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

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Lecture – 02
Overview of Indian regulatory system

Hello friends, welcome back to the course 1 Version 2. I am sure that you have enjoyed version 1 of this course and successfully passed the exams also. Dear friends with massive changes in the new drug and clinical trial rules, it was imperative need to come up with the version 2 of this course and were here with the version 2 of the course Current Regulatory Requirement for Conducting Clinical Trial in India for New Drug and Ind. So, the lecture first is regarding overview of Indian drug regulatory systems that is CDSCO and the State Licensing Authority.

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The learning objective of this course of this lecture and the excepted outcome is that from this lectures, the learners will be able to comprehend about the CDSCO and its different offices, then the laboratories of this CDSCO and the central government, then hierarchy at the CDSCO, then what is the State Licensing Authority, then responsibilities of the Central Government and the State Licensing Authority, then other ministries and department which are involve in the regulatory processes for approving the new drug with respect to the biological and others.

Also you will be come to know that what are the gaps and challenges for the regulatory systems and what the regulatory system has done in the recent year that that is the achievement and the initiatives.

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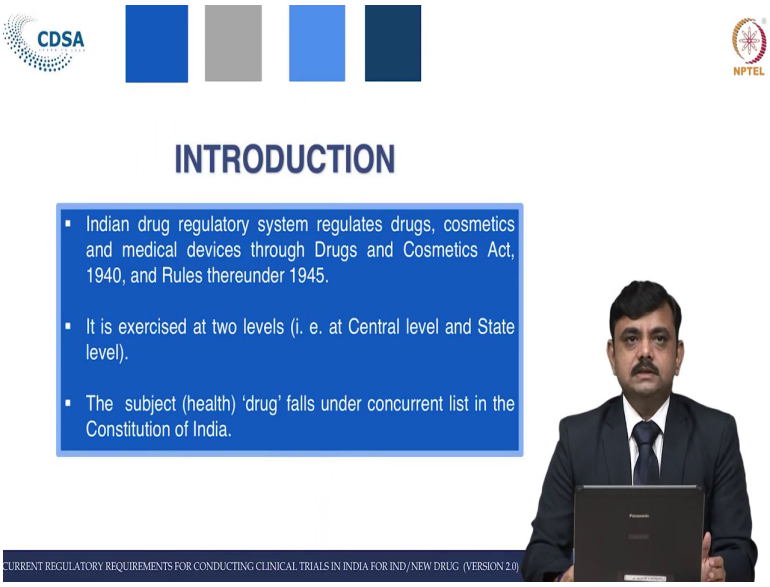

So, let us begin with the introduction of this lecture first. Dear friends, Indian drug regulatory systems regulates drug cosmetics and medical devices across the India under the act that is Drug and Cosmetic act which was established in 1940 and rules made their under in the 1945. It is exercised at two levels that is at the central government and at the state levels.

The excitants of these act at the two level that is Central level and the State level is because of the position of the subject drug in the Indian constitution. As you know there are three list in the Indian constitution in the 7th scheduled that is union list dead list and the concurrent list. The subject drug is in the list of the concurrent list of the Indian constitution. Hence, this act has been exercised at two level that is state level and the central government level.

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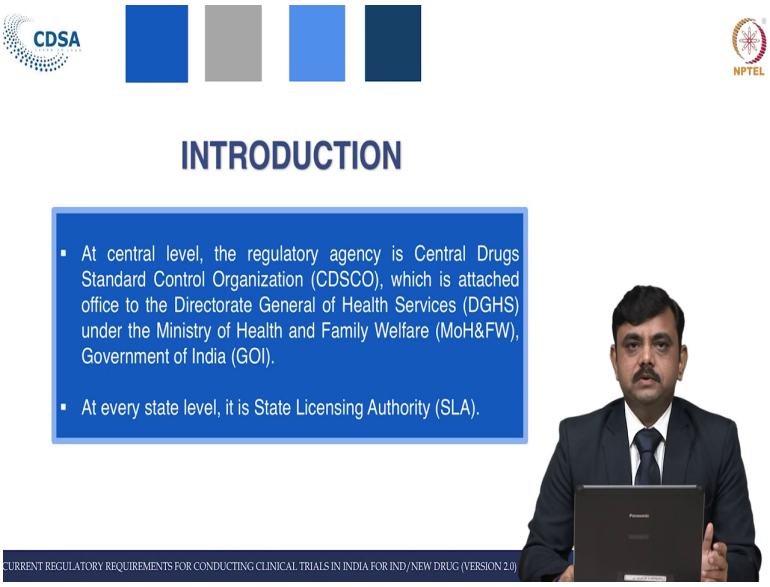

A state level authority may be called as a state licensing authority and a central government authority is a CDSCO which will see in the next slide.

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So, the CDSCO is the Central Drug Regulatory Authority which is headed by the Drug Controller General of India. This CDSCO institution is under the DGHS that is Director General of Health Services which is under the Ministry of Health and Family Welfare, Government of India. CDSCO is the national regulatory authority of the India. The headquarter of the CDSCO is located at FDA Bhawan, ITO Kotla road, New Delhi and the headquarter of the CDSCO which is at New Delhi is mainly responsible for giving the approval of new drugs, clinical, trials import export; then approval of the medical devices and other products. We will see in detail in our subsequent slides CDSCO has been supported by 13 zonal and sub zonal offices across the country which are also involved in the monitoring of the clinical trials.

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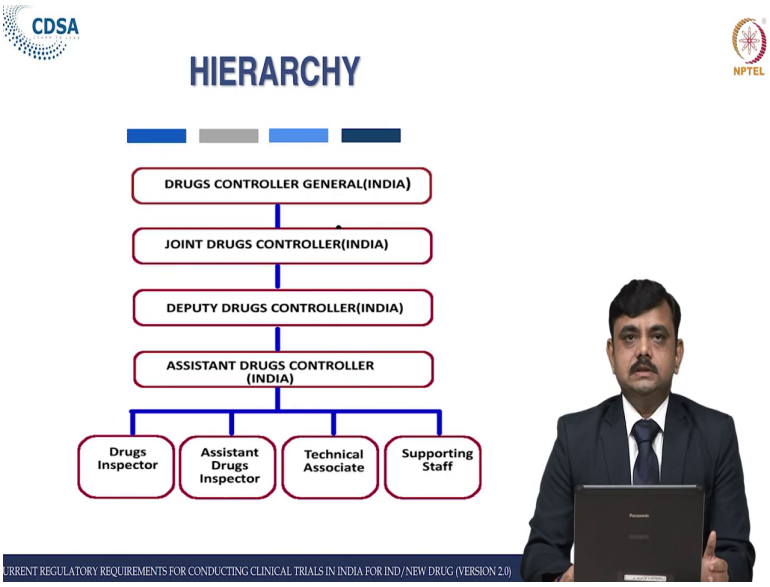

Let us see the hierarchy at the CDSCO at CDSCO headquarter at New Delhi. So, this is the hierarchy at CDSCO headquarter. The CDSCO this institution is headed by drug controller general of India.

We will so, called DCGI or the drug controlling authority or the central licensing authority and he supported by joint drug controller of India, deputy drug controller of India, assistant drug controller of India and they are supported by drug inspector who are actually responsible for conducting inspections and audit of the clinical trial sides and other.

They are supported by assistant drug inspector technical data associate and other supporting staff. Let us see the CDSCO offices and laboratories. So, where are these offices located across the country?

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So, as I have said there are 13 zonal and sub zonal offices. There are six zonal offices which are scattered throughout the India in a geographical distribution that is in the East, West, South and North zone to cover the whole of India. The office of the North zone is situated at Gahziabad and office for the West zone is situated at Mumbai and Ahmedabad. For the South zone the offices that is zonal offices are situated at Chennai and Hyderabad. There are also seven sub zonal offices. These are at Chandigarh, Bangalore, Goa, Jammu, Guwahati, Indore and recently added Varanasi.

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There are eight laboratories which are responsible for the testing of the drug cosmetic and medical devices. These laboratories are called as central drug laboratories and central drug testing laboratories. These are situated at Kolkata, Mumbai, Chennai, Hyderabad, Chandigarh, Guwahati, Kasuali, NIB Noida. These laboratories have been assign a different functions like some laboratories are involve in the testing and analysis of biological products, some laboratories are involve in the specific category of drug some laboratories are involve in the testing of cosmetic or medical devices.

Apart from these there are thirteen port offices and this port offices are mainly involved into the import and export of the drug cosmetic and medical devices. Let us see what are the various division at CDSCO headquarter.

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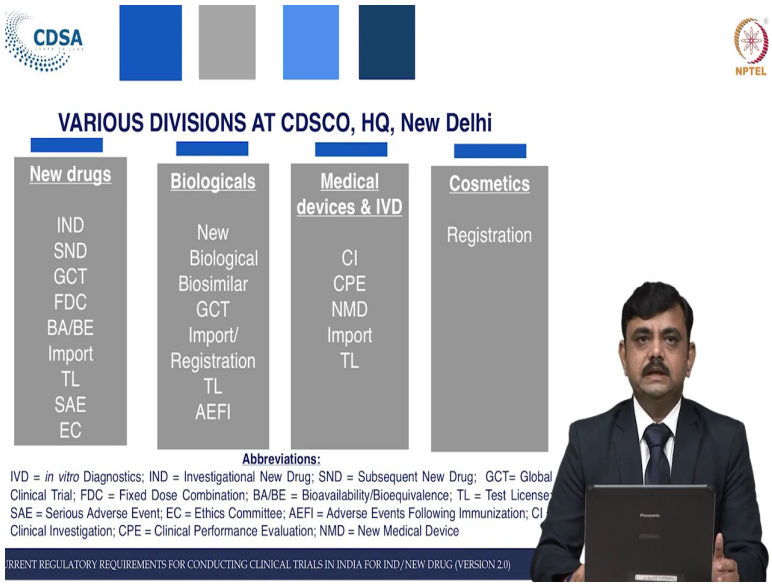

So, mainly there are four divisions; the new drug division, biological, medical device and IVD divisions. Then cosmetic division is also there at the CDSCO headquarter. Under this New drug division, there are again the subdivisions are also there.

The subdivisions are IND division that is which is which is looking after the investigational new drugs and its application, then Subsequent New Drug division, then Global Clinical Trial Division, Fixed Dose Combination Division, then bioavailability, bioequivalence division also it looks after the import and exports of the new drugs, then Test License division, SAE division and Ethics Committee division. Same is for the biologicals also whatever the applications per tempt to new biological, then biosimilar, Global Clinical Trial import registration, Test License, AEFI. These separate divisions are also there.

Then for the medical device and the in vitro diagnostic devices, the department like Clinical Investigation department, then Clinical Performance Evolution department. This is particularly with reference to the in vitro diagnostic. It then the division which look after the new medical devices, then import and test license devices. Cosmetic division is also there which look after the registration of the cosmetic which is required for the import of the cosmetic into the India.

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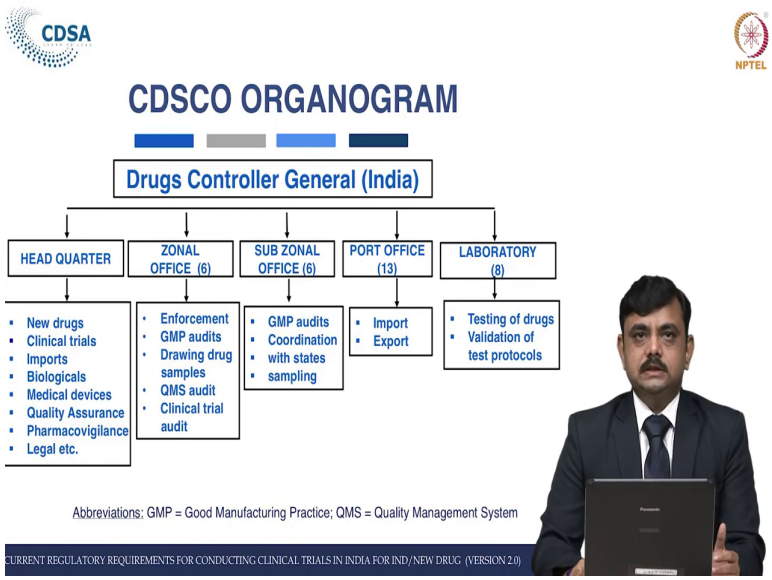

Let us see the organogram and what are the functions at zonal offices and the head quarter offices. So, at the head quarter as what I have mentioned, the different divisions are there. So, these different divisions, there having a different functions like approval of new drug, approval of the clinical trials, then import, export approval of the biological biosimilars,

medical devices. We are also having a quality assurance department which is responsible for maintaining and preparing the SOPs and the data base.

Then further these there is a pharmacovigilance department and the legal cell are also there which will look after the prosecutions matters and the matter related thereof. The zonal offices as I have mentioned in the previous slide, there are 6 zonal offices. Sub zonal offices also are 6 and port offices are 13 and there are laboratories which are 18 numbers.

So, zonal offices they are mainly responsible for enforcement activities and the GMP audit particularly who GMP, then drawing the samples available in the market, then QMS audit which is require for the medical devices and the city audit. The permission of the clinical trial is issued from the headquarter New Delhi and the audit mainly the zonal offices, they are responsible to monitor the clinical trials.

Sub zonal office, they are also having the similar function as that of the zonal offices. They are assisting to the zonal offices and they are also involve in the GMP audits, then coordination with the state licensing authority. The inspectors available, they are they are also drawing the sample and sending it to the test an analysis for the to the laboratories.

Then port offices where having the 13 port offices which are looking after for the import and export of the drug cosmetic and the medical devices and as we know the laboratories, these are responsible for the test and analysis of the drugs which are seen by the drug inspector or regulator or sometimes the customer and they will give the results of this drug and cosmetics. The laboratories are also responsible for validation of the test protocol. Now, we will see what is a state licensing authority.

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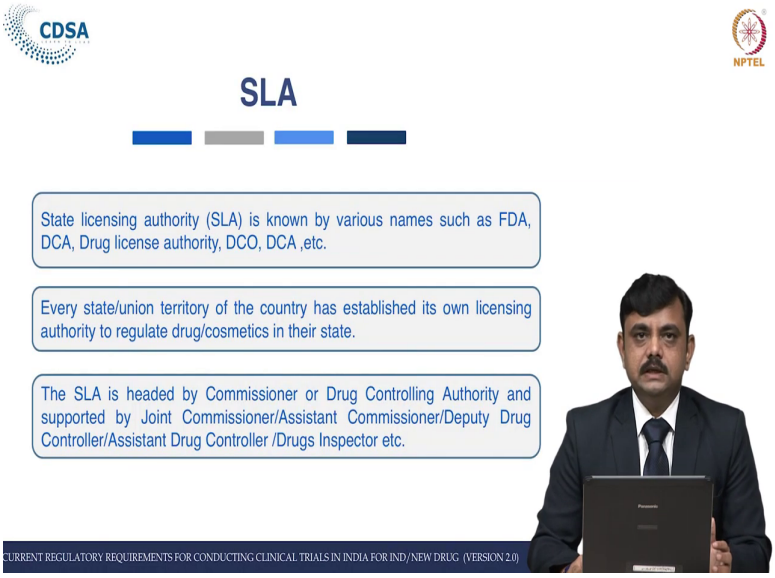

So, the SLA that is a State Licensing Authority is known by various names such as FDA that is Food Drug and Administration, then drug controller authority, drug licensing authority or somewhere it is called as a drug controller authority. Various names have been given in a different-different states. So, every state of the country has establish its own licensing authority to regulate drug cosmetic and medical devices in their state.

The state licensing authority is like unlike disease is headed by commissioner. Sometimes they are called as drug controlling authority and they are also supported by joint commissioner assistant drug controller or assistant commissioner and they are also having a drug inspectors and the supporting staff.

So, beside this CDSCO which is a national regulatory authority and the state licensing authority that is a FDA and DCO. Other department and other ministries are also involve in

the approval of the new drugs biologicals and directly and indirectly they are also involve in activities such as pricing and other activities. Let us have look which are these department administrates which are involve in the process of new drug approval.

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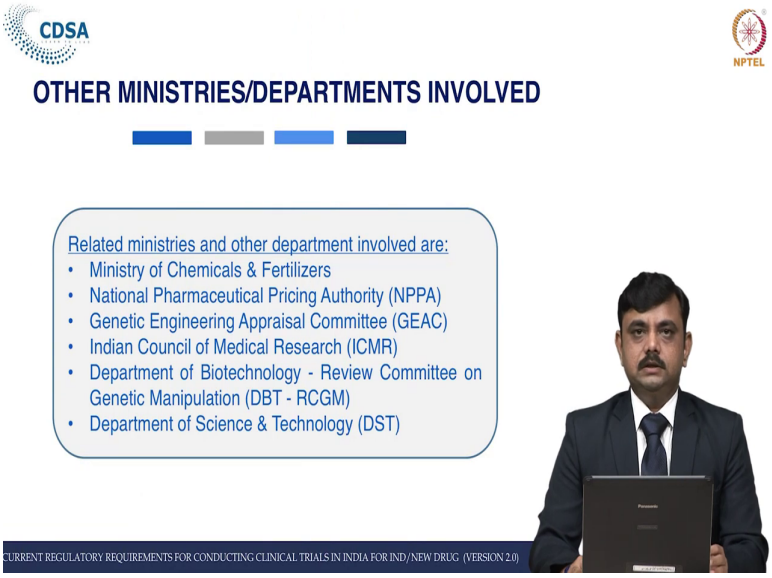

So, these are the ministries and the departments under them. Let us have a look on this slides.

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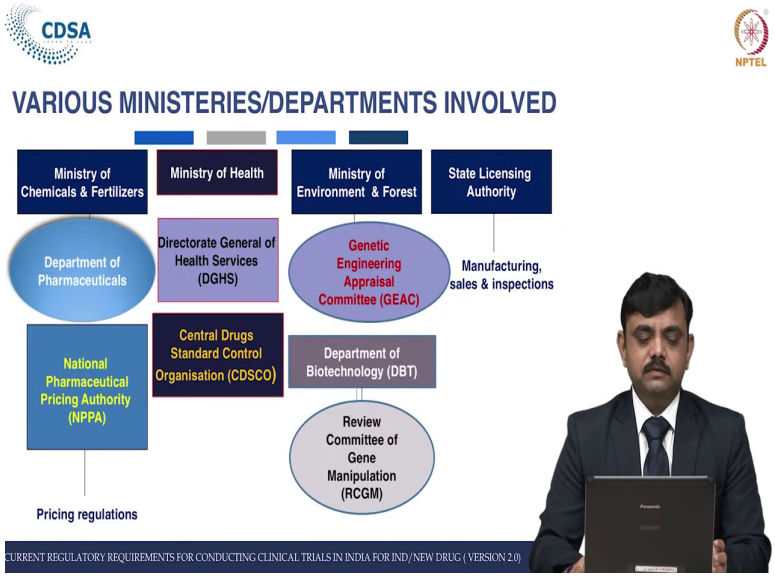

The Ministry of Chemical and Fertilizer under which the Department of Pharmaceutical is there. The Department of Pharmaceutical is having a division National Pharmaceutical Pricing Authority. The National Pharmaceutical Pricing Authority is mainly responsible for regulation of the prices of the drug. As we have seen the Ministry of Health and Family Welfare having a department DGHS under which CDSCO is there which is mainly responsible for giving the approval of the new drugs.

Then the Ministry of Environment and Forest is also involve under the Department GEAC and the DBT that is Department of Biotechnology. It is having a review committee for gene manipulation. So, the product which are related to the gene such as a RDNA and other biosimilar products. So, these ministries are involves in giving the approval of these products for the preclinical and sometime is they recommend for the clinical.

Apart from these we have seen the state licensing authority and these state licensing authorities are mainly involve in giving the permission for the manufacturing of the drug was the drug has become a old. These are also responsible for regulating the cells and the inspections. We will see in the detail what are the functions of the central licensing authority that is CDSCO and what are the functions of the state licensing authority.

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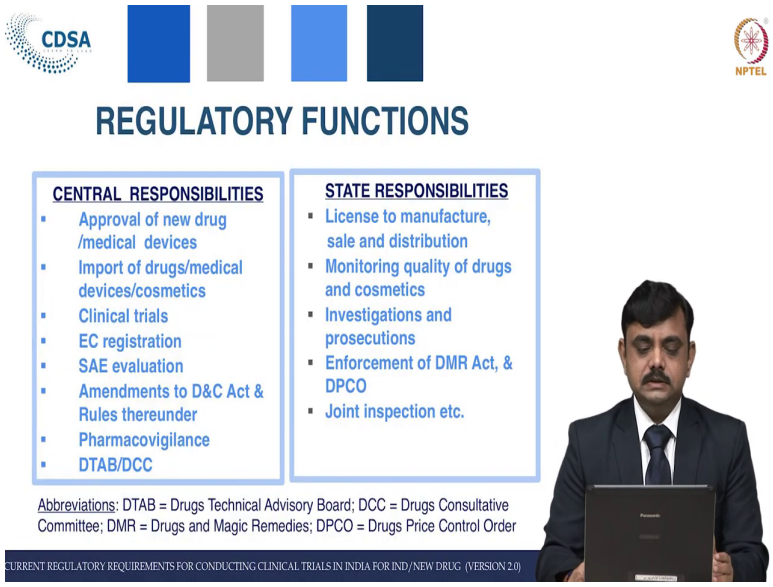

Moving to the next slide that is regulatory functions, the regulatory functions of the CDSCO we have seen in previous slides. The new drug approval, medical device approval, then import of drug, then import of the cosmetic, import of the medical device, then approval of the clinical trials, then ethics committee registration, SAE that is Serious Adverse Event evaluation.

So, that department is also there at the CDSCO headquarter, then amendment of the drug and cosmetic act and rules there under that is also the mainly the function of the central government authority that is a CDSCO. Then we are having pharmacovigilance. The pharmacovigilance is mainly for the collection and monitoring of the SAEs and the adverse events which are happening in the market. Beside these we are having the drug technical advisory board and the drug consultative committees. So, it is the function of the CDSCO to conduct drug technical advisory board meetings. The head of this drug technical advisory in board meeting is DG of in the health ministry.

And the DTAB that is Drug Technical Advisory Board meeting, these are conducted mainly for the giving the advise in the technical matters arising out of the act. For example, if the drug has to be ban or drug has to be prohibited then the proposal has to be put up into the drug technical advisory board and after the sanction or after the consent of these board members that can be enforced. DCC is the drug consultative drug consultative body and which is mainly responsible for bringing the uniformity in the enforcement of the drug and cosmetic act.

So, every drug controller of the state they participate in the drug consultative committee and give its opinion for the uniformity maintaining the uniformity in the state and maintaining the uniformity for implementation of Drug and Cosmetic Act. Let us see what are the functions of state authority. So, the state responsibility is to giving the license for the manufacturing.

So, once the drug has been approved by the CDSCO, then the manufacturing license is issued by the state licensing authority. Then sale and distribution is also the regulation is also the responsibility of state licensing authority, monitoring of quality of drug and cosmetic. So, they are having also the inspectors which are mainly conducting the inspection of the sides and they are also monitoring the quality of the drug and cosmetics available in the market.

Investigation and the prosecution is also the responsibility of the state licensing authority. So, the drug inspector in the consulstate, they pick up the samples and they send the sample to the laboratory for testing and analysis purpose. And if it found substandard or spurious or

misbranded, then it is the responsibility of the drug inspector to launch a prosecution against the manufacturer.

Enforcement of drug and magic remedies act and the DPCO that is Drug Pricing Control Order Act. So, this is also the mainly responsibility of the state licensing authority. The DMR act is mainly related to the misadvertisement of the drug or advertisement of the drug which is not acceptable legally.

The state drug inspector, they are also participate in the joint inspection that is inspection with the CDSCO for the giving WHO GMP certificate and in certain cases of medical devices for giving the manufacturing licenses for the medical device applicant. So, these are the responsibilities of state and the central government. Let us have a look on the initiative taken by the CDSCO and the achievements done by the CDSCO in the recent few years.

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As you know that the 344 irrational fixed dose combinations are prohibited under drug and cosmetic act by the CDSCO though the matter is subjudiced in the court. And with the make in India the various measures has been taken by the central government for ease of doing business. These are the various activities done for the ease of doing business. E-governance system introduced that is the we are having a SUGAM Portal which is also known as a Suraksha Gunavatta and Manatta.

So, most of the applications is now accepted through the online. Then government has published a New Drug and Clinical Trial rule which is effective from 19 -3-2019. Warlier there were no medical devices rule only three-four medical devices rules were there and these medical devices where consider as a drug and they are the permissions are given under the Drug and Cosmetic Act. Now, to bring the clarity in the medical devices a separate rules has been published which is called as Medical Device Rule 2017 and which is effective from first January 2018.

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In the recent years nation wide drugs survey also has been conducted by the CDSCO along with the national institute of biologicals and around 47000 drug samples have been randomly picked up from the market and tested in different government laboratories to see the extent of not of standard quality drugs see the misbranded drug and the spurious drug.

Then again central government has a started the pharmacovigilance department to see the SAEs and adverse event which are happening in the markets for the new drugs. Haemovigillance is also the same, but it is for the blood related products, then we have started the materiovigilance to see the SAEs and AVS with respect to the medical devices.

Testing of cosmetics on animals has been prohibited. So, wherever there is a no requirement of the using the animals and wherever there are alternative methods as per the OECD

guidelines are available so, in that cases and in the case of the cosmetics the testing of the cosmetic on animal that has been prohibited.

Earlier there were no timelines prescribed for the processing of application now, all the timelines has been prescribed for the speed processing and the disposal of the applications.

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Few of the offices which are at the port offices, they have been working 24 by 7 for the speed approval. This is one of the great achievement that CDSCO was declared by who as a functional National Regulatory Authority against stringent international indicators.

So, the who conducts audit for the every countries regulatory authority to assign them the maturity levels and the CDSCO has been audited by the WHO and other 14 countries people that is they are the regulators and they have assigned the maturity level 4 in most of the most

of the indicators and this maturity level 4 is the highest second of the maturity level available in the glob. CDSCO has established public relation office as a single window system for grievance redressal.

Then we have started the intelligence cell which is at CDSCO headquarter and this cells collect the information from the market and based on that the CDSCO has conducted various raid in the market and seized the drugs and cosmetic which are illegally available in the market. So, this is the achievement and initiative taken by the CDSCO and central government. While doing this functions the CDSCO is having many gaps and challenges.

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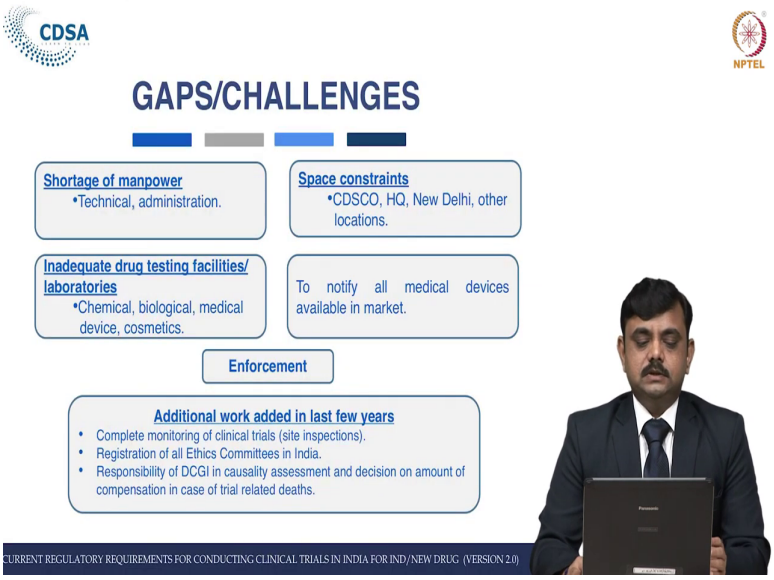

So, we will see the what are these gaps and challenges. CDSCO is with the shortage of manpower that is we are around only 223 inspectors across the country. So, this is a major shortage then inadequate drug testing facilities and laboratories. Though we are testing one

lack samples every year, but still it requires with the quantum of the industries and the product available in the market.

We require to still test more and more drug to value added, it is a quality and the efficacy. The whatever the laboratories they are available that are now inadequate. Then again there is a space constraint with the increase in the officers of the CDSCO and the manpower the space has remained same. So, it is a space constraint.

Then one of the major challenge the CDSCO and central government is facing to notify all the medical devices in market. Enforcement activity is little bit lagging behind because of the shortage of the manpower and the other constraint. CDSCO has been assigned with a additional work and this additional work is complete monitoring of clinical trials site inspections. Then registration of all ethics committee in India, those ethics committee which are giving the approval to the clinical trials.

Earlier there were no registration of these ethics committee and you know recently it has been started to register all the ethics committee. Responsibility of DCGI in causality assessment and decision on amount of compensation in case of trial related deaths. So, this is again the additional responsibility given to the DCGI to amount for compensation in case of clinical trial and clinical trial related in death. So, this is about the CDSCO and its offices the functions of the CDSCO and state licensing authority.

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Let us have look what we have learned in this lecture. So, in this lecture, we have seen the CDSCO, its different offices including its hierarchy, then what are the sub zonal offices and what are the laboratories there, its function, then various department at CDSCO headquarter New Delhi. These departments are new drug department, then medical device, cosmetic departments, biological department which are having again the subdivisions also. We have seen the responsibility of state and centre. The centre is having the main responsibility to give the approval for the clinical trial medical device, new drugs.

The state is having the main responsibility to give the approval for the manufacturing licenses and the GMP inspections drawing the samples. We have seen the achievement by CDSCO, then we have seen the regulatory gaps challenges faced by the CDSCO. So, this is all about the CDSCO.

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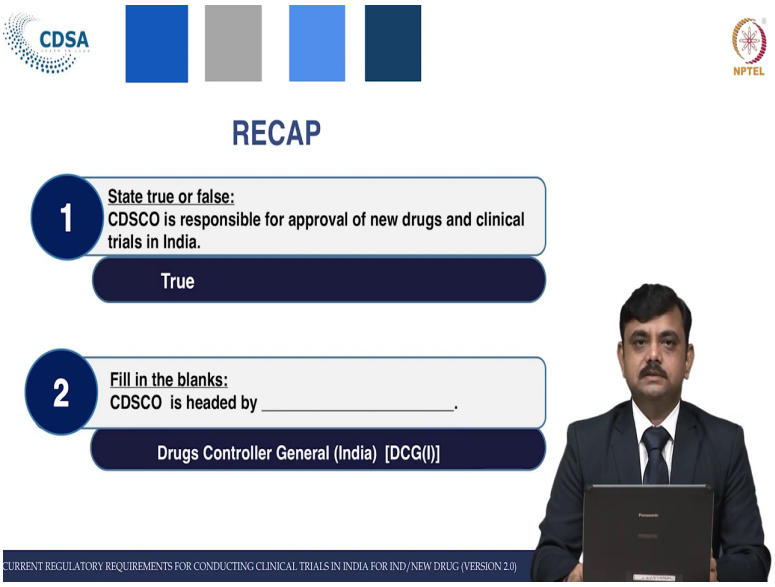

Now, it is time for you to give the reply of these question to check your memory. The first question for you, these are very simple questions. So, you have to tell the true and false. The first question is CDSCO is responsible for approval of new drug and clinical trials. So, your time start now, yes it is true; the CDSCO is responsible for approval of new drug and clinical trial in India. The next question CDSCO is headed by you have to tell the; what we call the head of the CDSCO. I will give you the hint, it is a DGCA, Commissioner or DCGI; yes DCGI is the head of this organization.

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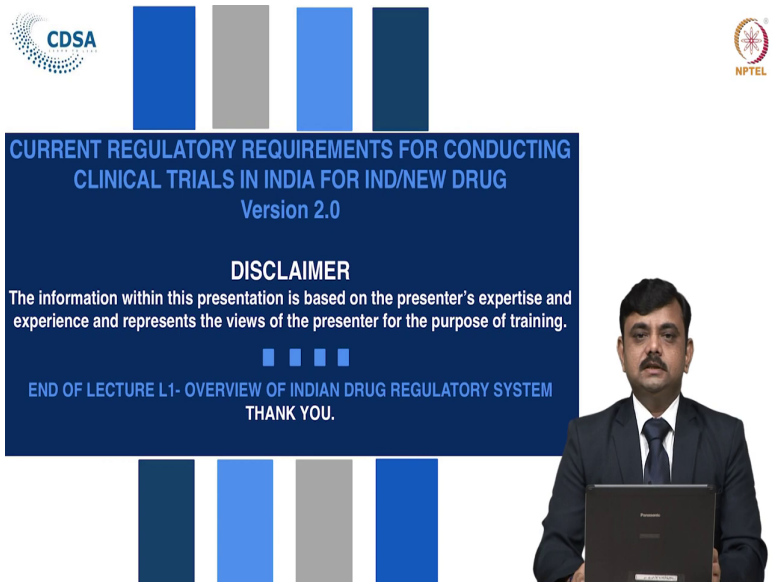

So, this is the first lecture of version 2 course current regulatory requirement for conducting clinical trials in India for new drug and the investigational new drug. We will be back soon with the lecture 2, till then you take care bye and all the best.

Thank you.