Current Regulatory Requirements for Conducting Clinical Trials in India

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Lecture – L1
Introduction

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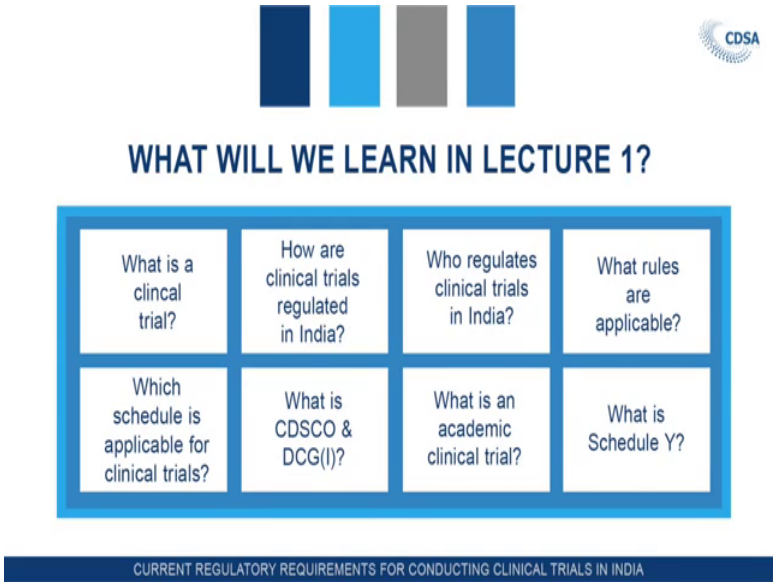

Hello everyone, welcome to the course Current Regulatory Requirements for Conducting Clinical Trial in India. [vocalize noise] This is the lecture 1 Introduction. In this lecture what will we learn in this lecture, what is clinical trial, what is academic clinical trial, who regulate clinical trial in India, what is CDSCO and DCGI, which rules are applicable for clinical trials, which schedules are applicable what is schedule Y and other things? So, let us start with the first what is a clinical trial.?

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Clinical trial has been define in Drug and Cosmetic Act and rules there under 122 DA. As per this definition a clinical trial is a systematic study of new drug in human subject to generate data for discovering and or verifying the clinical pharmacological including pharmacodynamics and pharmacokinetic and or adverse effects with the objective to determine safety and efficacy. Let us see word by word what is the meaning of this definition?

The first is systematic study. Systematic study it means the study which is appropriately designed with a scientific justification. The study is in principle with the good clinical practices and the study is in accordance with a schedule Y and with a prior approval of the licensing authority, that is called a systematic study of new drugs. New drugs we will see the definition of the new drug in our subsequent lecture. However, new drug is the drug which is not approved in country and it is approved in other countries.

In human subject it means the study should be in the human subject and not in animal. If it is in animal then it is called preclinical, to generate data for discovering and or verify. Discovering means if the data is not available or in the drug is not approved anywhere in the world then the data has to be discovered.

If the drug is already available in another country and if the data just has to be verifying specific population say for example, in Indian population, then it is a verifying the clinical pharmacological. It includes two things; pharmacodynamics and

pharmacokinetics. Pharmacodynamic it means what happens to the human body after taking a drug and pharmacokinetic it means, what happens with the drug after the drug getting into the body we call it as a ADME that is Absorption Distribution Metabolism and Excretion and or adverse effect with the objective of determining safety and efficacy. If the trial is proposed to verify the adverse effect only, that is also considered as a clinical trial and objective of all this study is to determine safety that is the drug is not toxic and efficacy.

Efficacy means whether the drug is effective or not. For its effectiveness the drug has to reach to the blood circulation and after reaching the blood circulation, it interact with some specific receptors and it show its pharmacological action that has to be ascertain. If the drug is studied for verifying its effectiveness in human subject, then it is also called as a clinical trial. These trial requires a regulatory permissions and hence this trials are called as a regulatory clinical trials. Now what are the other trials?

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Will see in our next slides the other clinical trials are maybe for the surveillance purpose or maybe for the research purpose. Let us see the example of the other regulate non regulating clinical trials for example, academic clinical trial. What is this academic clinical trials?

Academic clinical are clinical trial of drug already approved for certain claim and initiated by an investigator, academic or research institution for a new indication, new

route of administration or new dosage form where the result of such trial are used only for academic or research purpose and not for seeking approval of the central licensing authority, that is a DCGN or regulating authority of any country for marketing or commercial purpose.

In short what is means by academic clinical trail? The trail is with only for the approved drug for certain claim. It is only for the purpose of research and not for the commercial purpose and these trails do does not require any regulatory permission. So, this is all about clinical trial and academic clinical trials. Now let us see when this clinical trials rules and regulation came into existence and its evolution that is a brief history.

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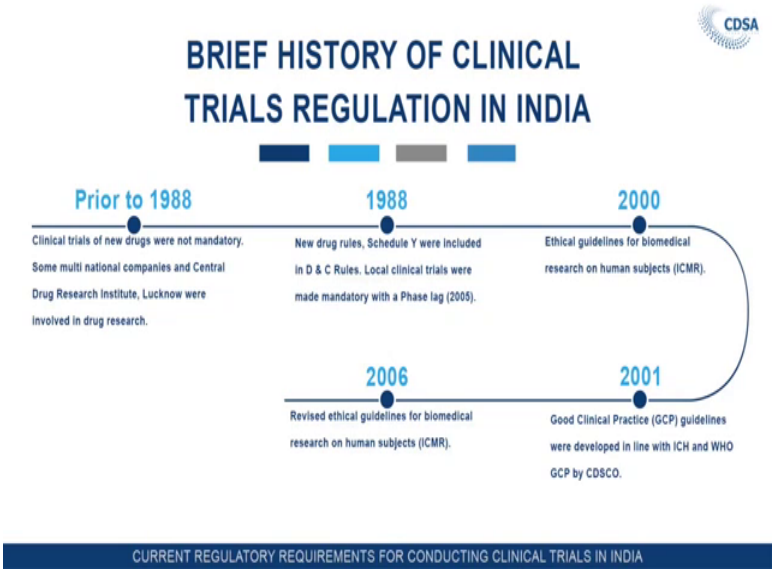

So, brief history of clinical trial in India prior to 1988, there were no rules and regulation as the research and development of the new drug was not that much up to the extent. Very few industries some of the multinational companies and some of the laboratories like CDRI Central Drug Research Institute Lucknow, they were involved in drug research.

In 1988 new drug rules; then schedule why were included in drug and cosmetic rules and since then the local trail where made mandatory with a phase lag. In 2000 ICMR has developed ethical guidelines for biomedical research on human subject. In 2001 CDSCO developed GCP guidelines that guidelines were in line with ICH GCP guidelines and WHO GCP guideline.

In 2005 the schedule Y was amended and in this amendment GLP that is a Good Laboratory Practices made mandatory for the toxicity studies, that is for preclinical trials studies. Phase lag in the clinical trial was removed in these 2000 period prior then product patent included in patent law.

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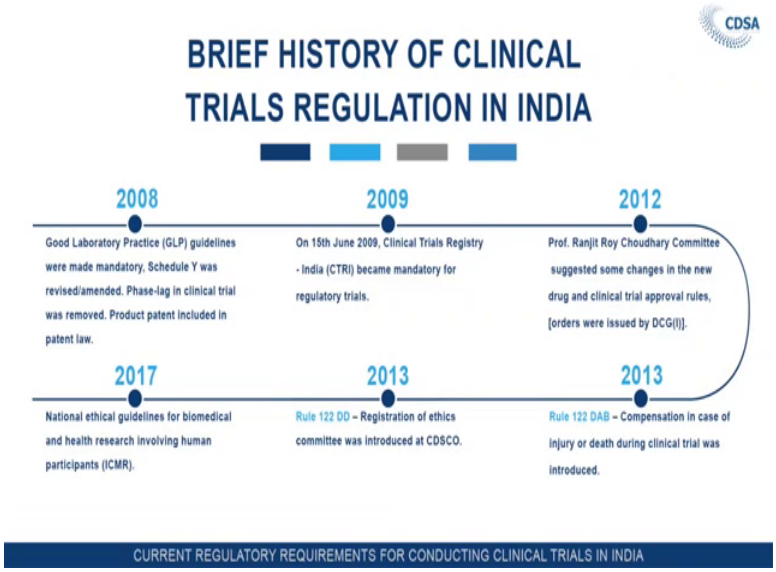

In 2006 ICMR has revised the guideline made and 2008 the GLP requirement and guidelines that is schedule l 1 inserted by GSR 780 which was effective from 2010. In 2009 on 15th June 2009 Clinical Trial Registry India that is CTRI became mandatory for regulatory trials to have the database and to enter each clinical trial on that side. In 2012 Professor Ranjit Roy Choudhary Committee changes in the new drug and clinical trial approvals. This changes were to streamline the clinical trial procedures. Based on that in 2013 rule 122 DAB and rule 122DD has been incorporated into the drug and cosmetic act and rules there under.

Rule 122DAB was related with compensation in case of injury or death during clinical trial. And rule 122DD is registration of ethics committee at introduced at CDSCO rules and act. In 2017 national ethical guidelines for biomedical and health research involving human participants was developed by ICMR. So, this is about the brief history of clinical trial in India.

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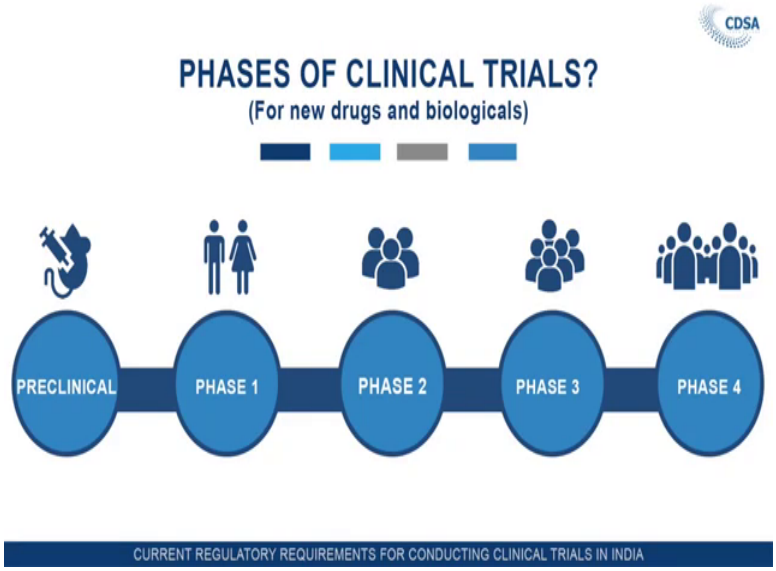

Now, let us see the phases of clinical trial. So, after drug has successfully completed research and development, it has to go through preclinical phase pre clinical phase means a phase in animals.

After completion of preclinical study and successful results in these animal, then there are 4 types of phases of clinical trial phase 1 phase 2 phase 3 and phase 4. In some other countries phase 0 is also considered, but that face 0 is not available in India. Phase 1 is with limited population size and mostly safety and tolerability has been ascertain in this phase 2 with little bit increase in number of size of the population and it is also called therapeutic or exploratory trials.

Phase 3 is therapeutic confirmatory trial. The number of subject in this trial increased and permission to market a drug can also be given after the phase. Phase 4 is a post marketing trial that is once the drug has been approved, then phase 4 is sometimes make mandatory this phase 4 is not consider mandatory at the time of giving the approval to the drug permission. However to optimise the dosage form and dose of the drug in wider population, this 4 phase 4 are considered.

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Let us see some important facts about the clinical trial. Cinical trial in India are considered as a one of the stringent trials. As these trials in clinical trial in India it involves compensation clause also it involves the AV that is Audio Video recording which is not available in many of the countries. Beside the sponsored then principal investigator and investigators, the regulator are also there to ensure that in a clinical trial the patients rights safety well being are fully protected and the data generated are accurate and credible.

Under the current regulatory framework clinical trial for new or existing drug or medical device can only be carried out at centre that have the appropriate facilities. The appropriate facilities means adequate number of the bed, then ICU unit emergency ward nearby hospitals and other ancillary facilities. The trials are allowed to be conducted only in such facilities having a staffed with a competent and experienced investigators that is doctor or nurses and the farmers is, there having the training of good clinical practice.

CDSCO which is a national regulatory authority of India, periodically carried out inspection of clinical trial sites in India. Foreign agencies like USFDA EMA PMDA they also carry out audit of the sides, if the drug is particularly proposed to be marketed in that country. Now let us see how clinical trials in India are regulated.

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The clinical trial on new drug are regulated under the provision of Drug and Cosmetic Act and rules there under 1945 as amended from time to time. The detail requirement and guidelines for conducting clinical trial are specified under rule 122 DA, 122 DAB, 122 DAC, 122 DD rule 122E that is a definition of new drug and schedule Y of said rules and other relevant provisions regarding the schedule Y we will see in detail in our subsequent lecture. Now, let us see who regulate this clinical trial in India and who are this regulators?

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So, Indian drug regulators CDSCO that is Central Drugs Standard Control Organisation is the central drug regulatory authority. This is headed by DCGI that is Drug Controller General of India sometimes it is called a central license approving authority. CDSCO is under the Ministry of Health and Family Welfare Government of India. CDSCO is also known as NRA that is National Regulatory Authority of India. Headquarter of the CDSCO is at New Delhi and the headquarter is mainly responsible approval of new drug clinical trial permission and some other functions.

CDSCO headquarter is also having its zonal and sub zonal officers. There are about 13 zonal and sub zonal offices across the country we will see in detail about CDSCO in our next lecture. This sub zonals and zonal offices are mainly involved in conducting the audit of this clinical trial site. Now let us see what is the hierarchy in this CDSCO.

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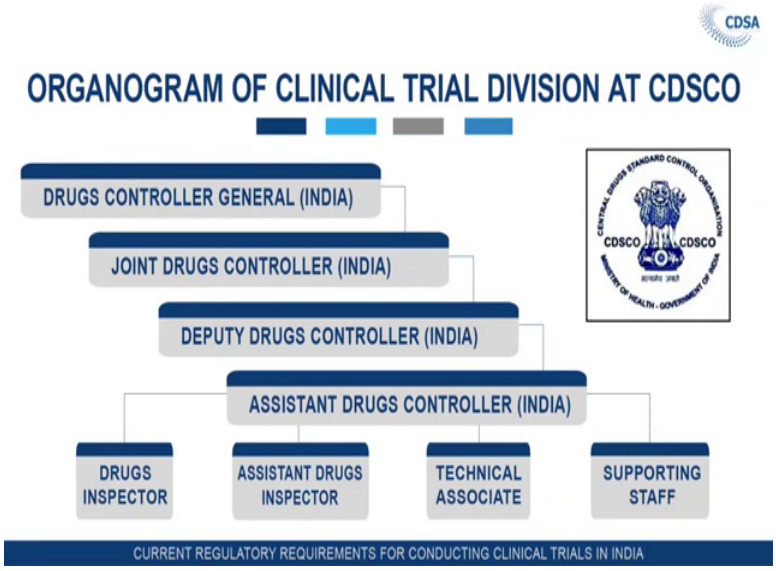

As I have said Drug Controller General DCGI that is central license approving authority is the head of the organization who is assisted by joint drug controller. Then deputy drug controller who are supported by assistant drug controller and they are supported by drug inspector assistant drug inspectors and other supporting staff. So, this is all about the clinical trials let us have quick recap to challenge your mind.

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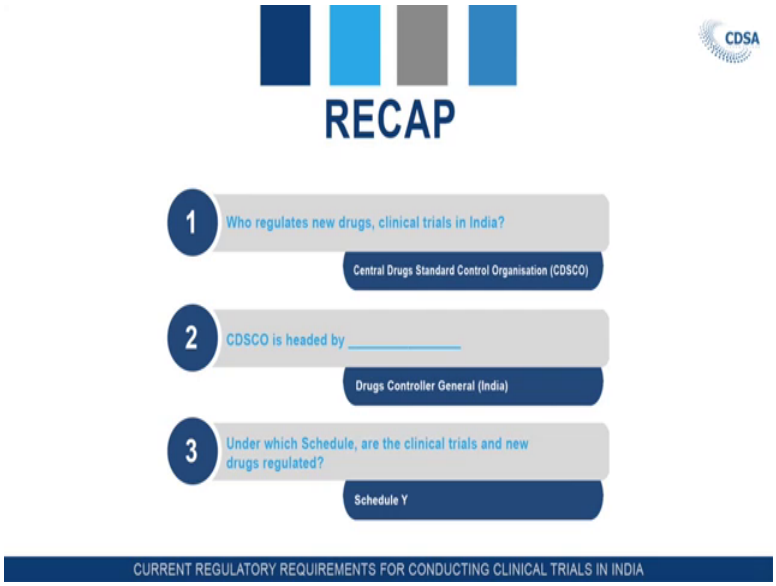

So, the first question to you, who regulates clinical trial in India? Yes CDSCO is the National Regulatory Authority of India who regulate clinical trial in India. The next question CDSCO is headed by that is who is the head of the CDSCO? Yes DCGI is the head of the CDSCO also called as central licensing authority. Under which schedule the clinical trials and new drugs are regulated? Schedule Y under schedule Y the clinical trials and new drugs are regulated. Now, let us see in lecture what we have learn in a brief.

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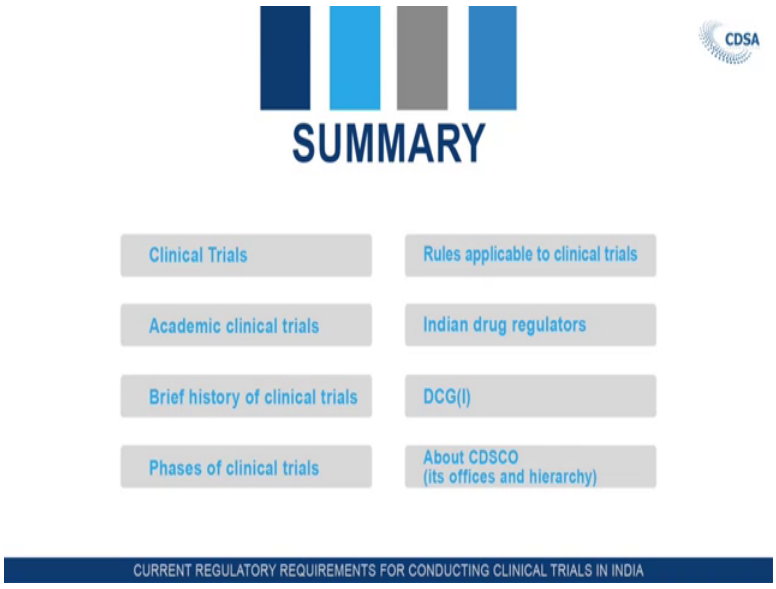

So, we have seen definition of clinical trial that is a clinical trial is a systematic study in human being and to have the, to determine the pharmacological effect that is pharmacodynamic and pharmacokinetic effect. Pharmacodynamic is related to the body pharmakokinetik what happens to the drug and the objective to determine the safety and efficacy.

Academic clinical trial the 4 things to keep in mind that, it is with a approved drug for the purpose of the research not for marketing or the commercial purpose and these are initiated by academic or the research institutions. We have seen the brief history of the clinical trial that prior to 1988, there were no regulation in 1988 the regulations schedule Y and neutral came into existence then we have seen the phases of clinical trial, that is after preclinical phase 1 phase 2 phase 3 and phase 4 the important thing is that after phase 3 the drug can be marketed with the permission of licensing authority.

Then rules applicable we are seeing the rule 122 DA, DAC, 122 DD, DAB E and other rules. Then we have seen the Indian regulators who are these Indian regulators from the DCGI to assistant drug inspector and in between that joint drug controller deputy drug controller and assistant drug controller. DCGI is the head of the organisation we have learn these in our this lecture. So, this is all about the introductory lecture, all these things you will learn in detail in our subsequent lecture, till then bye bye take care and all the best.

Thank you.