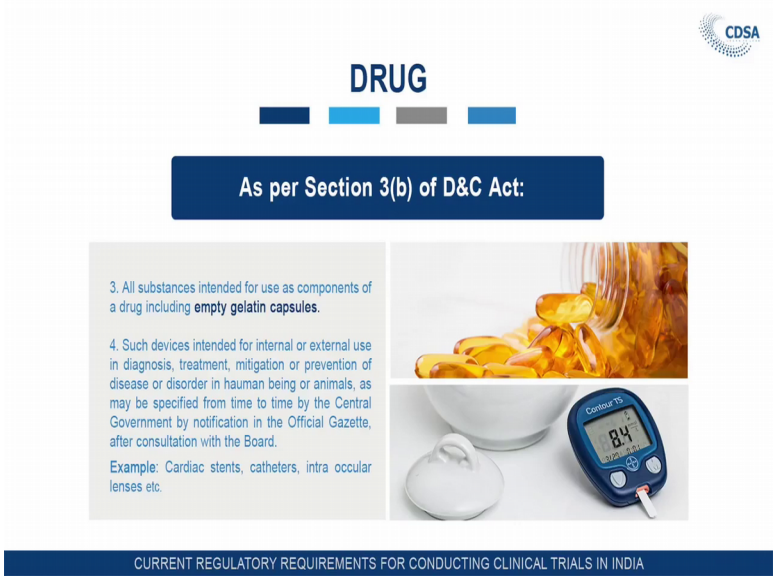
So, the first is the definition of the drug what is mean by drug, section 3 b of Drug and Cosmetic Act gives the definition of a drug. This definition has been divided in four sub clauses first sub clause specifies all medicines for internal or external use of human being or animal, and all substances intended to be used for or in the diagnosis treatment mitigation or prevention of any disease or disorder in human being or animal including preparation applied on human body for the purpose of repelling insect like mosquitoes, example all medicines what we take.

See this first part of thisdefi nition is quite exhaustive and inclusive. It has covered all medicines; all medicines means whatever the medicines who I had taking like paracetamol, ciprofloxacin, amoxicillin and other medicines what we take for the control of disease and disorder. Next it has given the all substances. So, all substances are also covered by this definition to include those which is not covered in medicines. All substances intended to be used the intended to be used is the key word because many of the substances they may be having they might be having therapeutic or curative activity, but unless they are intended to be used they are not drug.

So, it is given all substances intended to be used for example, ligatures, sutures, absorbent, cotton, wool all these are intended to be used for in the diagnosis treatment mitigation and prevention of disease and disorder that is in both that is human being and animals. Including preparation applied on human body for the purpose of repelling insect like mosquito like a Picard in drugs, these are also called in this clause. Let us see the second clause. Such substances other than food intended to affect the structure or any function of human body or intended to be used for destruction of vermin or insect which cause disease in human being or animal.

Such substances to intend affect the structure or any function of body. This is specifically given for the contraceptives, and these contraceptives are also considered as a drug.

(Refer Slide Time: 10:18)



The third clause it also mentions all substances intended for use as component of a drug including empty gelatin capsule. All substances intended for use as component it means the excipient are also considered and the empty gelatin capsule which is in direct contact with the active drug is also considered as a drug because to ascertain the safety of this component as these are also going into the body.

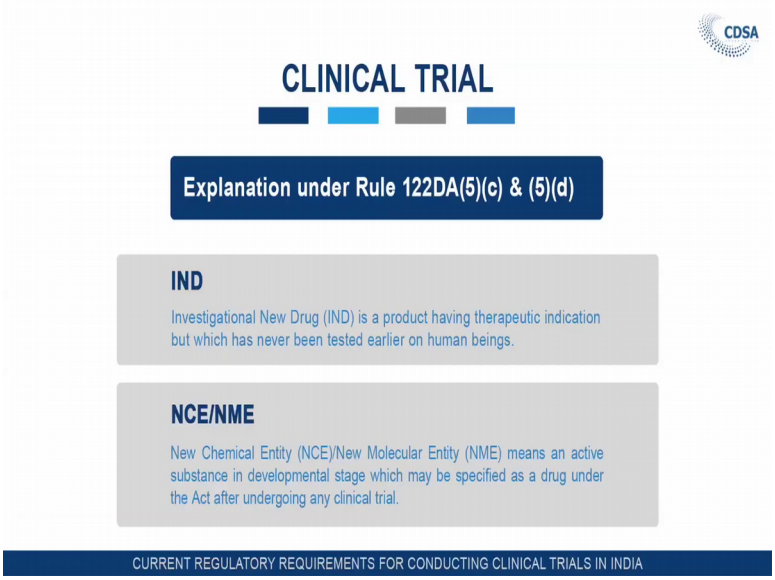
The forth clause is given for devices. Such devices intended for internal or external use in diagnosis treatment mitigation of prevention of disease or disorder in human being or animal. As may be specified from time to time by central government by notification in the official gazette, after consultation with the board; board means drug technical advisory board which is given in the Act or chapter II. Such devices means all devices which are used or intended to be for diagnosis treatment mitigation or prevention of disease and disorder. But not all the devices are considered as a drug unless they are notified by licensing authority that is specifically mentioned here. The example of this notified devices are cardiac stent, intra ocular lenses and many other devices which are notified by central government from time to time.

(Refer Slide Time: 12:08)

Let us see the definition of clinical trials. We have seen this definition of clinical trial in lecture first also. As per rule 122DA the clinical trial means a systematic study of new drug in human subject to generate data for discovering and or verifying the clinical pharmacological including pharmacodynamic and pharmacokinetic parameter and or adverse effect with the objective to determine the safety and efficacy.

The detailed explanation about this clinical trial we have seen in a our lecture first. Now the most important to see what is mean by IND, what is mean by NCE, what is mean by NME whether they are same or there is any difference.

(Refer Slide Time: 12:59)



So, let us see the first IND. IND is Investigational New Drug. IND is a product having therapeutic indication, but which has never been earlier tested in human being. So, IND is a product which after clinical trial therapeutic indication can be ascertained when the drug has came across the preclinical stage it means the preclinical study has completed and it has some therapeutic indication.

But it has never been tested in human being means clinical trial has not happen with that drug. What is NCE and NME? NCE is New Chemical Entity or New Molecular Entity these both are same. New chemical entity means an active substance in developmental stage, which may be specified as a drug under the act after going any clinical trial. So, which may be specified means it is not certain. So, new chemical entity it means it is a prior stage of the IND, means it has not yet shown any therapeutic indications and still it is in developmental stage it has not reached to the even preclinical stage and after going undergoing any clinical try, it may be specified or may not. So, that is a NCE.

Now, let us see what is a new drug.

(Refer Slide Time: 14:35)

This is the most important thing. So, the definition of new drug has been given in rule 122E. This definition also has been classified in four clauses. The first clause A state that, a drug as defined in the Act including bulk drugs substances or phyto-pharmaceutical drug. Phyto-pharmaceutical drug given in the bracket because it has been added lately in 2015; which has not been used in the country to any significant used under the condition prescribed, recommended or suggested in the labeling thereof and has not been recognized as effective and safe by licensing authority that is decisions (Refer Time: 15:23) mentioned under rule 21 for the proposal claim.

The simple meaning of these clause 1 the drug which is not approved in India, but approved outside the India or the drug which has not been tested or not been used in Indian patient or Indian subjects; however, it has been used outside the India. Let us see clause b, a drug already approved by licensing authority mentioned in rule 21 for certain claim, which is now proposed to be marketed with modified or nucleons namely indication dosage form including sustained release form and route of administration. What it mean by? It means by the drug is already approved in India now someone has propose to be marketed with different dosage form, different indication, different route of route of administration let us see one example.

For example paracetamol 500 milligram, tablet approved for the indication of antipyretic. Now someone has proposed the drug to be marketed with a different dose that is 600

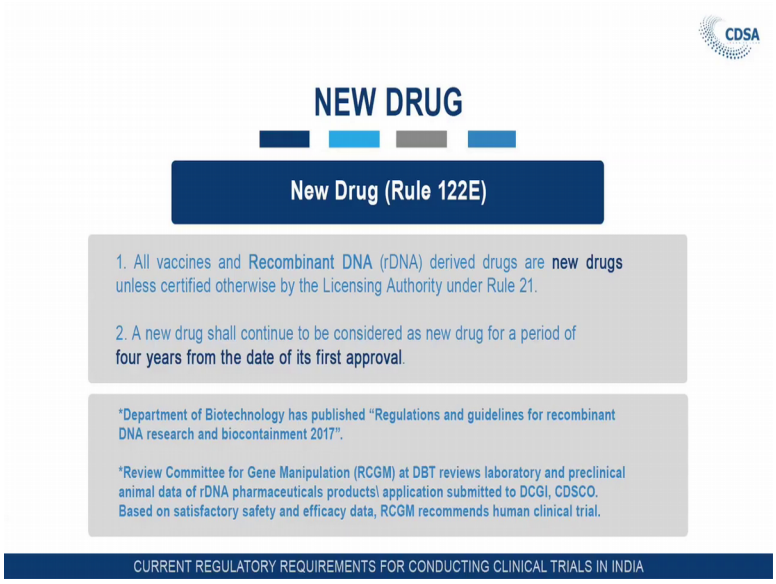
milligram then it become a new drug. If it is proposed to be marketed as a capsule then it is a new drug or any other dosage form. If the route of administration as in case of tablet it is oral somebody has proposed the i v route or i m route that is intravenous or any other route, then again it is considered as a new drug. If the drug is proposed to be marketed for a different indication if it is approved for antipyretic, now if it has been proposed for the analgesic then also it is a new drug. Why we are considering new drug? Because, every new drug require a clinical trial permission.

(Refer Slide Time: 17:38)

Let us see clause 3 that is a c. A fixed dose combination of two or more drugs individually approved earlier for certain claim which now proposed to be combined for the first time in a fixed ratio or if the ratio of the ingredient in an already marketed combination is proposed to be changed with certain claim such as indication, dose, dosage form including sustained release form and route of administration, then it is also new drug and it is called the FDC new drug. For example, paracetamol 500 milligram tablet as antipyretic is approved as we have discussed. And new (Refer Time: 18:24) 100 milligram tablet as analgesic has been approved both the drug approved in country individually. Now someone proposed to market the combination of these drug that is one tablet including paracetamol and new slide, then it become a FDC and every FDC is a new drug.

If someone has to change its a ratio for example, if it was paracetamol 500 milligram and now it has to be changed as 600 milligram, then is also considered as a new drug and FDC. If the ratio has changed then it become a FDC and new drug. If its indication is changed then again it become a new drug.

(Refer Slide Time: 19:13)



The last that is clause D it is very important. In this clause it is mention all vaccines and recombinant DNA derived drugs are new drug unless certified otherwise by licensing authority under rule 21. It means all the vaccines and recombinant DNA product derived products, all the time they are considered as a new drug. As these vaccines and recombinant DNA derived product they are derived from some sale lines or the microorganism which may continuously change or there is a may there may be a variation in the quality and the composition all these vaccines are considered as a new drug every time.

So, once this drug has been approved as a new drug, the drug shall continue to be considered as a new drug for period of 4 year from the date of its first approval. Regarding this recombinant DNA product, department of biotechnology has published regulation and guideline for recombinant DNA research and biocontainment 2017. RCGM that is Review Committee for Gene Manipulation at DBT reviews, laboratory and preclinical animal data of rDNA pharmaceutical product submitted and submitted

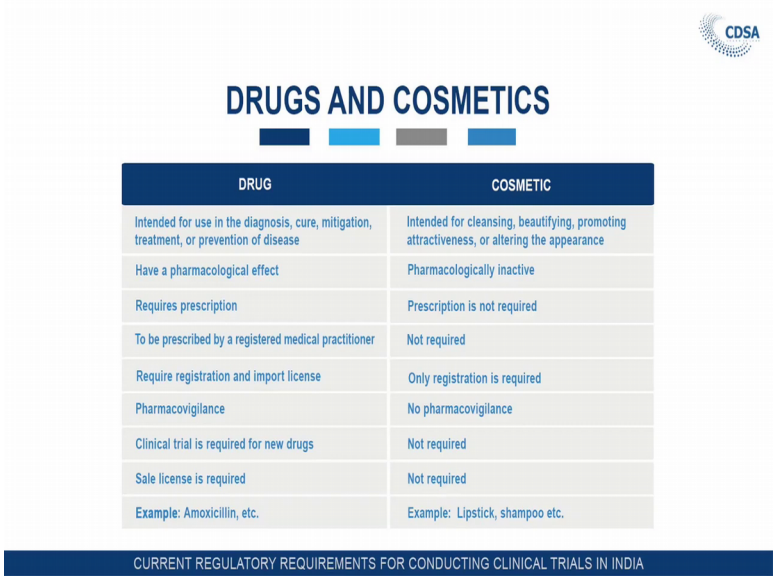
application to DCGI CDSCO. Based on satisfactory safety and efficacy data RCGM recommend for human clinical trials. So, this is about drug, new drug, IND.

Now, let us see what is mean by cosmetics.

(Refer Slide Time: 21:07)

So, the definition of cosmetic is given under section 3 a a that is triple a of Drug and Cosmetic Act. According to this definition cosmetics are any article in the definition of drug we have seen the all medicines, all substances and all devices here it is any article. Intended to be rubbed, poured, sprinkled or sprayed on or introduced into or otherwise applied to the human body or any part there off or cleansing for the purpose of cleansing, beautifying, promoting attractiveness or altering the appearance and include any article intended for use as a component of cosmetics. Here the purpose is changed in the drug definition we have seen the purpose for the diagnosis treatment mitigation and prevention of disease and disorder any human being and animals. Here it is only in a human beings as the animals do not use cosmetic.

(Refer Slide Time: 22:20)



Let us see in detail what is the difference between drug and cosmetic. So, as I have stated drugs are intended for use in the diagnosis cure, mitigation treatment or prevention of disease and disorder in human being or in animal. In case of the cosmetic it is the purpose of the cosmetic is for cleansing, beautifying, promoting attractiveness or altering the appearance. Drug act by having a pharmacological effect that it reaches to the blood circulation combine with the receptor and then elicited its pharmacological effect to you have the prevention or treatment of particular disease and disorder.

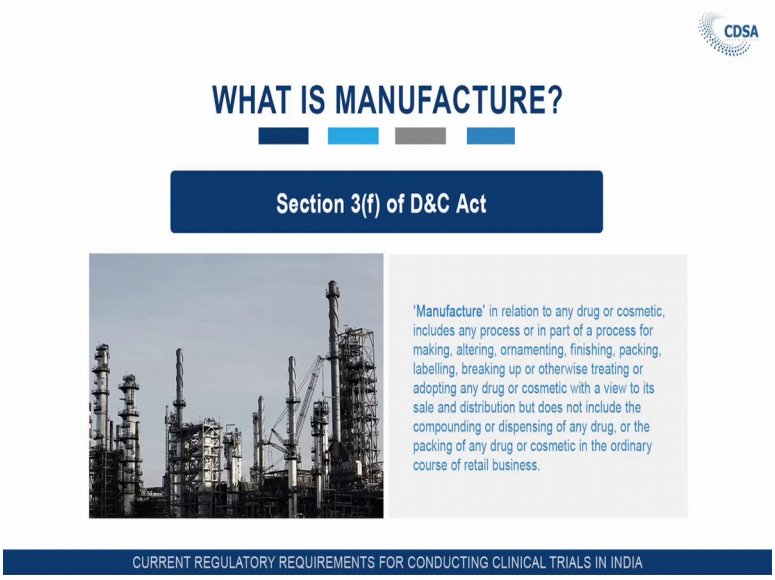
In case of cosmetic, as it is for the beautifying purpose or altering appearance there is no pharmacological activity. For the drug prescription is required and for the cosmetic prescription is not required you can buy it from any retail or a wholesaler. The drug has to be prescribed by the registered medical practitioner, the drug you cannot buy at your own it require as per the act and rule. The prescription by registered medical practitioner for the cosmetic it is not required. For the import of the drug, it require import license and registration is certificate issued by the DCGI or CDSCO.

In case of cosmetic this is also regulated, but in case of cosmetic only registration certificate is required. In case of the drug to see the adverse drug reaction there are there is a pharmacovigilance programme and there are many centres of this pharmacovigilance in case of cosmetic it is not there. In case of the drug clinical trial required for new drug we have seen the new drug and to import it or to manufacture it, it required the clinical

trials in case of cosmetic it is not there. Let us see what are the drug and cosmetics. So, drug we know all the drugs amoxicillin, cloxacillin, metformin, paracetamol, domperidone and other all the drugs, blood is also considered as a drug.Cosmetics we know lipstick, shampoo, foundation, kajal, mascara, eyeliner and many more of the cosmetics.

Coming to the next slide that is what is manufacture. See if you remember we have seen in schedule y. Schedule y is regarding guideline and requirement to undertake clinical trial for new drug to manufacture or to import a new drug. So, we have seen the definition of clinical trial, we have seen the definition of new drug now let us see what is means by a manufacture or what is mean by import. Manufacture is defined in section 3 f of Drug and Cosmetic Act.

(Refer Slide Time: 25:36)

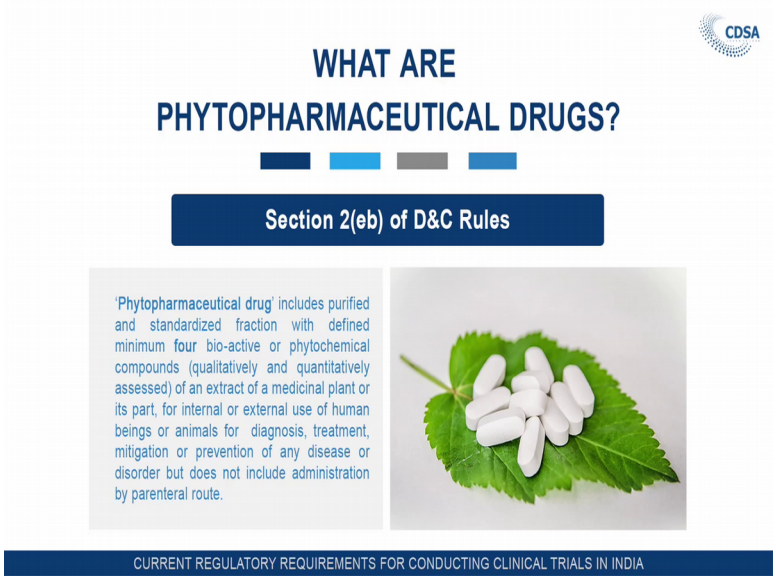


According to the definition manufacture in relation to any drug or cosmetic include any process or in part of process for making, altering, ornamenting, finishing, packing, labeling, breaking up or otherwise treating or adopting any drug or cosmetic with a view to its sale and distribution, but does not include the compounding or dispensing of any drug or the packing of any drug or the packing of any drug or cosmetic in ordinary course of retail business. In ordinary course of retail business means if in the drug has been breaker if for the dosage or in hospital pharmacy, if the dose adjustment has been done that is not consider as a manufacture.

(Refer Slide Time: 26:26)

Let us see what is mean by import. Section 3 g of Drug and Cosmetic Act mentions about import. To import with its grammatical variation and cognate it is mean to bring into India. We have also seen in new drug definition phyto-pharmaceutical drugs. So, it is important to know about phytopharmaceutical drug also.

(Refer Slide Time: 26:51)

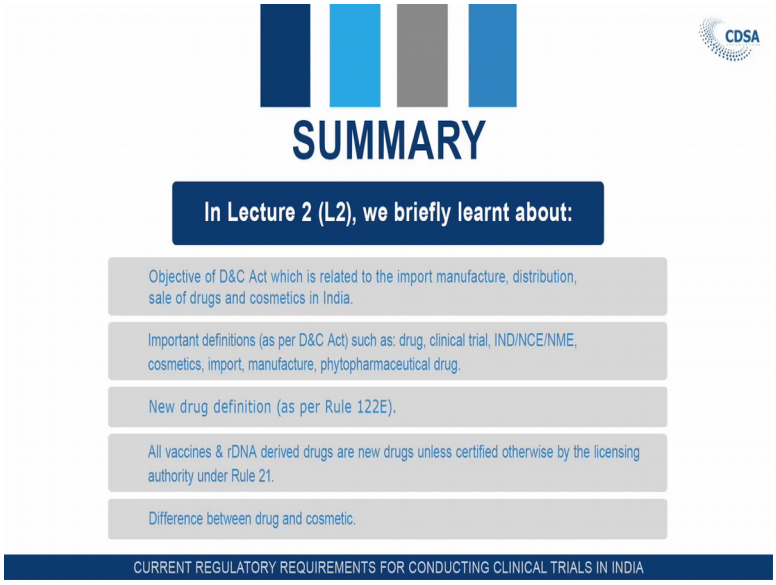


In section 2 eb of D and C rules, the definition is given in the rules. Phyto-pharmaceutical drug includes purified and standardized fraction with defined minimum four bioactive phytochemical compound, qualitatively and quantitatively assessed of an

extract of medicinal plant or its part for internal or external use of human being or animal for diagnosis, treatment, mitigation or prevention of any disease or disorder, but does not include administration by parenteral route.

So, if we see the difference between drug and phyto-pharmaceutical drug, the things we have to keep in mind about phytopharmaceutical drug. These are the drug having four bioactive phytochemical compound and this drug is the standardized extract of medicinal plant, it is not mean for the parenteral administration. So, this is all about the definitions. So, in this lecture what we have learn let us see in brief.

(Refer Slide Time: 28:09)



In this lecture we have a seen the objective of Drug and Cosmetic Act, the objective is to regulate the import manufacture sale and distribution to avoid substandard in drug. We have seen important definition such as a drug in the drug definition we have seen all medicines, substances, notified (Refer Time: 28:29) intended for diagnosis treatment mitigation and prevention of disease and disorder in animal or in human beings.

Clinical trial we have seen in first lecture also and this lecture also it is a systematic study, with the define objective of safety and efficacy. Then IND you have a seen; IND is a investigational new drug having therapeutic indication, but not tested earlier in any human being is a IND. New chemical entity, new molecular entity these are the same and it is the substance in a development stage and may or may not be ready for preclinical or clinicalness stage.

Cosmetics we have seen; the purpose of cosmetic it is for cleansing beautifying promoting attractiveness or altering any appearance it is maybe any articles. The definition of import we have a seen that is to bring into India is import. Manufacture definition we have a seen, manufacture means process of making a turning ornamenting finishing, packing of labelling is considered as a manufacture phyto-pharmaceutical definitions we have a seen. It is a standardized except of medicinal product with a minimum four bioactive components and it is not for a injections unlike a drug. We have seen a new drug definition as per rule 122E. As per this definition the drug which is not approved in India, but approve outside India is a new drug.

In the second any FDC combination is also a new drug, if the drug is already approved, but now it is proposed to be marketed with new dosage form, new route of administration, new indication or new strength is also considered as a new drug. We have a seen the third that is all DNA product and vaccine there all time new drug unless otherwise certified by licensing authority. We have also seen the difference between drug and cosmetic.

Drug is for the purpose of diagnosis treatment mitigation and prevention of disease and disorder in human being and in animal; however, the cosmetic is not for that purpose, it is just for the promoting attractiveness, beautifying for the purpose of beautification and the other purposes and it is specifically in human being and other differences. So, this is all about the lecture 2 we have seen, we will see in our next lecture till then bye bye take care and all the best.

Thank you.