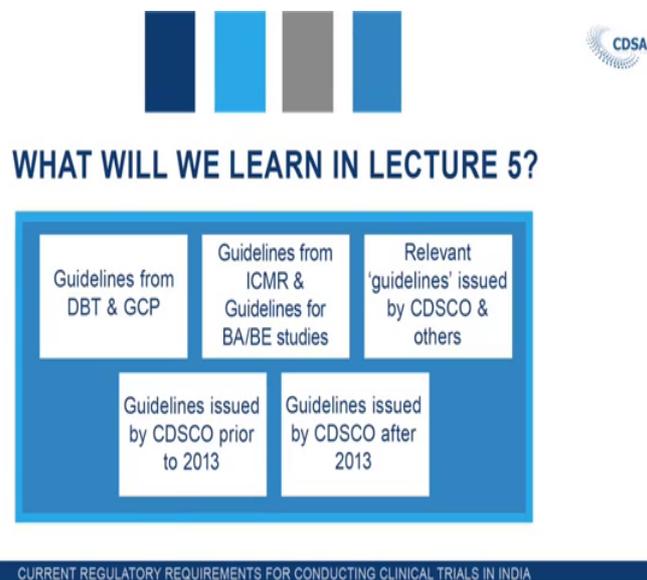


Current Regulatory Requirements for Conducting Clinical Trials in India
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Department of Higher Education, Ministry of Human Resource Development

Lecture - L5
Guidelines Relevant to Clinical Trials and New Drugs

Hello friends welcome back to the course Current Regulatory Requirement for Conducting Clinical Trial in India. So, this is a lecture 5; in this lecture we are going to see Guidelines Relevant to Clinical Trials and New Drug.

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So, in this lecture we are going to see the different guidelines that is guidelines from DBT, then guideline from ICMR, then what is GCP, then what are the guidelines for ethics committee, which are developed by the ICMR, what are the guidelines for bioavailability and bioequivalence studies? Guidelines which are developed by CDSCO prior 2013 and guidelines which are developed by CDSCO after 2013.

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LEARNING OBJECTIVES

Upon completion of this lecture, the participants will:

- Be able to understand the **guidance documents** issued by the regulatory authority (CDSCO), and the expert bodies like ICMR, DBT related to clinical trials and new drugs in India.
- Be able to understand the main objective and tenet of GCP.
- Know where to find out these guidelines.
- Be able to understand which guidelines to be followed for BA/BE studies, for biosimilar products, medical devices etc.
- Be able to understand the handbook for clinical trial.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

So, the learning objective of this lecture upon completion of this lecture the participants will be able to understand the basics of the guidance document issued by the regulatory authority that is a CDSCO; we have all seen it and the expert bodies like ICMR, DBT. The guidelines related to the subject clinical trial new drug in India. The learner will be able to understand what is good clinical practice and why the compliance is required?

What is the aim of the good clinical practice, what is the tenet of this GCP? We will be able to understand where to find out this guidelines for example, BA, BE studies are there, then the other guidelines like GCP stem cells. So, where these guidelines are available that would be understood and which guideline to be followed? Many of the time there is a confusion whether to follow the BA, BE studies guideline or clinical trial guideline.

So, after having this lecture you will be able to understand which guideline to be followed, then there is one handbook of clinical trial you will be understand what is that handbook.

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**GCP FOR CLINICAL RESEARCH
IN INDIA (2001) BY CDSCO**

Introduction

- Good Clinical Practice (GCP) is an **ethical and scientific quality standard for designing, conducting and recording** trials that involves participation of human subjects.
- Compliance with this standard **provides assurance** to public that the rights, safety and well being of trial subjects are protected, consistent with the principles enshrined in the 'Declaration of Helsinki' and ensures that clinical trial **data are credible**.
- GCP is a set of **guidelines** for biomedical studies which encompasses the design, conduct, termination, audit, analysis, reporting and documentation of the studies involving human subjects.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

So, let us start with the introduction of a Good Clinical Practices for clinical research in India. So, good clinical practices is an ethical and scientific quality standard for designing, conducting and recording trial that involve the participation of human subjects whichever the trials wherein the human participants are there we called it as a clinical trial; we have seen it and if there are animals then it is a preclinical.

So, the good clinical practice it is a ethical and scientific quality standard. Compliance with this standard provides assurance to the public. So, if one has followed this good clinical practice while conducting the clinical trial then it will provide a assurance to the public that the right safety and well being of the participant that is a study subject has been protected and then whatever the data they have from this research that data is credible and reliable.

GCP as I have said is a set of guidelines for biomedical studies which encompasses the design conduct, termination, audit, analysis reporting and documentation of the studies involving human subjects.

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**GCP FOR CLINICAL RESEARCH
IN INDIA (2001) BY CDSCO**

Introduction

- The fundamental tenet of GCP is that in research on human subject, the interest of science and society should never take precedence over considerations related to the well being of the study subject.
- It aims to ensure that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical substances under investigation are properly documented.
- The guidelines seek to establish two cardinal principles: **protection of the rights** of human subjects and **authenticity** of biomedical data generated.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

The fundamental tenet of GCP is that in research on human subjects the interest of science and society should never take precedence over consideration related to the well being of the study subject. So, the well being of the study subject is at higher priority and the science and society that should not take the precedence of it.

The aim of this good clinical practice to ensure that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical substances that we call it as investigational substance also IP under investigation are properly documented. The guidelines seeks to establish two cardinal principles; there are two main principles. First is the protection of the right of human subjects and authenticity of biomedical data generated. So, these are the two basic principle based on that many principles are developed by the GCP guidelines.

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It has been widely recognized that India offers unique opportunities for conducting clinical trial.

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GOOD CLINICAL PRACTICES FOR CLINICAL RESEARCH IN INDIA

CDSA

Large patient pool, well-trained and experienced investigators, premier medical institutes along with considerable low per patient trial cost makes India an attractive destination.

Therefore, there was a need to develop our own Indian guidelines to ensure protection, promote uniform quality of clinical research throughout the country and to generate registration data for new drugs before they are released for commercial usage.

An expert committee set up by Central Drugs Standard Control Organisation (CDSCO) in consultation with clinical expert has formulated this GCP guideline for generation of clinical data on drugs.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

In view of the large patient pool then well-trained and experienced investigator and premier medical institute available in the country along with considerable low per patient trial cost as compared to the developed countries; that is why the clinical trials are more in the India.

However, a need was failed to develop our own Indian guidelines. So, these are some of the guidelines they are developed by WHO then ICH, but the India need to develop a guidelines which are suitable for the Indian population. So, that need failed to develop guideline to ensure uniform quality of clinical research throughout the country and to generate data for registration for new drug before used in the Indian population. For that an expert committee set up by the CDSCO that is a central government in consultation with clinical expert and they have formulated the GCP guidelines for generation of clinical data on a drug.

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The slide features the title "GOOD CLINICAL PRACTICES FOR CLINICAL RESEARCH IN INDIA" in bold blue text, with the CDSA logo in the top right corner. Below the title are four colored bars (dark blue, light blue, grey, dark blue). The slide contains two text boxes with the following content:

The history of GCP statute traces back to one of the oldest enduring traditions in the history of medicine: The Hippocratic Oath. As the guiding ethical code it is primarily known for its edict to do no harm to the patient. However, the complexities of modern medicine research necessitate a more elaborate set of guidelines that define a physician's ethical and scientific responsibilities such as obtaining informed consent or disclosing risk while involved in biomedical research.

These guidelines have been evolved with consideration of WHO, ICH, USFDA and European GCP guidelines as well as the ethical guidelines for biomedical research on human subjects issued by the Indian Council of Medical Research (ICMR). These guidelines should be adhered while carrying out all biomedical research in India at all stages of drug development, whether prior or subsequent to product registration in India.

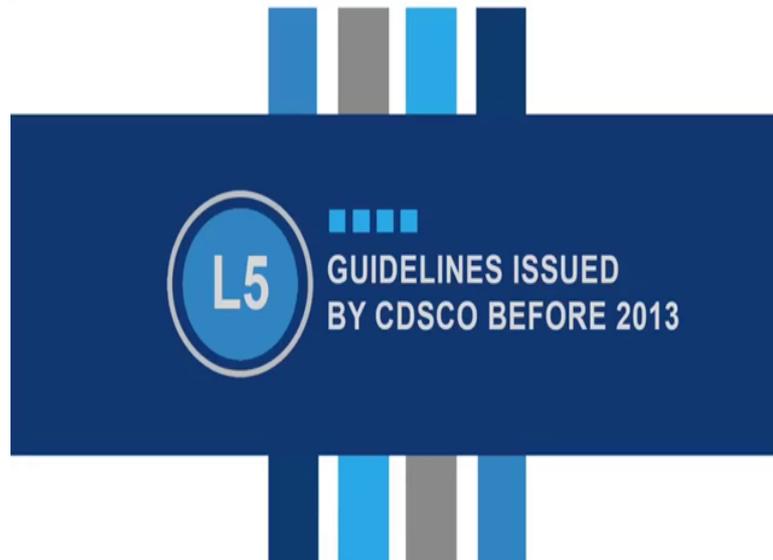
CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

The history of GCP statute traces back to one of the oldest enduring tradition in the history of medicine that is the Hippocratic Oath. As the guideline ethical code it is primary known for its edict to do no harm to the patients. So, that was the main principle to do no harm to the patient. However, the complexities of modern medicine research necessitate a more elaborate set of guidelines that address a physicians, ethical and scientific responsibilities such as obtaining informed consent form or disclosing risk while involved in biomedical research.

So, these guidelines have been evolved with the consideration of WHO, ICH, USFDA new guideline that is European Good Clinical Practice guideline and also the ethical guidelines for the biomedical research on human subjects issued by the ICMR. So, they

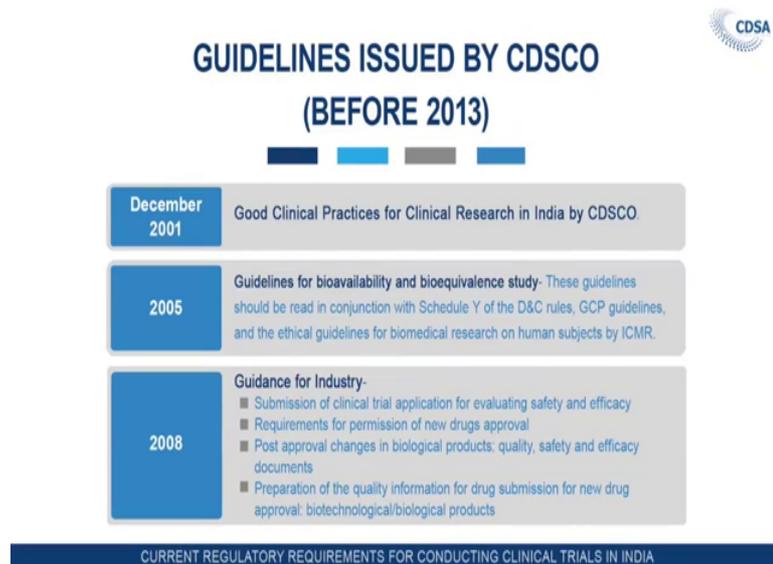
should be followed for carrying out all biomedical research in India at all stages of drug development whether prior to subsequent to product registration in India.

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So, let us see which are these guideline.

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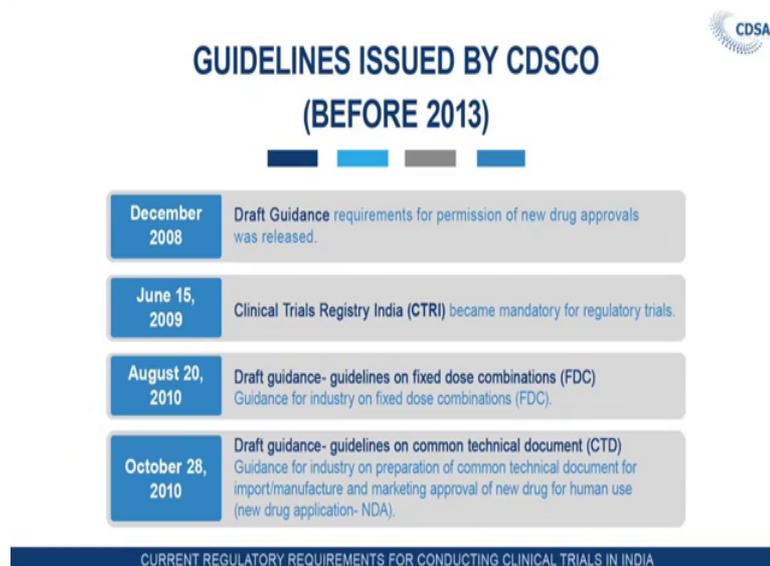
So, guideline issued by CDSCO before 2013; good clinical practices guideline for clinical trial on pharmaceutical product in India by CDSCO December 2001. In the year of 2009 we have seen that clinical trial registry, then guidance for industry on submission of clinical trial application for evaluating safety and efficacy.

So, in this there is a requirement for permission of new drug approval what are the requirement that has been given. Post approval changes if there are after the approval of the trial and after approval of the marketing authorization.

If there is a changes then what are the changes, how they have to be applied regarding that post approval changes in biological products; the guideline mentions. Then preparation of the quality information for drug submission for new drug approval. So, this has also been uploaded in 2008. Guidelines for BA, BE study this guideline though it is exclusively given for the bioavailability and bioequivalence studies.

This guideline should be read in conjunction with the schedule Y because schedule Y is having the more specific information about the clinical trial also the GCP guideline and ethical guideline for biomedical research on human subject by ICMR. So, this specific guideline with respect to the bioavailability and bioequivalence is there; this was hosted in 2005.

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The next is guidance for industry; the Draft Guidance that is for the preparation of CTD; for import manufacture and marketing of approval of new drug for human use, so, this was posted in 2010. Further the draft guidance requirement for a permission of fixed dose combination. There was confusion regarding the fixed dosage combination whether new drug or old drug, whether required clinical trial or not; for that the draft guidance has been published on the website that is requirement for permission of FDC.

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GUIDELINES ISSUED BY CDSCO (BEFORE 2013)

May, 2011	Draft Guidance- for issuance of no objection certificate (NOC) for export of new drug (unapproved/approved/banned).
July, 2011	Draft guidance on approval of clinical trials and new drugs.
December 21, 2011	Draft Guidance- requirement of chemical & pharmaceutical information including stability study data before approval of clinical trials/BE studies.
August, 2012	Draft Guidance- requirement for determining quantum of financial compensation to be paid in case of clinical trial related injury or death.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Draft guidance for issuance of NOC for export of new drug. So, the export of new drug; new drug whether it is approved, unapproved banned for that the draft guidance is there on the site which was posted on May 2011. Draft guidance requirement of chemical and pharmaceutical information including stability study data before approval of clinical trial BA, BE studies posted on December 2011.

So, what are the data is required with respect to the chemical and pharmaceutical including stability study? So, whatever the data that has been given in this guideline? Draft guidance that is requirement for determining quantum of financial compensation to be paid. In case of clinical trial related injury or death this is there in the site and it has been hoisted in August 2012. Then the draft guidance 2018 so, this is exclusively for the bioavailability bioequivalence study for the purpose of only export.

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GUIDELINES ISSUED BY CDSCO (AFTER 2013)



February 2013	Guideline for registration of ethics committee -CDSCO 2013.
January 2014	Draft Guidance on audio-visual recording of informed consent process in clinical trial -CDSCO 2014.
2015	Guideline for specifying the procedures for payment of compensation to the subjects of clinical trial in case of injury or death -CDSCO 2015.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Some of the guidelines issued after 2013 and we have seen in many lecture; 2013 was a landmark in this year and after this there has been a many changes in the Drug and Cosmetic Act and Rules. So, some of the guidelines are published these are like this. So, the draft guidance on a-v recording of informed consent process in clinical trial. So, this is published in Jan 2014.

This talks about the audio-video recording. We have seen it is required for the vulnerable population and for new chemical entity. So, all these things regarding how to record and what are the criteria this is given in this draft guidelines.

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GUIDELINES ISSUED BY CDSCO
(AFTER 2013)

2015 Guideline formula on how to determine the quantum of compensation in case of SAE of deaths occurring during clinical trial -CDSCO 2015.

2016 Guideline on similar biologics (regulatory requirements for marketing authorisation in India) -DBT-CDSCO 2016.

2017 National Guidelines for stem cell research -ICMR-DBT 2017.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

National Guideline for stem cell research; this has been given by the ICMR in 2017. So, all the types of stem cells and the bodies involved; how to apply, where to apply that has been mentioned in this guideline. These are the national guidelines.

Guideline on similar biologics; so, biosimilar after the biological there were the guidelines for the biologics that we called the biosimilar. For the guideline on similar biologics that is regulatory requirement for marketing authorization in India. So, this guideline was developed by DBT and CDSCO and now it has been revised in 2016 which is available in our site.

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GUIDELINES ISSUED BY CDSCO (AFTER 2013)

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January 2017	Handbook for applicant and reviewers of clinical trials of new drug in India.
2018	Draft guidance document for medical devices -IPC 2018.
July 2018	Guideline for application processing by officials in new medical devices, (CDSCO-CDAC).
2018	Draft guidance- BA/BE for export.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then handbook for application and reviewers of clinical trial of new drug in India. So, one book has also been web version is available in our site, that book is also related to the clinical trials guideline.

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CDSCO GUIDELINES

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The CDSCO Guidance documents were earlier available at the CDSCO website, www.cdscsco.nic.in
The new CDSCO portal is www.cdscsco.gov.in

All above guideline will available at new portal in due course of time.



CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

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GUIDELINES ISSUED BY CDSCO (AFTER 2013)

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January 2017	Handbook for applicant and reviewers of clinical trials of new drug in India.
2018	Draft guidance document for medical devices -IPC 2018.
July 2018	Guideline for application processing by officials in new medical devices, (CDSCO-CDAC).
2018	Draft guidance- BA/BE for export.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

This has been published in January 2017.

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GUIDELINES ISSUED BY CDSCO (AFTER 2013)

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February 2013	Guideline for registration of ethics committee -CDSCO 2013.
January 2014	Draft Guidance on audio-visual recording of informed consent process in clinical trial -CDSCO 2014.
2015	Guideline for specifying the procedures for payment of compensation to the subjects of clinical trial in case of injury or death -CDSCO 2015.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Guidelines specifying the procedure for payment of compensation to the subject of clinical trial in case of injury or death. So, these are the guidelines related to the compensation class how to remerge the give the compensation in case of the injury or death. So, this is given in 2015. Then guideline for formula to determine the quantum of compensation in case of SAE of death occurring during clinical trial. So, there are two three formulas in case of death, in case of injury, in case of the serious adverse events.

So, this formulas how to formulate, how to put the values that is given in this guideline; then guideline regarding the ethics committee registration.

So, what are the composition, who should be the member, who should be the chairman? That is given in the guideline that is registration for ethics committee. So, this was published by CDSCO in Feb 2013. In draft guidance document for medical device by IPC that is Indian Pharmacopoeia Commission they have published a draft guidance for the medical devices. Guideline for application processing by official in new medical devices by CDSCO.

So, this guideline actually; this guideline has been developed by the CDAC. CDAC is a team which is available in CDSCO and they are involved in making all the applications online. So, likewise they have made the medical device application and approval is also online. So, how to apply, what are the precaution to be taken, how to register, how to apply; so, they have developed the guidelines in this regard.

So, as I have mentioned these all are available in our websites. So, the website for this is earlier it was cdsco.nic.in. Now we have developed a new web portal that is www dot cdsco.gov.in. So, most of the guidelines are available and those guideline which are not available that will be available soon on this website.

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RECAP

1 What are guidelines?
Guidelines are directives containing relevant rules for stakeholders prepared by the experts.

2 In which year the national guideline for stem cell research was developed and by whom?
The national guidelines for stem cell research was developed by ICMR and DBT in 2017.

So, let us have quick recap with the questions as usual. So, the first question; what are guidelines? So, the guidelines are the details of relevant rule for stakeholders prepared by the expert bodies. The second question in which year the national guideline for stem cell research developed and by you have to tell the who has developed the guideline and in which year for the stem cells? So, the answer is the national guideline for stem cell research have been developed by ICMR and it is in 2017.

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RECAP

3 What is full form of CTD?
Common technical document.

4 What is good clinical practice?
GCP is an ethical and scientific quality standard for designing, conducting and recording trials that involve the participation of human subjects.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

Then the next question is; what is the full form of CTD? So, CTD is a Common Technical Document. The next question that is, what is good clinical practice? We have seen in the second slide. So, GCP is an ethical and scientific quality standard for designing, conducting, recording, reporting of the clinical trial that involve the human participation.

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SUMMARY

In Lecture 5 (L5), we briefly learned about

- The guidelines are specified by the CDSCO to streamline conducting clinical trials/new drug approvals in India.
- These guidelines are available for biosimilar drug products, stem cell research and bioavailability/bioequivalence studies.
- There are guidance documents to help assess and compute compensation in case of a serious adverse event (SAE)/death during clinical trial/trials.

CURRENT REGULATORY REQUIREMENTS FOR CONDUCTING CLINICAL TRIALS IN INDIA

So, let us summarize briefly in lecture 5 what we have learn about. So, in this lecture we have seen the different guidelines developed by DBT, developed by ICMR, developed by CDSCO, the guidelines before 2013, the guidelines after 2013, then the guideline for biosimilar product, then guideline for stem cell product, then guideline for good clinical practice. There are the guideline for the compensation, then the formula how to report the SAE. So, we have seen all almost all the guidelines and guidance document developed for the industry and stake holders. So, this is all about this lecture.

Thank you for your kind attention; we will see in the next lecture, till then bye bye all the best.