Regulatory Requirements for Medical Devices and IVD's in India

Prof. Aseem Sahu
Prof. Malay Mitra
Department of Biotechnology, Ministry of Science and Technology,
Department of Higher Education, Ministry of Human Resource Development,
Government of India

Lecture – 11
Inspection of Medical Devices and IVD Establishments

Welcome to Regulatory Requirement for Medical Devices and In Vitro Diagnostics in India, lecture 9. Lecture 9 that is the Inspection of Medical Devices and In Vitro Diagnostics Establishments.

So, in this lecture you will be understand, what is the inspection? What is inspection? Inspection of the establishment or the manufacturing site; why inspection is required to be carried out at the premises? Inspection of the medical devices and in vitro diagnostic, what is; what will be the conformance with respect to the quality management system for manufacturing of medical devices and in vitro diagnostics? Who does the regulatory inspection? Inspection, there are different types of inspection. It is not [FL] all the inspection is considered as a regulatory inspection. Regulatory inspection means for the purpose of grant of manufacturing license for import, for manufacture into the country.

So, that all those inspection, what types of the inspection are there? Where it is required? What in the inspection? What need to be verified? All those part we will discuss in the, in this lecture. And in this lecture, the lecture will be again done by Dr. Malay Mitra, who was the former Deputy Drug Controller in CDSCO; having lot of regulatory experience and knowledge in the medical device and in vitro diagnostics.

So, in that lecture why the inspection is done; you will be understand inspection of the establishment licensed or to be licensed under the drugs and cosmetics are carried out. Why it is carried out? To evaluate, if the facility have been set up according to the norms or the provisions as stated in the fifth schedule of the medical device rule, 2017. What is fifth schedule? We have already discussed that in the general discussion on the medical device rule.

Fifth schedule is the quality management system; requirement of the quality management system for manufacturing of medical devices and in vitro diagnostics. So, under this

lecture you will understand types of the inspection, what different types of inspection are carried out at the manufacturing premises or establishment? Some inspection that you can call as regulatory inspection that inspection is required for before grant of manufacturing license. Some is inspection carried out for the verification of the non compliances which were observed by the inspection team.

Some inspection based on the complaint, if somebody has raised complaint or some concern was observed by the regulators. As a part of investigation they will again inspect the premises that will also called as a regulatory inspection. Self inspection that is the responsibility of the manufacturer; that is the one of the responsibility being conformist with the quality management system; the manufacturer may have the provision for self inspection or self audit. In that audit, he can hire the external experts for inspection to verify whether the conditions of the license, given by the licensing authorities is complied or not.

So, these are the various different types of the inspection that you will learn more about this inspection in this next lecture; which will be given by the Mister Malay Mitra. And who does the inspection to the manufacturer premises? Also you will be and you will be knowing that already we have discussed the in the medical device from 2017.

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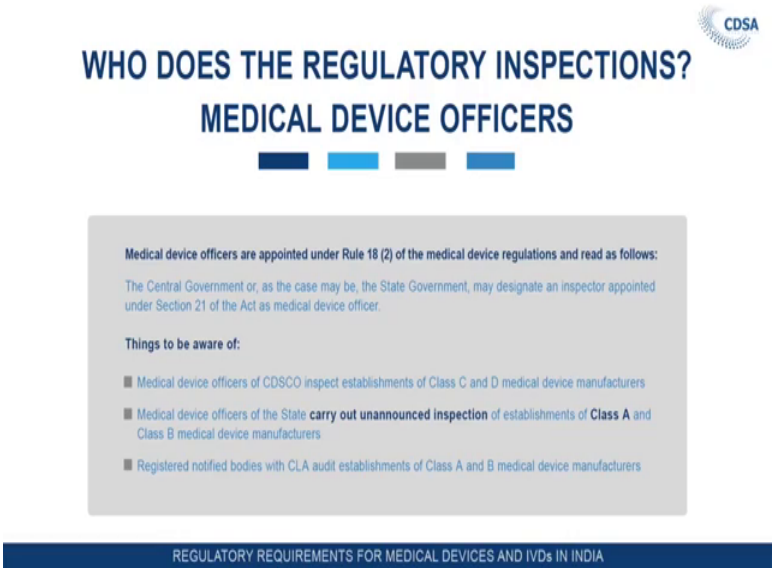

The person appointed as a medical device officer under Rule 18, sub rule 2 of the 18 will be responsible for inspection of the premises. It is not anybody can go there to inspect

the premises. Only as per the medical device rule, medical device officer he will be responsible. Medical device officer engaged in the center with central assessing authority. They will be responsible for inspection of Class C and Class D manufacturing unit.

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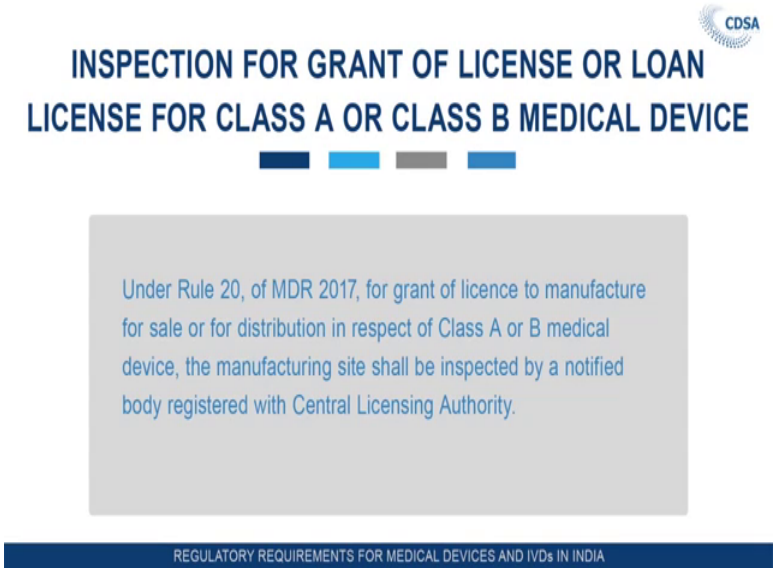

And notified body also we have discussed. How notified body will be responsible for audit of Class A and Class B medical devices. Who will be the notified body? The notified body, who have already registered with the Central Licensing Authority, only will be responsible for audit of Class A and Class B medical devices.

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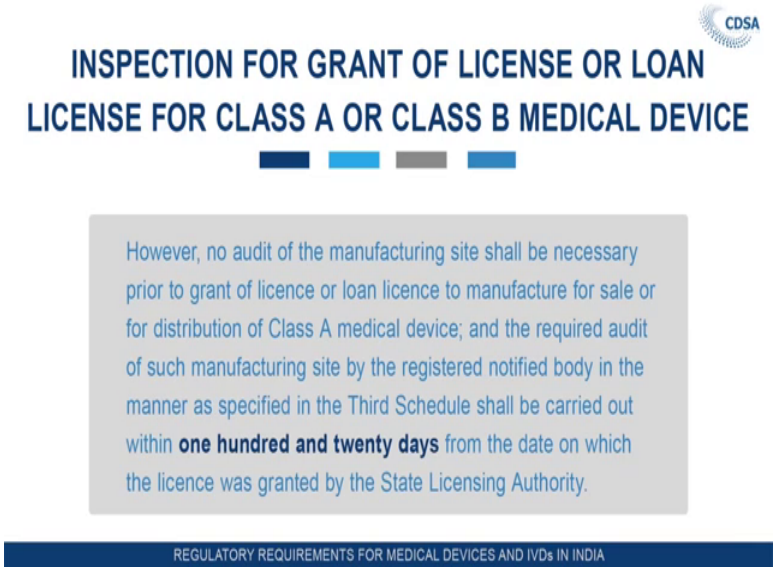

And also the medical devices of medical device officer appointed by the State Licensing Authority; they will verify the 2 percent of the inspection carried out by the notified body with respect to the conformance of the QMS.

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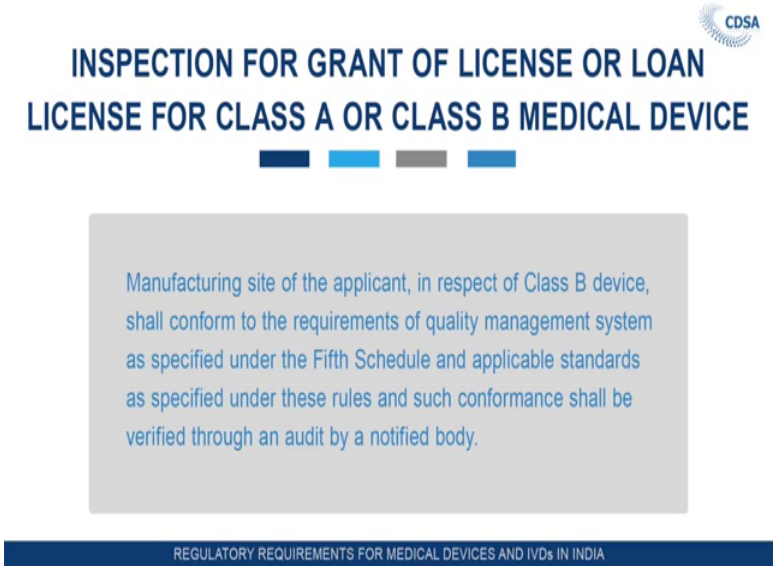

So, these are the competent technical staff personnel appointed under the medical device rule, 2017. Who will be responsible for inspection of the manufacturing site? And based on the inspection of these officials the licensing authority can grant the manufacturing license for a manufacturer of medical devices and in vitro diagnostics. So, all these

details you will be, understand in the detailed presentation on the lecture 9 that is the inspection of the medical device and in vitro diagnostic establishment. So, concentrate on the lecture and again, I will again tell you. If you have any doubt, you please come back to us. We will be further clarified. Thank you very much and enjoy the lecture.

Thank you.

Hello friends, this is one of those inspections in a series of inspections on medical devices. And, this time we are going to talk on inspection of the medical device and IVD establishments. We know inspection is one of the most important aspects during licensing.

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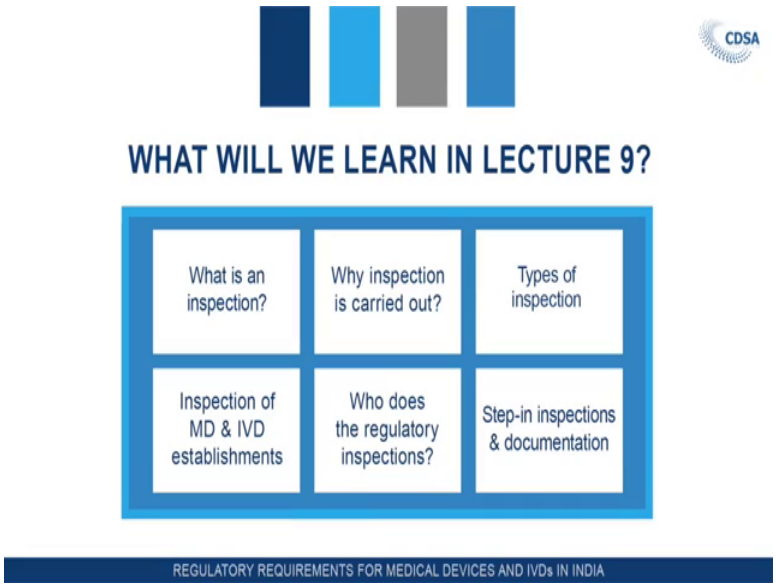

And any manufacturer or an applicant for manufacturer medical devices has to go through inspection or inspection of their establishment. And this particular presentation will explain the overview of, how the inspections are carried out? And types of inspections and who carried out the inspections? And a general view of what is actually expected a few to get inspected on?

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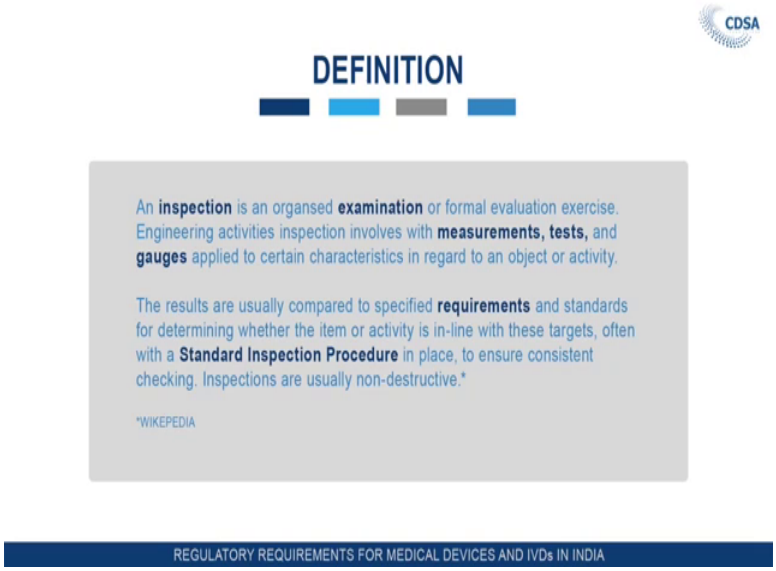

Let us see the definition of inspection as per Wikipedia; inspection is an organized examination or formal evaluation exercise. In engineering activities inspection involves the measurement tests and gauges applied to certain characteristics in regard to an object or activity. The results are usually compared to specified requirements and standards for determining with that item or activities in line with these targets often with the Standard Inspection Procedure in place, to ensure consistent checking inspections are usually non-destructive.

So, what is an inspection? Inspection is not testing; testing is actually destructive practice, but in the inspection what happens is your plant, equipment, manpower, procedures go through a series of examination by certain trained people and what they do is they compare what you are doing with standards, standard practices and objectives that. Those activities should meet up to. In case they meet up to you pass a standard and your inspection is successful; if not then, you have to go the extra mile to comply with the requirements.

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Why inspection is done? Inspection of established, establishes license or to be licensed under the drug and cosmetics act are carried out to evaluate if they have been set up according to norms as stated in the regulations. The establishment of various arms in person are compared with this prescribed conditions and a conclusion is reached whether it can be licensed or not. The following slides include the requirements for obtaining a license which are examined during an inspection.

Now, this is basically, a inspection procedure based on inspection of a manufacturing plant for medical devices. However, the same criteria is applied in any inspection under drug and cosmetics act broadly. So, the slides are specify specific from medical devices, but can be applied to any inspection required.

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Now, this is actually the inspection cycle. There is no cycle of inspection and audit is carried out and deficiency find out. A short coming to find out obtained in the inspection. And these are removed by the applicant and then re audit is carried out. This cycle goes on until and unless all the deficiencies are removed and the audit becomes successful.

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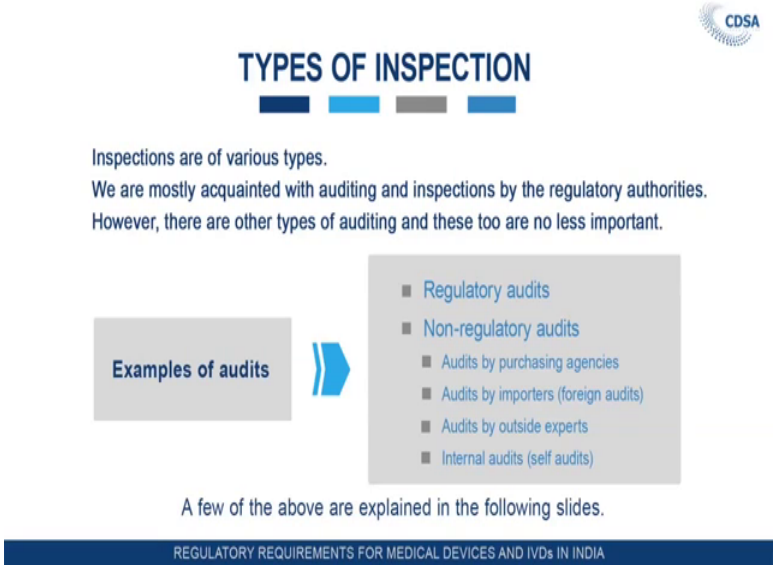

Inspections are the various types; we are mostly acquainted with auditing inspections by regulatory authorities. There are other types of is auditing also and are no less important. They are broadly as follows. Regulatory audits we shall describe this in the subsequent

slides; audits by purchasing agencies. When your product has to be purchased by a vendor, he can audit your facilities which is known as the vendor audit or a pre-purchase audit. Audits by importers by foreign agencies you want to export to foreign country they can come and audit you, that is an audit similar to the regulatory audit; audits by outside experts, an expert from outside is hired by you to carry out a specific audit on qualities and that is also an inspection.

Internal audit or self audit is done by the manufacturer himself to find out the compliance with regulatory requirements or any other requirement that is essential in for your manufacturing. Some of the above we explained in the following slide; especially, the regulatory audits. We are not concerned about audit by purchasing agencies etcetera. Those are separate chapters all together and are not in the scope of this particular presentation.

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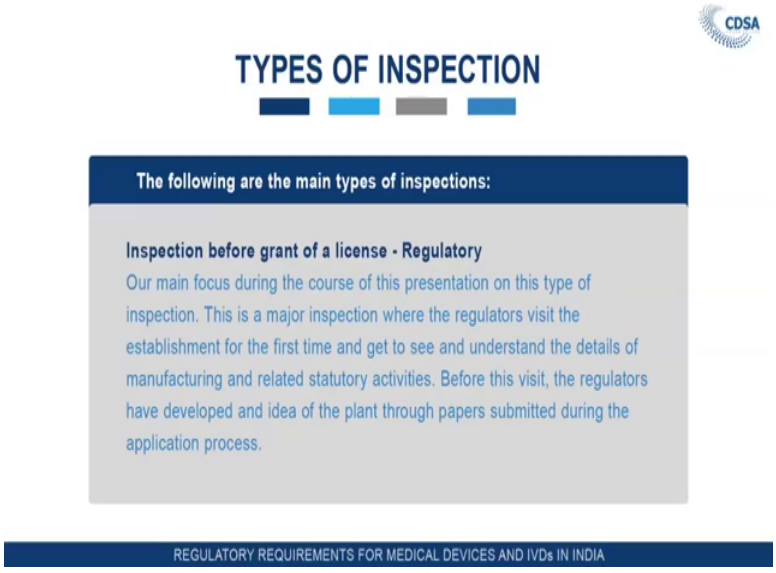

The following at the main type of inspections; before or inspection before grant of a license. This is a regulatory audit. Our main focus during the course of this presentation is on this type of inspection. This is the major inspection where the regulatory visits establishing for the first time and get to see and understand the details of manufacturing related statutory activities.

Before this visit, the regulators have developed and developed the idea of the plant through paper submitted during the application process. Remember, an auditor or a

inspector or a medical device officer in this case will visit your plant after you apply for a license along with document. And those documents have the details of your plant and equipment and process and procedures. He has studied those things and he has come to your plant to actually verify whether you submitted everything in a proper and honest manner.

Second especially, inspection for continuation of a license; this is also a regulatory inspection. And license is issued to manufacturing medical device or IVDs is valid perpetual; that means, it does not have the expiry date. And it is valid indefinitely; however, its continuation has to be maintained by payment of fees and if necessary undergo an inspection. These inspections are actually re-evaluate the system of an establishment for continuation of its license; the inspection of a medical device session have to be carried out once a year on routine. So, your license is a perpetual; however, before 5 years you have to apply for it and get the license continuation carried out. So, it is perpetual every 5 years, renew it.

Second is the law says, the medical resolution says apart from the inspections for continuation of license; your plant has to be inspected every year on the routine. So, whether you like it or not every year some officer will enter your plant and check them. These inspections that actually to maintain the systems in your plant and the GMP procedures, that you carried out. And these inspections will find out and tell you also whether you are missing out or certain things or you slipped on certain areas where, you have to pull a pull yourself up. Then, we come to investigative inspections. This is also regulatory inspection.

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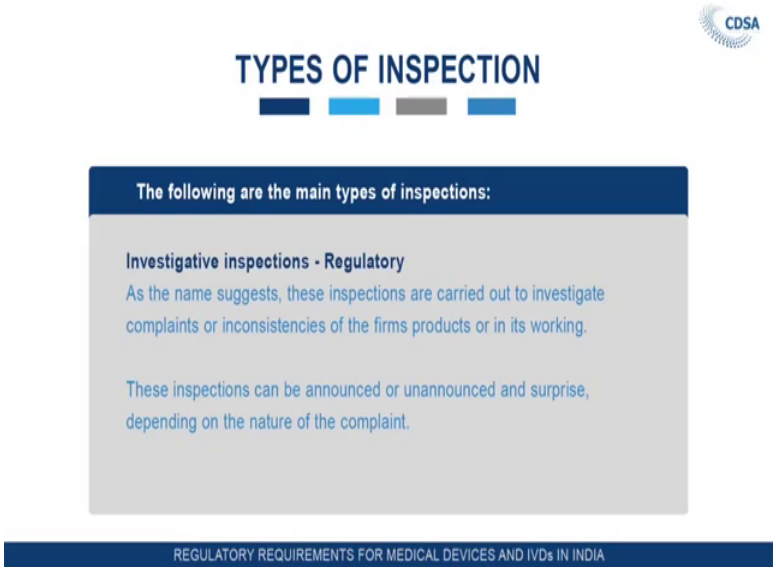

In this case, what happens is as the name suggests, these inspections are carried out to investigate complaints or inconsistencies of the firm's products or in its working. These restrictions can be announced or unannounced and surprised depending on the nature of the complaint. So, in case you have one of your products is found to be causing some reaction in some patients somewhere, in the country or abroad. The regulator may visit your plant without even announcing and carry out a detailed audit over that particular product and we have planned to find out whether it is or united from your plant or not.

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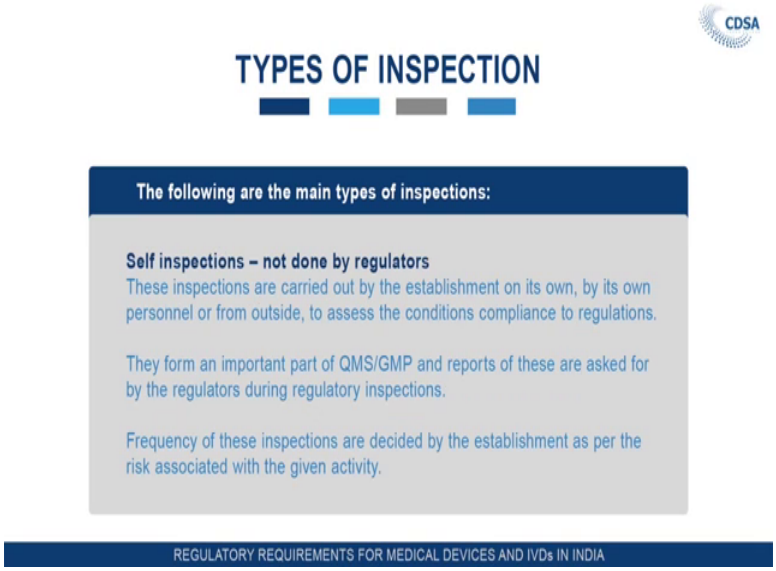

So, this is actually investigative inspections. Self inspection; this is not a regulatory inspection. In this case of course, as the name suggests these inspections are carried out by establishment on its own by its own personnel or from outside to assess the conditions compliance to regulations. They form an important part of QMS GMP and reports of these are asked for by regulators during regulatory inspections.

Frequency of these restrictions are decided by the establishment as per risk associated with the activity. And this particular self inspection has been mentioned in the regulations very very clearly. So, this is also a compulsory inspection to be done by you. And self inspections are not necessary; a fixed period inspection, a plant may have self inspection or a particular risky area every three months or four months and generally stable area every year as per the requirement.

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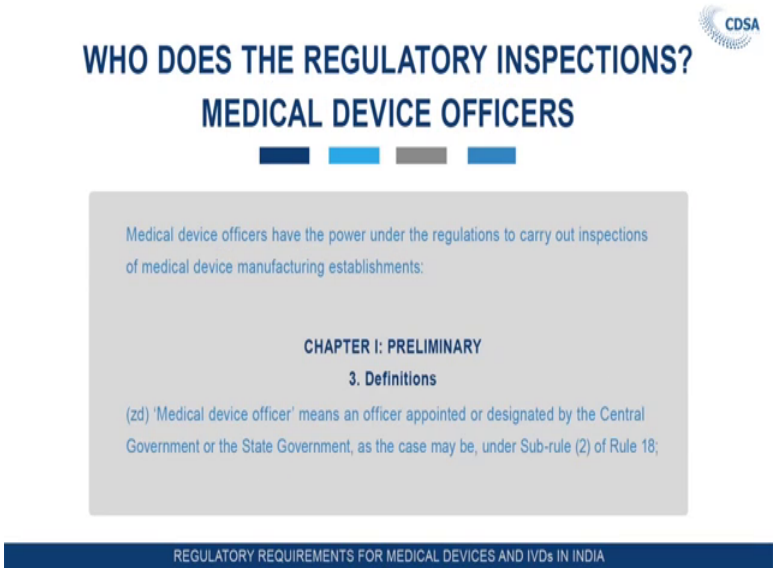

So, this is decided by the firm itself. Who does the regulatory inspection? Now, we come to regulatory inspections because this is for our focus. Medical device officers, who are medical device officers? They have the power under regulations to carry out inspections of medical device manufacturing establishment. This is chapter I Preliminary in the regulations. The definition of medical device as mentioned by zd; at z d whereas, indeed medical device officer means an officer appointed or designated by the central government or the state government as the case may be under sub rule 2 of rule 18.

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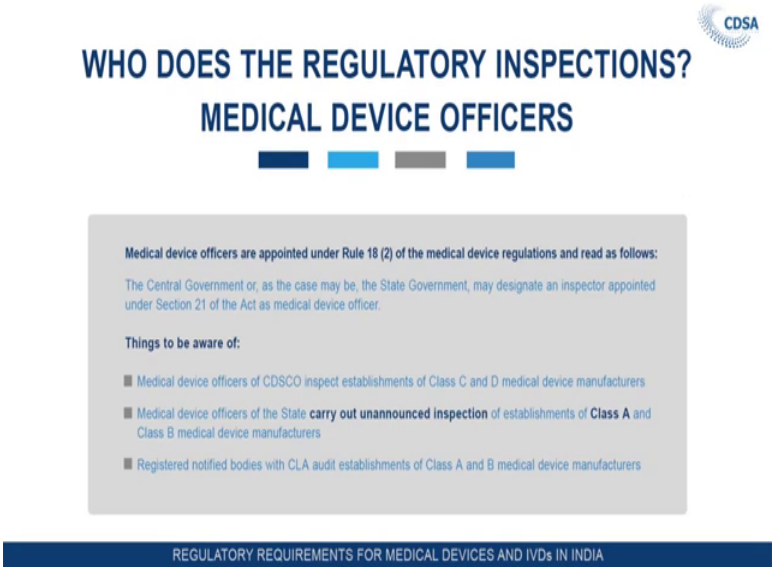

Medical device officers appointed rule 18 2 of the medical device regulations and read as follows. The central government or as the case may be the state government, may designate an inspector appointed under section 21 of the Act as medical device officer. So, what does section 21 say, section 21 of the drug and cosmetics act, which is the mother act of the regulation. All regulations section 21 says the government can appoint inspectors to carry out inspections of facilities under the drug and cosmetic act.

Now, that inspector has been designated as a medical device officer in the regulations. And under that section, they are appointed under rule 18 2. So, they have the powers as per the drug and cosmetic act. The powers, powers include, power of medical device officers under the act include inspection search and seizure, taking samples etcetera. Important to mention that medical device officers are expect a establishment of Class C and the medical device manufacturers. This is a CDSCO inspector, who has the power to inspect Class C and D medical device manufacturers.

Because the C and D D medical device manufactures are licensed by CDSCO and not by the state government. Similarly, medical device officers is also the state inspect establishing of Class B medical device manufacturers. I recruited notified bodies auditing establishment of Class A and B medical device manufacturers.

Now, this does not mean that Class B medical device manufacturers cannot be inspected by particularly by the officers of Class C and D because the application goes through

both of them in case of class B medical device manufacturers and both can carry out the joint especially required.

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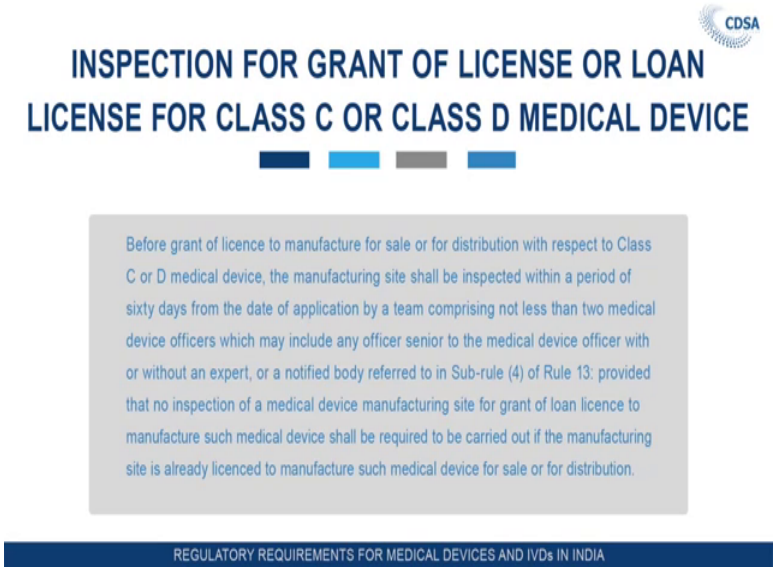

Inspection for grant of license or loan license for Class C or D medical device; before grant of license to manufacture for sale or for distribution with respect of Class C or D medical device, the manufacturers site shall be inspected within a period of sixty days from the date of application by a team comprising not than the two medical device officers which may include any officer senior to the medical device officer or with or without an expert or notified body referred to subsection 4 of Rule 13.

Now, this is the power given for inspection to the CDSCO. The CDSCO under this particular provision can carry out an inspection. And it comprises of a minimum of two persons and a maximum of three persons. I mean the two persons, who are the two persons, a team comprising not less than two medical device officers; one is senior to the other. And, if required an expert on the medical device can accompany them.

So, it will be a team of maximum three officers, who will visit and carry out the inspection. Provided that no inspection of a medical device manufacturing site or for grant of loan license to manufacture; such medical device shall be required to be carried out. If the manufacturing has already license to manufacture such medical device for sale or for distribution; this actually means that if there is a plant which manufacturing safe hypodermic syringes, plastic, disposable hypodermic syringes on their own for

marketing. Now, I as a manufacturer who does not have a plant; I apply for a loan license the same plant where, this is manufactured and I get a license to manufacture a plastic disposable syringes; a similar type that can parent for manufactures.

In that case I the plant may not be inspected for my product sake. I may be granted license looking into the mother plants capabilities to manufacture the products.

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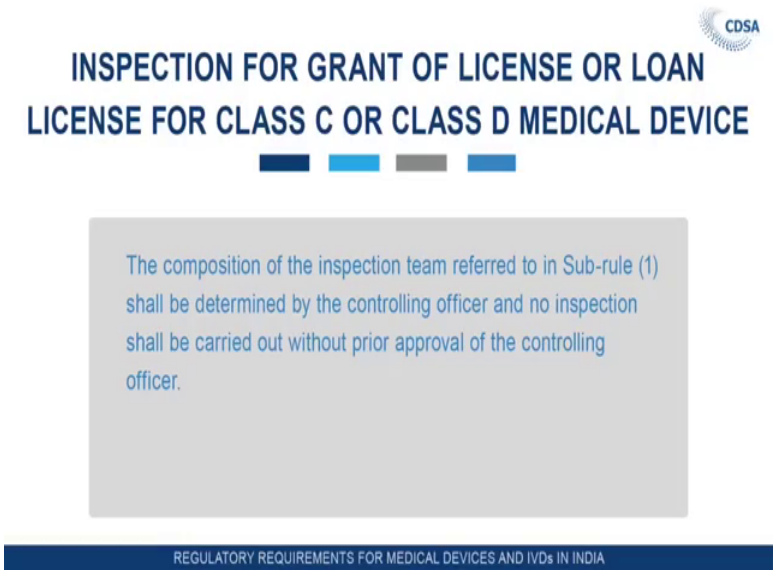

The composition of the inspection team referred to in subsection sub rule 1 shall be determined by the controlling officer and no inspection shall be carried out without prior approval of the controlling officer. So, the controlling officer is a person who is also mentioned in the drug and cosmetic act who can be a controlling officer.

He can be a drug controller; he can be a person under the drug controller with this all the powers come delegated to somebody under the drug controller. So, drug controller has to authorize an inspection to be carried out. So, inspector cannot be enter a enter a plant; he cannot enter a plant without the prior approval of this, his senior controlling officer. What is inspected?

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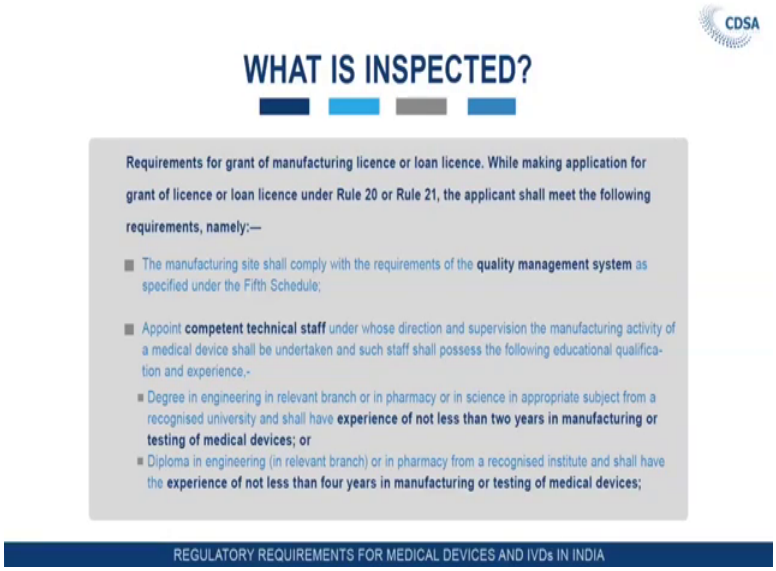

Now, we lets come to the actual inspection portion and what is respected by medical use officers? While making application for a grant or license or loan license under Rule 20 Rule 21, the applicant shall meet the following requirements namely; the manufacturing site shall comply with the requirements of quality management system as specified under the fifth schedule. That means, quality management system is also inspected while the inspection is going on because you apply for a grant of license and you have to comply with QMS.

Appoint competent technical staff under whose direction and supervision the manufacturing activity or medical device shall be undertaken and such staff shall possess the following educational qualifications. Now, this competent technical staff will read means that you have to appoint certain people who have got knowledge and who are able to manufacture those products. And, they are competent to do that by virtue of their experience and education qualification as mentioned. So, this is something also which is examined by the time of inspection.

Now, what did you; what these competent technical staff should possess? A degree in engineering or in the relevant branch or in pharmacy or in science or in appropriate subject from a recognized university and shall have experience of not less than two years in manufacturing or testing of medical devices. Now, you require a person, competent

person for manufacturing as head of manufacturing and a competent person head of testing.

So, you should have two persons of that level, who have got a degree in the engineering etcetera and has got at least two years experience in the type of product that is going applied for to get a license. Number 2 is b diploma, if we; if you if you have a person with diploma not a degree then, the same; same qualifications are required in diploma with an experience of not less than 4 years; that is earlier for degree, it was two years; for diploma, it is four years for testing, on a testing of medical device and manufacturing medical devices.

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Appoint competent technical staff with degree or diploma in engineering in relevant branch or in pharmacy or in science or relevant subject and having experience of not less than two years in testing of medical devices under whose direction and supervision, testing activity of a medical device shall be undertaken.

So, a person who is actually having an experience of less than two years not less than two years and has a degree in diploma in a relevant field has to be appointed as head of the testing of the, of the medical device in the plant. So, this is very clearly mentioned and these portions experience and qualification are also part of the inspection system, in which these are examined in detail by way of examined documents and experience

certificates etcetera. And only then, the regulatory authorities the inspectors can take a decision whether they are competent to manufacture that for products or not.

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Inspections are basically based on QMS. and gmp. Every aspect of an establishment is inspected in detail by the medical device officers are include, but is not limited to such aspects at the buildings, manpower, equipment etcetera. Though, examination of the manufacturing and testing aspects is given focus. So, inspection is carried out of the buildings; what kind of factory or building you have got walls etcetera? The (Refer Time: 24:05) system, the equipment that you procured to manufacture this product etcetera.

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Steps in inspection, what is the general step carried out everywhere including all over the world in the inspection? The following steps are actually carried out. First is your introduction meeting; there is a preliminary meeting for introduction and outlining the plan of the inspection, discussion on technical matters are also taken up. This is the first step when, a medical device officers team enters a plant.

The second phase is your inspection phase. In this case, the actual walkthrough inspection of the premises is carried out examining the facilities, machinery and procedures. So, they walk through the whole facility right from the raw materials stage to the finished stage, going to the laboratories etcetera and recording everything that they see and any deficiencies that they see in the process. Examination of documents is the next stage and interviewing people is done after the walkthrough inspection.

So, after the walkthrough inspection; they sit down at a particular place. They will ask for documents for backup. For backing up what they saw during the inspection also backing up because that they have submitted in the application. And in this; this is the particular stage when, they come in contact with the technical personnel or other personnel whether they are trained or not, whether they know their subject or not. And this is also recorded in the inspection report.

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Then, the report is prepared; a report is prepared summarizing the outcome the inspection documents are collected. Then, at the end of the day you have a closing meeting; in which general discussions carried out over the plant and the inspection is as usual ends over there.

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Now, let us come to the specifics of, what is actually seem to be inspection? The plant master file, this is prepared by the plant and submitted to the regulators before a inspection is carried out. This gives actually a birds eye view of the plant right from the

very beginning; what is generally inspection personnel premises? So, very concise document, crisp document not a very lengthy document. And before a regulator enters a plant, he can go through the document. And gets a nice picture of the plant, what is going to expect when he goes in the plant?

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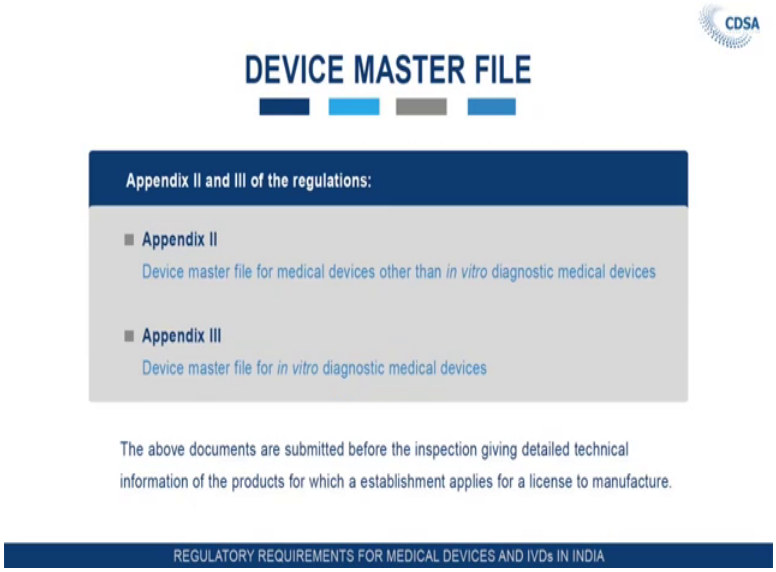

Then, we come down to a device master file. The Appendix II and III of the regulations describe this. The Appendix II is the device master file for medical devices other than in vitro diagnostic medical devices. Appendix III is device master file or in vitro diagnostic medical devices which is actually reagents.

The above documents are submitted before the inspection giving the detailed technical information of the products for which establishment applies for a license. This document, the device master file document is gone through with a lens in the regulators office before the inspection is carried out. And any queries regarding the product detail is answered at that point of itself. It is asked by the regulator and the applicant replies to that. And only after complete such a session that the product is as per the device master file; that the inspection stage is carried out.

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Fifth schedule rule 20 3, 20 5, 20 8, 22 i quality management system for Medical Devices and in vitro diagnostic Medical Devices. This is the most important portion in the regulations, which actually guide the inspectors and also the applicant to set up their plant according to the norms.

The most important part in the in the inspection, compliance to this schedule ensure that inspection will be successful. Compliance ensures the safety and effectiveness of a device. This is more or less the same as ISO 13485 which is internally accepted QMS, internationally accepted QMS for medical devices and in vitro device devices. So, you have to follow 13485 completely; which is actually the QMS as mentioned in the Medical Device Regulation, 2017.

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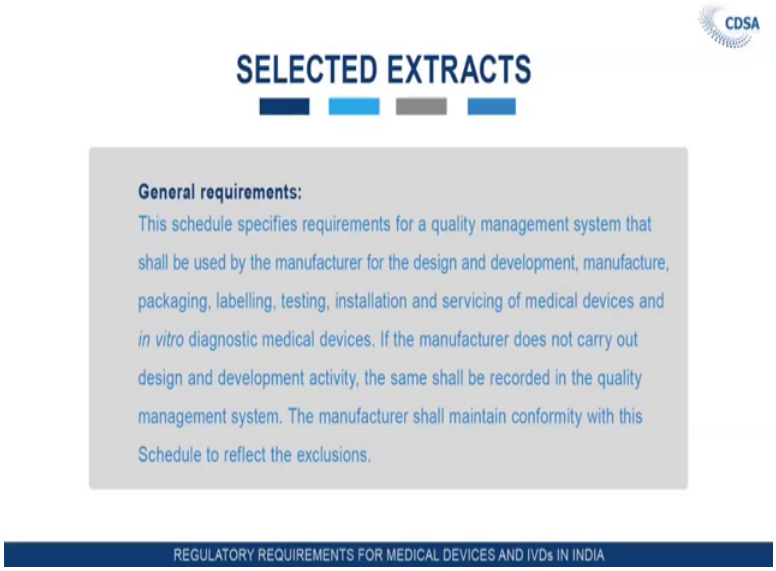

Now, selected extracts of this quality management system is explained over here. So, that we get an idea what is actually seen during the inspection. General requirement, this schedule specifies requirements for quality management system that shall be used for the manufacturer for the design and development manufacture, packaging, labeling, testing, installation and servicing of medical devices and in vitro diagnostic medical devices. If the manufacturer does not carry out design and development activity the same shall be recorded in the quality management system.

The manufacturer shall maintain conformity with the schedule to a reflect exclusions. So, this actually what does the general requirement require? It says that it shall be used to design and develop the manufacture packaging, labeling, testing, installation and servicing of medical devices. All these areas are very clearly at the requirement under the general requirements of the QMS the system of the Medical Device Regulation, 2017. And, each one of them has been given in detail everywhere.

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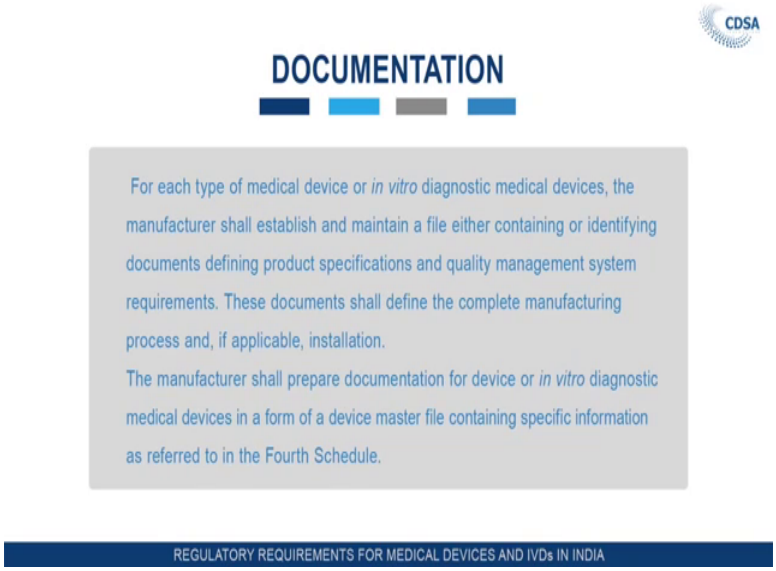

Another very important portion that is inspected is the documentation. Each type of medical device or in vitro diagnostic medical device, the manufacturer to establish and maintain a file either containing or identifying documents defining product specification and quality management system requirements. These documents shall define the complete manufacturing process and if applicable, installation. The manufacturer shall prepare documentation for device or in vitro diagnostic medical device in a form of a device master file containing specific information and referred to in Fourth Schedule.

So, documentation being one of the most important portions of important parts of a manufacturing plant; documentation actually will clearly mention anything that is carried out in the plant and that is recorded again. So, that there is a traceability on activities carried on the plant. Documentations are actually prepared with care and they are authorized for you. You cannot keep on changing documents day in and day out. They are all fixed documents and cannot be changed that easily.

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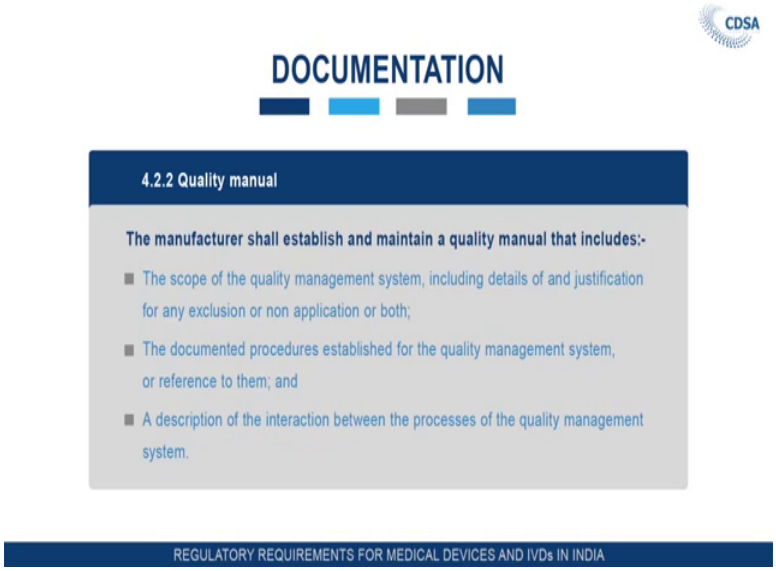

Quality manual, the manufacturer shall establish and maintain a quality manual that includes the scope of the quality management system including detailed of and justification for any exclusion or non application or both. The documented procedures established for the quality management system or referenced to them and discretion of interaction between the process of the quality management system.

So, quality manual has these three functions and they have to prepare a quality manual and show it to the inspectors when, the inspectors visit the plant.

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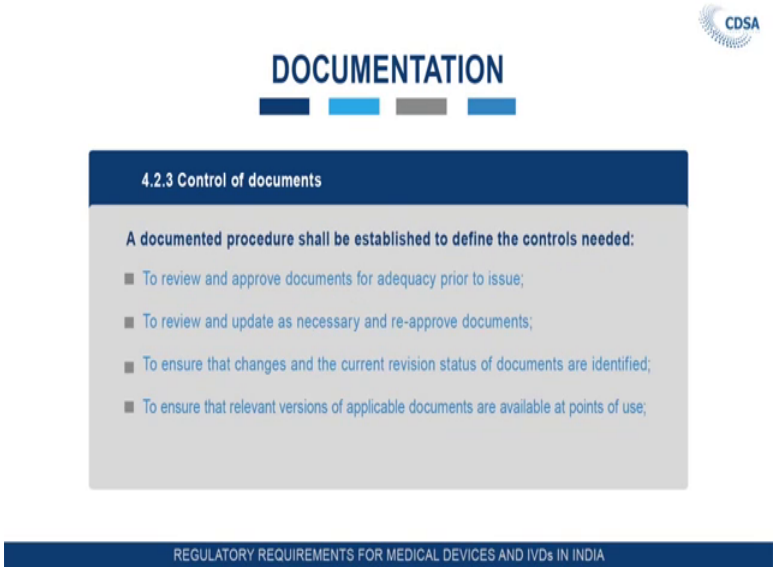

Control of documents; now, you again we come back to documents again; because document is one of the most important things along with other activities that the plant carried out. A documented procedure shall be established to define the controls needed. To review and approve documents for adequate prior, advocacy prior to use; to review and update as necessary and reprove documents; to ensure that changes and current revision status of documents are identified. To ensure that relevant since versions of applicable documents are available at points of use.

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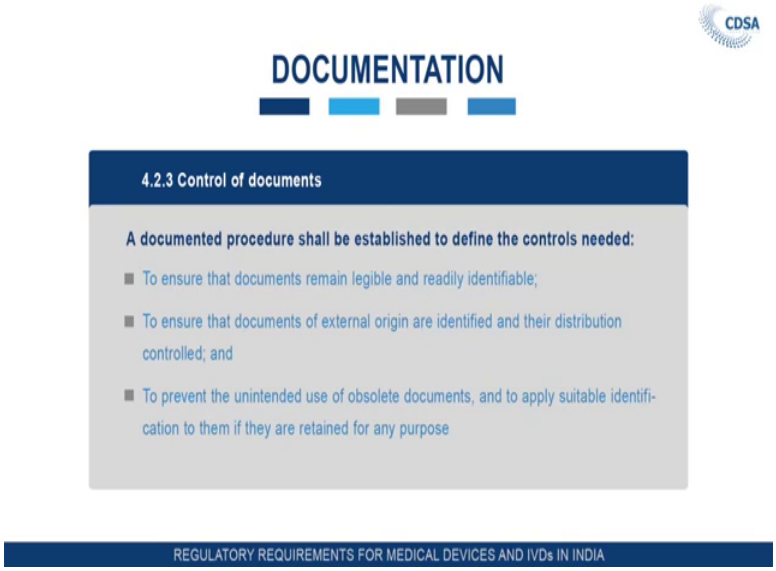

To ensure the document remain legible and readily identifiable. To ensure the documents are of external origin identified and the distribution controlled; and to prevent the unintended use of obsolete documents and to apply suitable identification to them if they are retained by any purpose. Now, where are the documents used actually? We have to control the document, but what; where are they used?

The documents are used at every stage in the plant and every procedure that is carried out; right from the time a raw metal enters the plant to the time that a product goes out as a finished product for marketing, all is controlled by documents. There shall be standard operating procedures for the it activities and each activities of this carried out have to be recorded and signed and kept as a record. Now, if there is a change in the procedure the older procedure the older SOP has to be withdrawn back and a new document has to be

written. This is all controlled on the under control of documentation. And any slip in the documentation is very clearly identifiable during the inspection.

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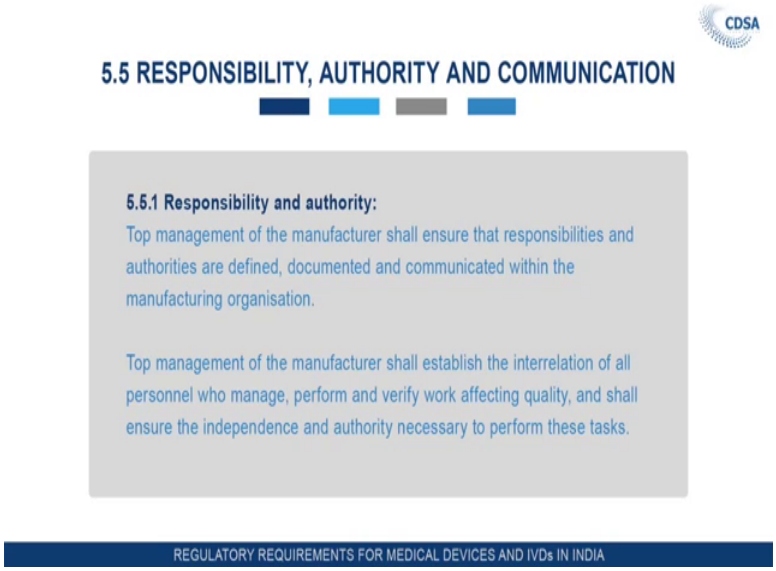

Responsibility authority and communication 5.5 5.5.1 responsibility authority under the MDR; top management of the manufacturer shall ensure the responsibilities and authorities are defined, documented and communicated within the manufacturing organization. Top management of the manufacturer shall establish the inter relation of all personnel who manage, perform and verify work affecting quality and shall ensure the independence and authority necessary to perform these task.

That means, there should be a organization chart which shall show the flow of authority from the top management to the lowest level of workmen who is working. And this responsibility authority has included the top management who cannot nor shut the responsibility of quality of a product we use manufactured over there.

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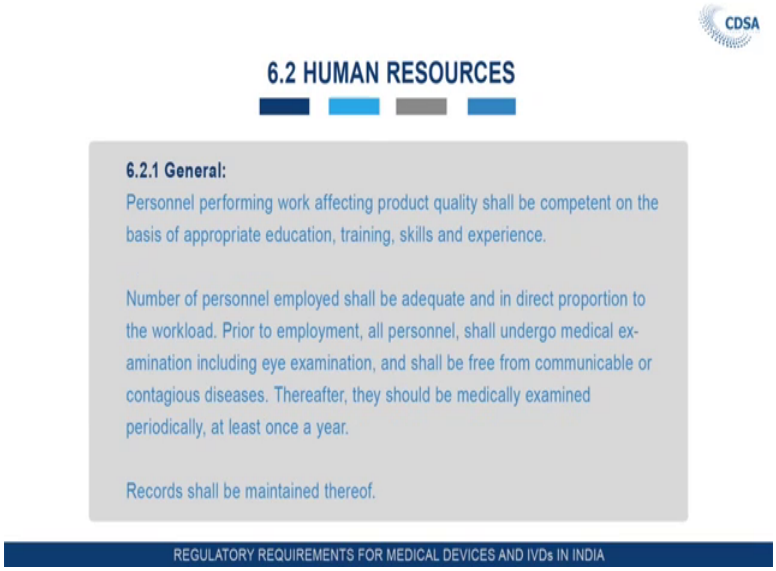

Human resources, human resources are actually the people working in the plant, the workmen, the people the workers who are working in the plant and also including technical personnel and non-technical personnel. 6.2.1 General says, personnel performing work affecting product quality shall be competent on the basis of appropriate education, training, skills and experience. Number of personal employed shall be adequate and in direct proportion to the workload. Prior to employment, all personnel shall undergo medical examination including eye examination and shall be free from communicable or contagious diseases.

Thereafter, they should be medically examined periodically or at least once a year; records should be maintained thereof. Now, all these activities; all these activities and what are these activities? Undergo a medical examination they should be fit to work, they should be trained, they should be skilled, they should have experience, appropriate education all this is examined during the audit. So, then, the auditors may ask for the details of training carried out for the workmen; when they were carried out? What was the assessment of the people who are trained?

They shall also find out by way of direct interaction with the top floor workmen to know their experience and skill. And whether they are working mechanically or they have a general idea what they are doing. And this is all recorded in the record. So, that over overview of a general human resources is got over there. If the song that the workers are

not trained adequately; it is recommended in the report that the workers are not adequately trained, they should be trained properly in certain areas. So that, they do not miss out on the quality parameters during manufacturing.

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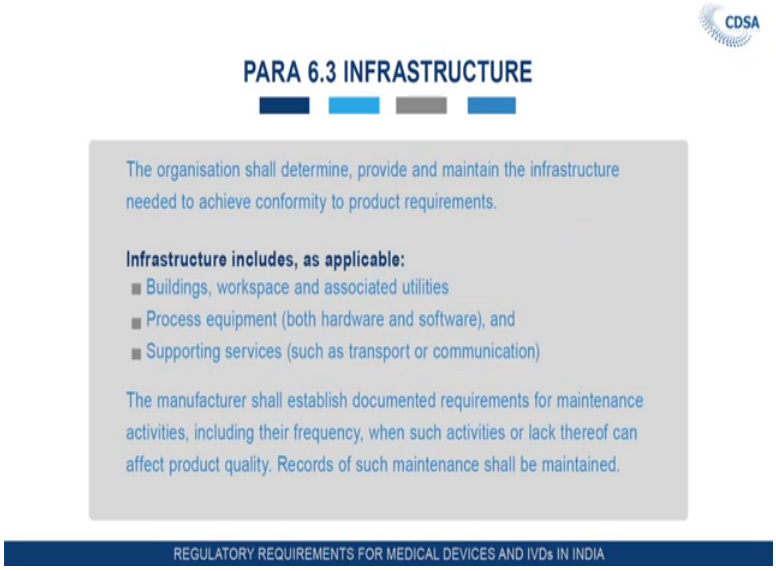

Infrastructure, this is actually the hardware of the plant. The organization shall determine, provide and maintain the infrastructure needed to achieve conformity to product requirements. Infrastructure includes as applicable building, workspace and associated utilities; process equipment both hardware and software and supporting services such as transport or communication. The manufacturer shall establish documented requirement for maintaining activities, including their frequency, when such activities or lack thereof can affect better quality. Record of such maintain shall be maintained.

Now, building, workspace, associated utilities include your right from the beginning you can have stores with required storage, space workspace means where, the manufacturing is carried out with machineries kept over there associated utilities maybe steam or your what you call electrical supplies, generator systems etcetera and water supply, process equipment both hardware or software process equipment permission is required for manufacturing and associated computers and things like that. And all this is examined while the while the auditors are going through your plant right from the entry to the exit. They will actually go through everything of this infrastructure and note it down.

If you find that, if they find that the entry procedure to your plant is wrong; you need a change over for workmen to change their clothes and wash their hands; and if it is not there; they will record it down and that will be a deficiency which you have to rectify before you can get a license. So, infrastructure is actually very very important in case of plants which are manufacturing (Refer Time: 37:24) products or products which are of critical nature.

For other products, it is not that critical, but that is also important because this is a part of your QMS system. So, you cannot ignore this one.

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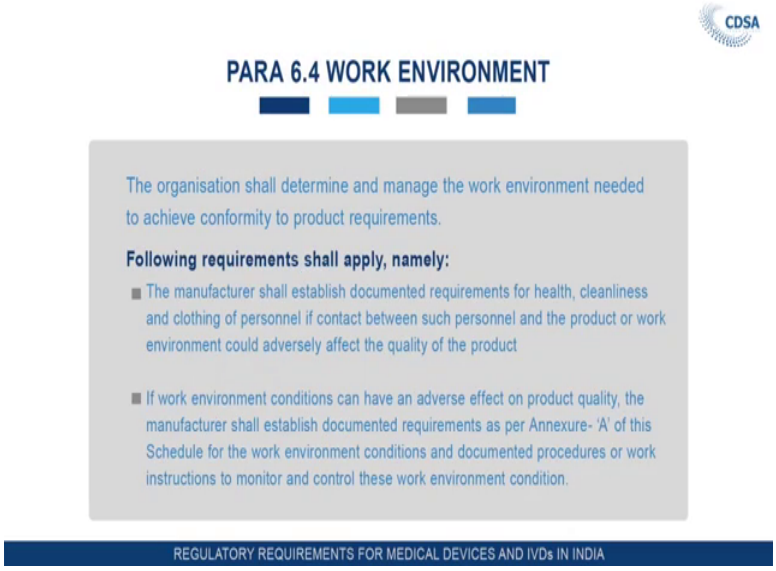

Work environment, the organization shall determine and manage the work environment needed to achieve conformity to product requirements. Following requirements shall apply namely; the manufacturer shall establish documented requirement for health, cleanliness and clothing of personnel if contact between such personnel and the product or work environment could adversely affect the quality of the product.

This actually means that whether the product requires that the personnel should change over to clean uniforms, wear gloves before touching the products, change their shoes and things like that. And if not, why it is not required? If the, if the medical device officers feel that the product environment in this case, the personal and product contamination is there and the firm has not provided adequate protection then, the medical device officers

can very well ask, why you have not done it? And they have to have a proper answer for that.

If the work environment conditions can have an adverse effect the product quality, the manufacturer shall establish documented requirements as per Annexure A of the Schedule for the work environmental condition and documented procedures or work instructions to monitor and control these work environment condition. That is in simple terms they should have SOP for people working over there.

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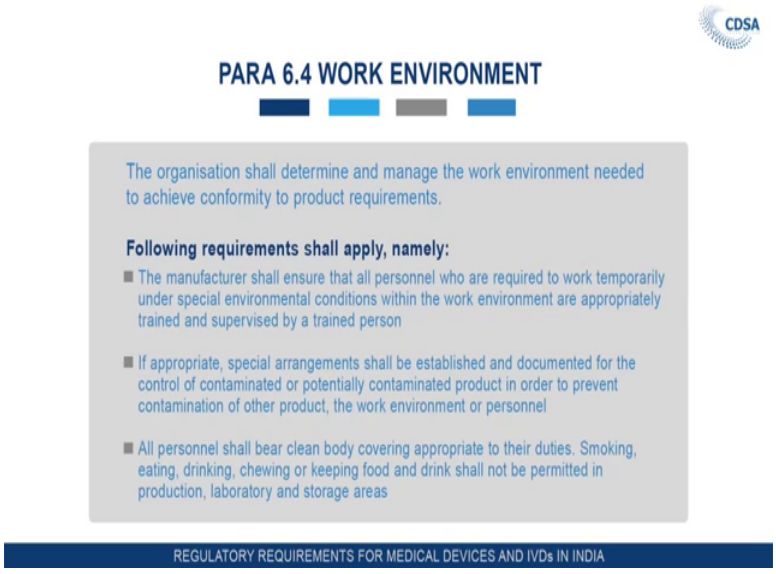

The manufacturer shall ensure that all personnel who are required to work temporarily under special environmental conditions within the work environment are appropriately trained and supervised by trained person; that means, all contractual workers or casual workers who are employed over there they should be trained. You cannot have untrained people working over there excepting for a few manual labour jobs like lifting and loading trucks etcetera.

All the personnel should be trained properly whether they are regular employees or whether they are casual workers. If appropriate special arrangement shall be established and documented for the control of contamination or potentially contaminated product in order to prevent contamination the other products the work environment of personnel; so, what is the contamination?

Contamination of a product or product means you have, you have a batch of products which is defective medical devices. Now, that has to be protected from other devices. So that, there is no one of those defective may not get mixed up with the contaminate the proper products and go to the market or for that matter you have a batch of trial products which has failed in (Refer Time: 40:01) and they are stored separately.

Now, these non trail products, which are failed (Refer Time: 40:08) actually should not get mixed up with product which have been sterilized and go into the market and cause CDS hazard the patient that are there being used in. All personnel shall bear clean body covering appropriate duties. Smoking, eating, drinking, cheering or keeping food and drink shall not be permitted in production laboratory storage areas. So, this is very clear, simple language. The worker, who are entering the plant should actually carry out the work they are assigned to do and not do anything else other than that.

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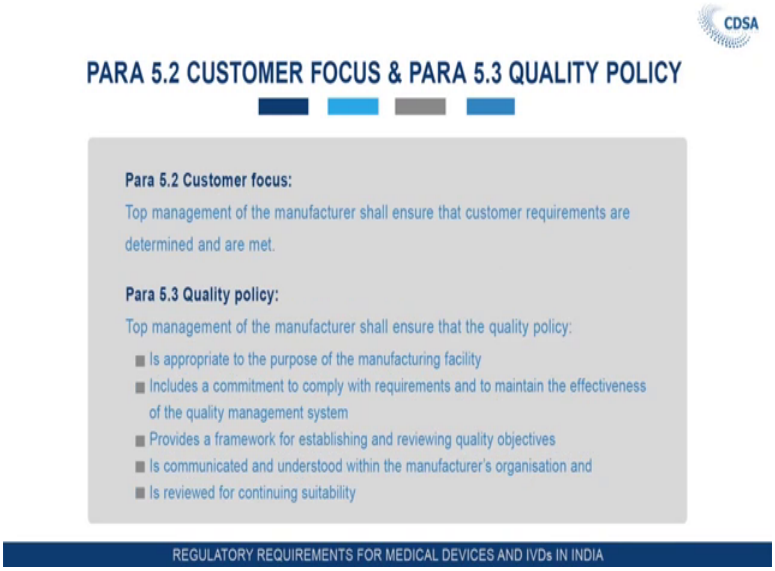

Customer focus, top management of the manufactures shall ensure that customer requirements are determined and are met. What is the customer requirement? Customer this actually line is a ISO 9000 line, which is over here. Customer requirement in this case is, the product which is being used by a person whether a patient or an unhealthy person. That product should actually help that person for a particular activity to be carried out. Now, the customer can be patient, in case of say insertion of a cardiac stent. So, the requirement of the patient has to be met by the manufacturer and the top

management is responsible for that; anything that goes wrong with the requirement of the product (Refer Time: 41:28) the customer the top management shall be responsible for that.

Now, the manufacturer shall prepare a quality policy for as per Para 5.3; top management the manufacturer shall ensure that the quality policy is appropriate to the purpose of manufacturing facility; includes a commitment to comply with the requirements and to maintain the effectiveness of the quality manual system; provide a framework for establishing and reviewing quality objectives. Is communicated as understood within the manufacturers organization and is reviewed for continuing suitability.

The quality policy is usually made by the manufacturer; it can be one liner or a three paragraph policy twists, but encompasses everything and that is actually placed at strategic in intervals in the plant for everybody to see and get a sense of what they are doing over there. So, this is also examined; the auditor may ask that, where is your quality policy? And you have to show that quality policy to him at that point of time.

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Control of production and service provision specific requirements 7.5.1.2 is the control and.1 of this control is cleanliness of product and contamination control. The manufacturer shall establish documented requirements for cleanliness of the product if, the product is cleaned by the manufacture prior to sterilisation or it is use or the product is supportive, supplied non sterile to be subjected to cleaning, cleaning process prior to

sterilisation or it is use or the product is supplied to be used non sterile and its cleanliness of significant in use.

Or the process agents are to be removed from product during manufacture. If the product is clean in accordance with Clause a or Clause b above, the requirement content in Clause a and b of Sub paragraph 6.4 do not apply prior to cleaning process. So, this actually decides the type of product contamination; that can be there in the product which will affect the final user. The product can be manufactured sterile and this is a medical device remember. So, medical device products have various types of cleanliness levels. For instance, your products there are certain products which are actually to be sterilized, when it is released from the plant.

That is your cardiac stent (Refer Time: 43:57) intraocular lenses they have to be sterilized with the manufactured by appropriated method before they released for use. There can be other products which are, which have to be cleaned and sold in a cleaned manner, but not sterilized. And these products can be automatic implant, which are actually sterilized by the hospital before they are used. So, they have to be cleaned, but not sterile. So, there are, these products are also re sterilizable products the in plants. So, they should be able to withstand constantly re sterilisation in a plant, in a in a hospital premises. So, all this is contamination control in a product and this is also examined during the audit.

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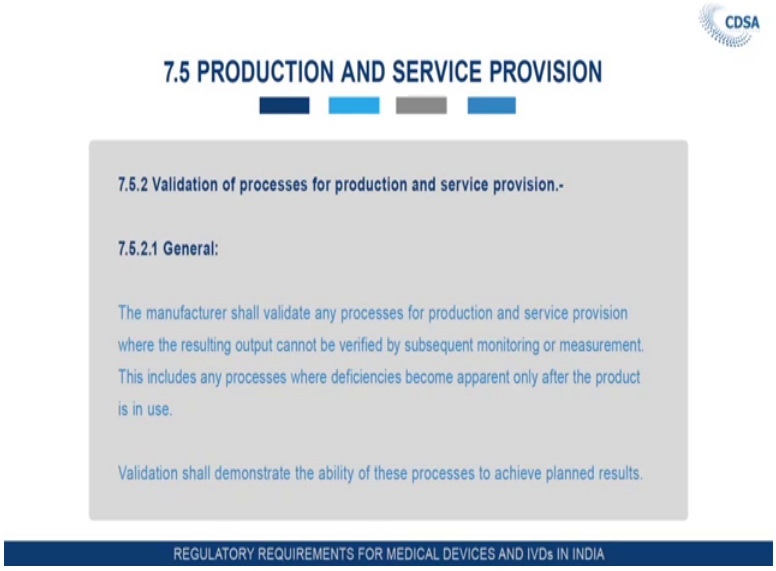

Validation of processes and production and service provision; the validation is very important. General; the manufacturer shall validate any process of production and service provision where the resulting output cannot be verified by subsequent monitoring and measurement. This includes any processes that deficiencies become apparent only after the product is in use. Validation of shall demonstrate the ability of these processes to achieve planned results.

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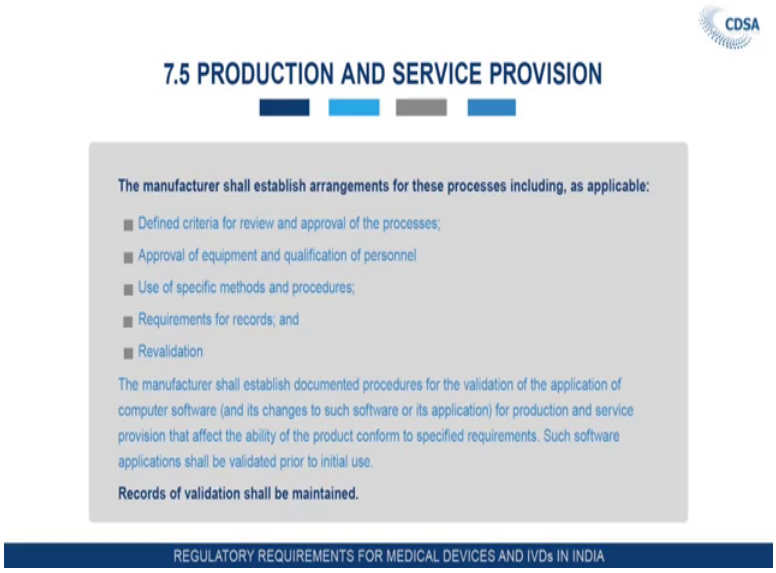

The manufacture shall establish arrangements for these processes including as applicable; defined criteria for review and approval of the process; approval of equipment and qualification of personnel; use a specific methods of procedures; requirement for records and revalidation. The manufacture shall establish document procedures for the validation of the application of computer software.

And its changes to such software or its application for production and service provisions for that affect the ability of the product conform to the specific requirements. Such software application shall be validated prior to initiate use. Records of validation shall be maintained. So, what is the validation, validation the first line if you read very carefully? Validation of for processes, for production and service provisions where the resulting output cannot be validated by subsequent monitoring and testing; that is you cannot test and find out the whether the process has gone through properly or not.

In such cases the processes have to be verified and validated repeatedly. So, that the end result remains the same. In such cases, you do not require a final testing of the product, but each process if it is validated properly by various means your product at the end of the day will be the required product that you require to be; this is the market.

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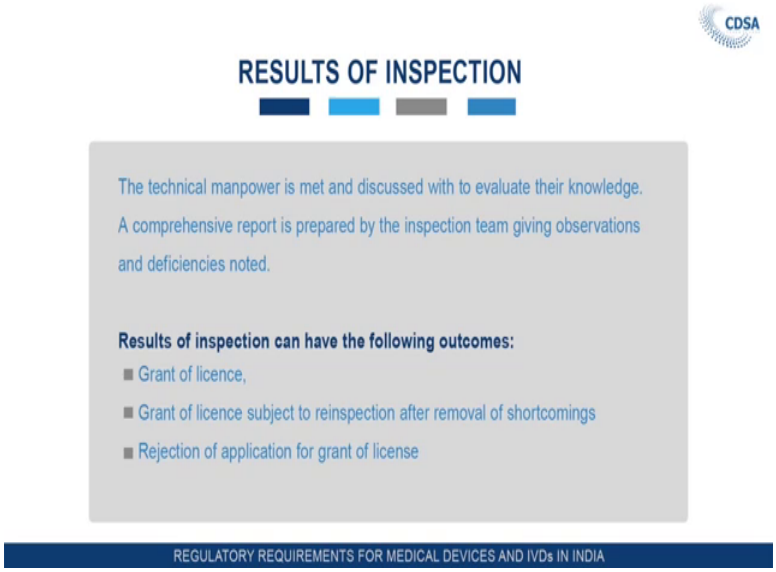

Technical manpower is met and discussed with to evaluated their knowledge. In this case, what happens is? The technical manpower is discussed is interviewed in the audit a comprehensive report is prepared of the inspection team giving observation and deficiencies noted. So, after all this is done the inspection, the walkthrough inspection, the observations are made.

The workmen interacted with the technical manpower interviewed. The product is detained, detail is examined; a comprehensive report is prepared by the medical device inspection team. The result of the inspection can have the following outcomes; it can either requirement of grant of license or it can requirement grant of license subject to re inspection after removal of shortcomings or rejection application for grant of license. The third case is usually a rare case because one who was actually invested a lot of money will actually see that he gets a license.

So, it is the second case which is usually the case because there is a bit of a gap between understanding of the applicant and the requirement. So, what happens is, there are certain

deficiencies which are usually noted and these are removed. And the team re inspect to check for the removal of that shortcomings and grants a license.

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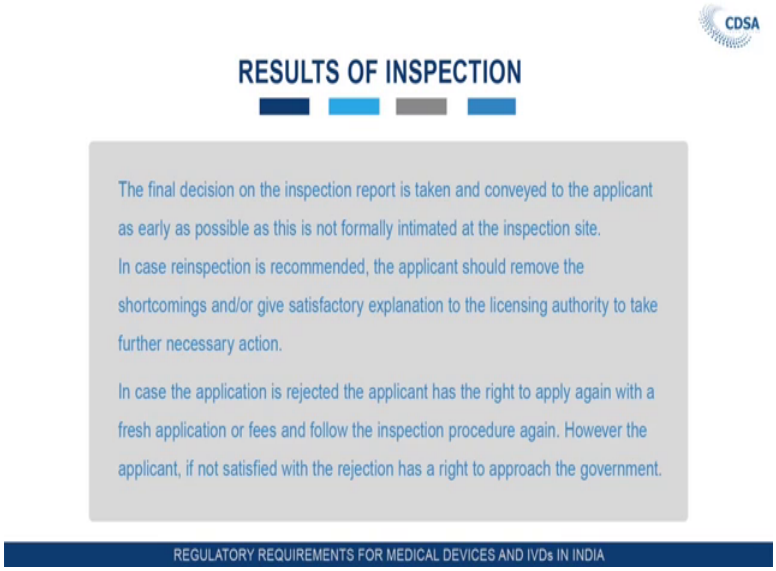

Final decision on the inspection report is taken and conveyed to the applicant as early as possible as this is not formally intimated at the inspection site. Nobody, no inspector or auditor will tell after inspection whether he is getting a license or not because it is not in his hands to say it. And it also creates a sort of problem in the inspection schedule and the relationship between the inspected and inspector. In case the inspection is recommended, the applicant should remove the shortcomings and or give satisfactory explanation to the licensing authority to take further necessary action.

In case the shortcomings are noted, the manufacturer may feel that the shortcomings have not been understood. And mean wrongly mentioned by the auditors in that case he can go in for an explanation and explain to the regulator that this is this short come is not shortcoming; it has been wrongly interpreted. And its reaction taken; in case the application rejected the applicant has the right to apply again with the first application fees and followed by inspection procedure again.

However, the applicant if he is not satisfied with the rejection has a right approach the government for a review. Government in this case is not CDSCO, but the government, respective government state government or central government. This actually is a

nutshell the inspection. And what the inspection procedure goes through? And what is inspected during the inspection?

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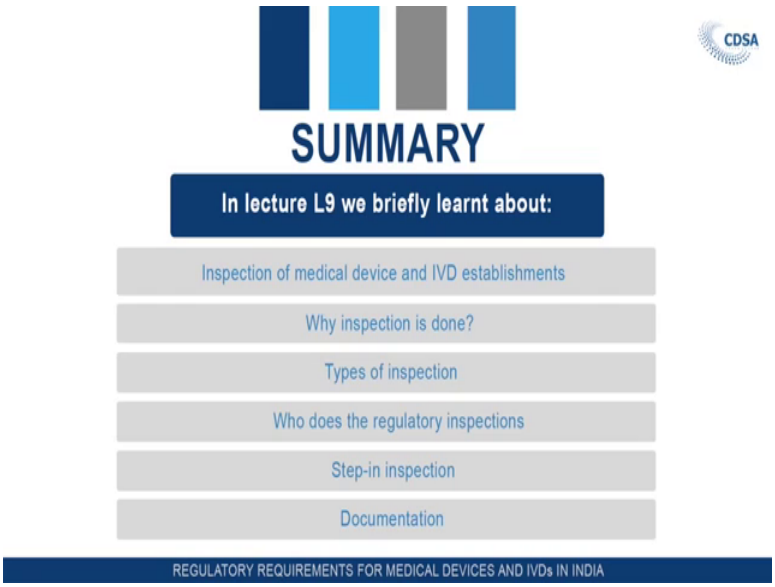

This is, this is very scanty and small; however, once you go through the medical device regulation details; you may find out the QMS gives you much more scope to understand the whole thing and what is required.

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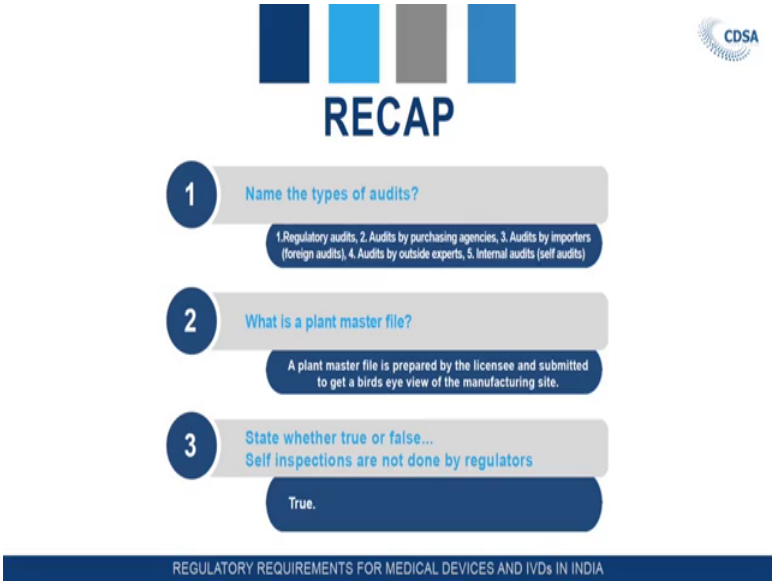

Now, some of the question and answers over are over here very simple one. However, you will be getting much more question and answers we have to submit later on for

assessment. In case you require further clarifications, you can always get back to us for a detailed answer to your quarries.

Thank you very much.