Regulatory Requirements for Medical Devices and IVDs in India

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Lecture – 09
Quality Assurance & Quality Management System

Dear friends, welcome to Regulatory Requirement for Medical Devices and In Vitro Diagnostics in India, lecture 07. Lecture 07 that is Quality Assurance and Quality Management System; what is the quality management system? What is the quality assurance and quality control of the medical devices? You will understand in this lecture. This lecture will be given by Mister Malay Mitra former Deputy Drugs Controller, who have lot of exposure and experience in the regulation of the medical devices and in vitro diagnostics.

In this lecture you will also understand, where the provisions of the quality management system has been given in the medical device regulation? In the previous lecture, we have discuss that the quality management system Medical Device Rule, 2017 fifth schedule has been prescribed. Fifth Schedule as given the details of the quality management system for manufacturing of in vitro diagnostics and medical devices in the country; this quality management system where that; which is in the line of the internationally accepted quality management system as per ISO 13485 that has been prescribed with certain modification.

What modification we have included in the fifth schedule of the medical device regulation? To have the harmonized or (Refer Time: 01:42) on the device master file and the plant master file. What will be the details of the requirement? All clearly prescribed in the fifth schedule that is the one of the additional part which have been included in the fifth schedule. So, the manufacturer, indigenous manufacturer of the medical devices; manufacture of the medical devices which are presently regulated has to conform the requirement of the quality management system as prescribed in the fifth schedule of the Medical Device Rule, 2017.

So, why this quality management system has been incorporated? Why not the quality management system? Because, the quality management system have four different major

component; what will be the component for the quality management system? GMP is one of the part of the quality management system; in the GMP, there is a interaction between the development of the medical devices and GMP.

But there is a no interaction between design of the medical devices and the good manufacturing practices. And also if you see the quality risk management of the medical devices, the minimum all; there is a minimum interaction between the risk management of the medical devices and the GMP. However, in the quality management system there is a interaction between the design of the medical devices, development of the medical devices with the quality risk of the medical devices and also GMP.

GMP also included in the quality management system. So, the detail of the quality management system, that you will understand in this lecture; why GMP was replaced with the QMS? The reason also you will understand in the forth coming that lecture which will be given by Mister Malay Mitra And also during the presentation you will understand, what are the quality control parameter for the medical devices and in vitro diagnostics? What is the difference of quality control and quality assurance?

So, all, those topic you will be understand in the lecture; this detail lecture which will be given by Mister Malay Mitra, Deputy Drugs Controller. So, concentrate on the lecture and enjoy the lecture. If you have any doubt you ask; we will try to clarify that information further in future; thank you very much.

Today, we are going to, go through the quality assurance and quality management system under the new regulations of medical devices. This is part of the series of presentations on medical devices. And, this forms of bedrock of the manufacturing of medical devices. This forms part of the ISO 13485 which is universally accepted and applied on medical devices all over the world.

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Now, before we proceed further; let us first understand, what is quality assurance? WHO definition of quality assurance is: it is a wide ranging concept covering all metals that individually or collectively influence the quality of a product with regard to pharmaceuticals. Quality assurance can be divided into four major areas that is quality control, production, distribution and inspection. This can be applied to devices also; because all this four parameters in the manufacture of a medical device drug are also applied to medical devices. In applying QM QA system; every aspect the manufacturing system it is controlled at every step is such a manner.

So, that the final product conforms to requirement. Quality assurance system covers design and development, manufacturing procedures, packaging, manpower, training release, testing, documents and its control and in any other activity related to the whole process of manufacturing. What it means is that the QA system is a all encompassing system, which covers everything in the manufacture of a medical device right from the time the raw material enters the plant and it is released as a finished product to go into the market. Even the distribution is covered under QMS system. It is; it covers, what does it cover? The quality assurance cover the design of the medical device; its developmental stage before, its product wise approved for manufacture.

The manufacturing procedure, the packaging, containers, the manpower, the people that are working in the plant the its covered by that, training of the manpower testing etcetera etcetera.

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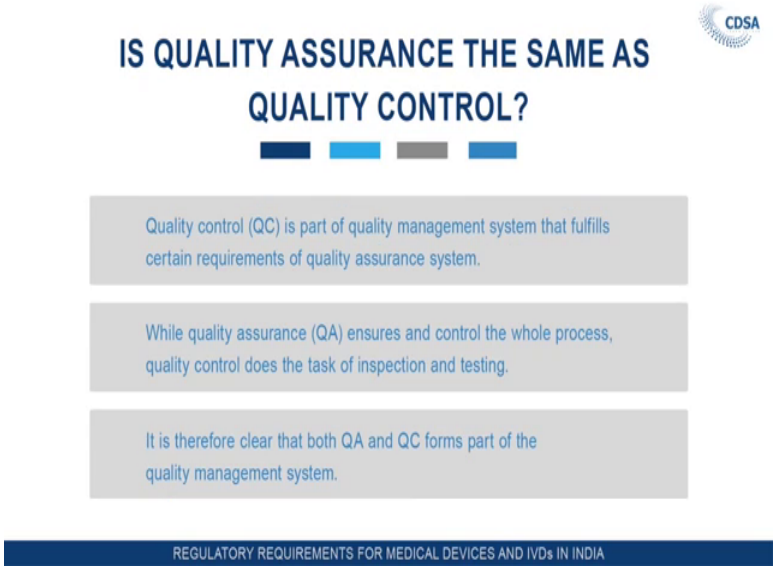

Is quality assurance the same as quality control? This is one of the very very major confusions in the mind of people who are working in the manufacturing of drugs and medical devices. Is quality assurance the same as quality control? Let us see, quality control is part of quality management system that fulfill certain requirements of quality assurance system. It means that quality management system has called various politicals; one of which is quality control system; part of it is quality control system.

And along with quality control stable other important parameters, the QMS becomes a whole. While quality assurance ensures than controls the whole process. Quality control does the task of inspection and testing. It is therefore, clear the quality control forms part of the QA system. Quality assurance ensure the control of the whole process, the whole plant, whole everything; while quality control inspects a particular area and the finished product under the quality management system.

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It is frequently queried, if the product is tested at the end of production; why control the whole process? That is a very common question; I manufacture a medical device in my plant and at the end of the day will manufactured and packed. I send it to my laboratory for a complete testing of the medical device. And it complies to the standards required. So, why do I required QA system at all? This was very common in the earlier days; however, it was seen that the medical device failed while in use.

And therefore, it was ensure that quality assurance during manufacturing ensures that each step, each component, each procedure is under documented control to conform to the requirements. Final testing at the time of release can only ensure the conformance of the product the physical parameters; what it means is that quality assurance doing manufacture ensure the each step remember, each step means.

Manufacturing is a combination of different steps in the whole process. So, each step, each process it is controlled and it is controlled by people who are trained for that process and whatever they are doing is written down and documented. And therefore, what happens is that you built in quality right from the very beginning to the end. So, in case you are QMS is very very strong, you may not required to test the final product at the end of the day and it happens quite by often when the product is very very costly product; you cannot tested by destroying it. You have to put quality into it. For the final product that goes out conforms your requirement.

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Now, a bit of schedule M III; schedule M III GMP for medical devices was effective under the drug and cosmetic rules, 1945 as long as the medical device rule, 2017 was nonexistent. It helped the manufacturers as a guide in the earlier regulations. So, till 2017 and all manufacturers where, following schedule M III as a good manufacturing practice document. That document was a simplistic document and it gaves you yes or no's in manufacturing; what you have to do, what you have not do, but it was not a comprehensive multi management system as required under 13485 ISO which is applicable all over the world.

So, for are manufacturers to follow 13485. So that, we are in sync with the rest of the world; this ISO has been adopted by the new regulation. Relevant areas of schedule M III; however, has been incorporated in the QMS system. So, you are not missing out on anything without the schedule M III not being there, but you are adding value to the Schedule M III by way of accepting Schedule ISO 13485.

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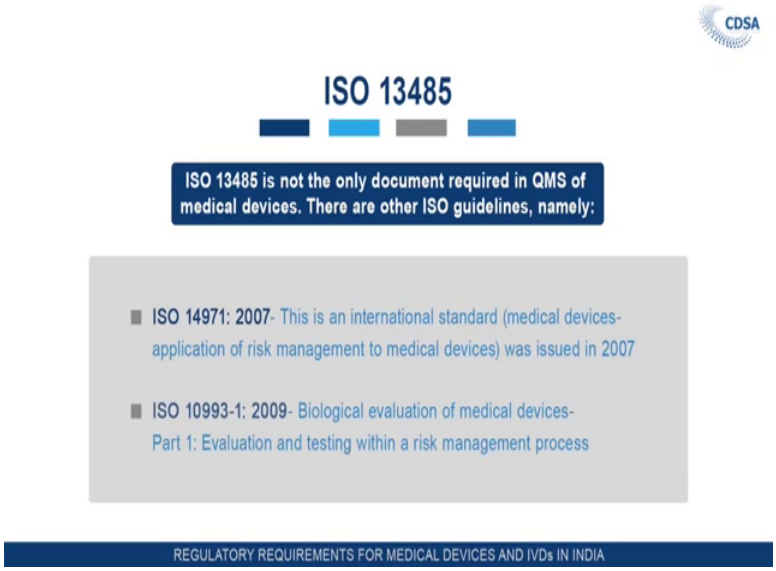

Now, ISO 13485 is a mother document; you have to follow 13485, if you want to manufacture medical device. The ISO has also got a equivalent ISO 13485, which is it has adopted in to a two. Now, what are the other ISO required under this umbrella 13485? You require ISO 14971 which is an international standard that ISO issued in 2017. The title is medical devices application of risk management system. So, risk management is covered under this ISO 14971; in case you have to you encounter a risk in the in the whole process.

This will apply and guide you to manage that risk. ISO 10993 is the biological evaluation medical device. If the medical device has to be evaluated biologically then, this ISO is required to be applied over there. IEC 62366 is applicability of usability of engineering to medical devices. That is, this is basically engineering a portion of the ISO, under the ISO 13485.

ISO also has issued ISO 149694004 medical devices quality management system guidance. Now, this ISO is a guidance to the application of 13485. So, if you want to apply 13485 into your system in a plant; you have to go through this ISO to understand how to apply that. So, it is become very user friendly iso in case you want to apply 13485. We will; however, confine ourselves to ISO 13485 which is a quality management system because going into all this ISOs at a go will it is not possible in one presentation till required days and days of understanding and presentations.

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ISO 4 and 5 which is mother for our quality management system is in the fifth schedule of quality management system for medical devices and in vitro diagnostic medical devices motion of the medical device regulation, 2017. The fifth schedule of the Medical Device Rule, 2017 describes in detail the quality management system that has to be followed by a medical device establishment.

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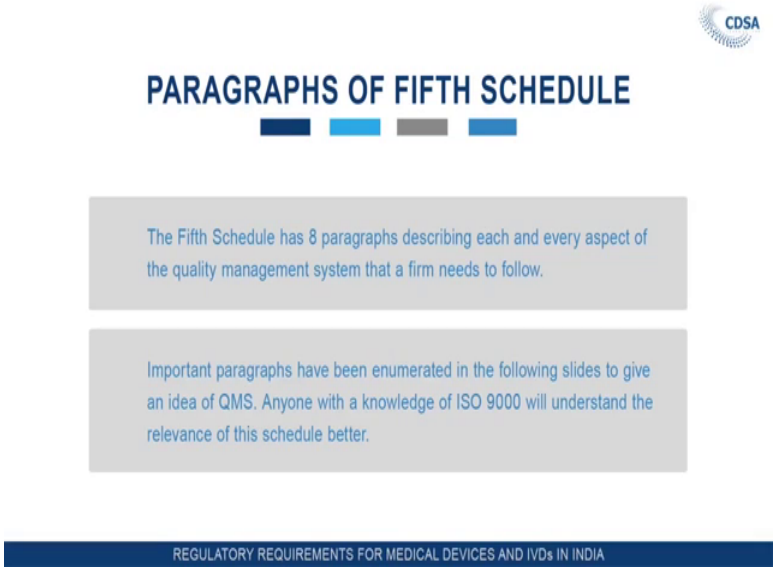

The fifth schedule has 8 paragraphs describing each and every aspect of the quality management system that a firm needs to follow. Important paragraphs have been

enumerated in the following slides to give an idea of QMS. Anybody having some interaction with the ISO 9000 will understand the relevance of the schedule.

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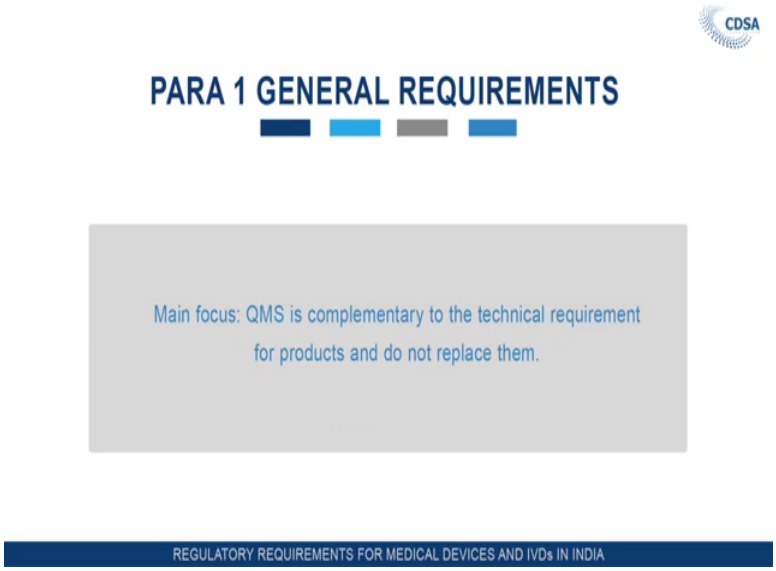

Part I general requirement; some other thing it say the QMS complementary to the technical requirements for products and do not replace them; this is important. If you have technical requirements of a product, they are not to be replaced with QMS. QMS will complement and help those technical requirement reaches ultimate goal.

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Part II is applicability; the provisions of the schedule shall be apply, applicable to manufacture of finished devices, in vitro diagnostic medical devices, mechanical contraceptives condoms, intrauterine devices, tubal rings, surgical dressing, surgical bandages, surgical stapler, surgical sutures and ligatures blood and blood component collection bags with or without anticoagulants.

These items have been notified in the drug and cosmetics act. And under the act and in case there are other items added under the act and notified; they will also following this part II applicability portion.

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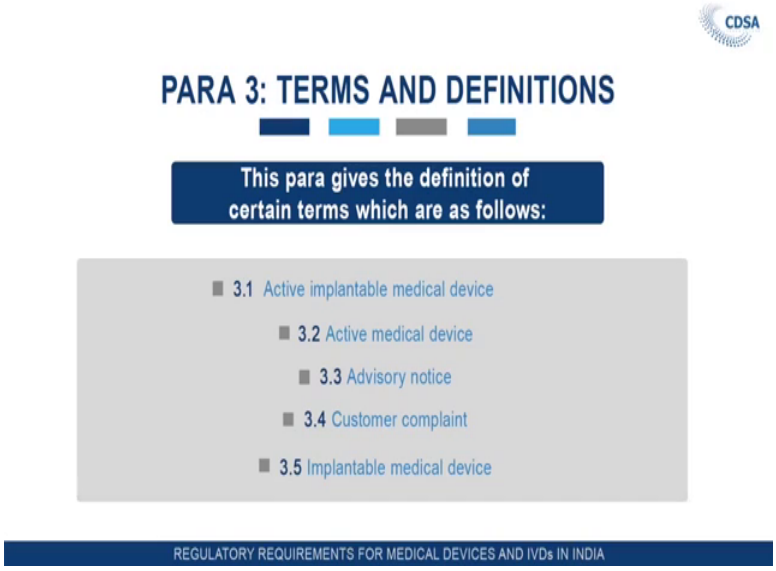

Terms and definition; part III is the terms and definitions in the regulations. The para gives the definitions of certain devices which are as follows. 3.1 is active implantable medical device, 3.2 is active medical device, 3. is advisory note, 3.4 is customer complaint, 3.5 is implantable medical device.

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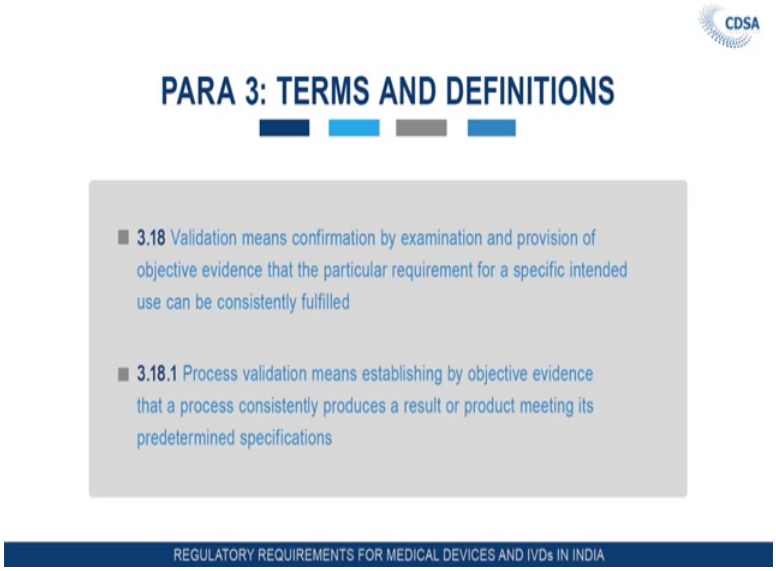

3.18. I have picked up the relevant paragraph. So, there are; there may be a few paragraph in between which are not as important as these, but if you go through these paras you can understand those paras also. 3.18 is a very important para; validation means confirmation by examination and provision of objective evidence that the particular requirement for a specific introduce can be consistent to fulfill; that means, you may come across the word validation in this whole regulations here and there or not even here may be in other documents that you go through internationally.

Now, what does validation mean; validation means you conform by examination and provisions of objective evidence that whatever you are doing in a particular manufacturing activity can be consistently fulfilled. 3.18.1 is the process validation which means establishing by objective evidence that a process consistently produces a result or product meaning its predetermined specifications.

I am sure the language is very simple to understand, but in case you want to understand further from this I can explain that. Process validation is a system by which you have to divide; first of all you can divide the whole process a to z into small segments. The each segment does its small work to change the raw material into the final product. Each of those segments have to be validated as a simple process, separate entity and the process. Now, once you do that that process validation will prove or it will verify that the end result of that process is consistent batch after batch product of the product.

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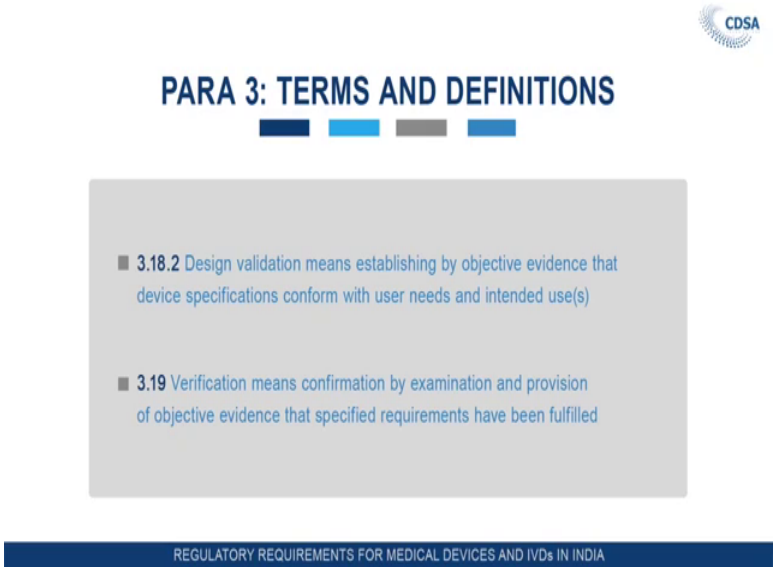

3.18.2 design validation means establishing by objective evidence that device of specifications conform with user need and intended uses. Design validation comes into place when you design the product; you have to design the product before it goes in to commercial manufacturing. Therefore, when you are the drawing board designing a product for a particular activity in the human body; you have to have this design qualification done and validate that whole design before you going for actual manufacturing. 3.19 is verification means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

In this case verifications means actually in a way, in a simple language it is testing basically. We have to have objective evidence has specific requirement; that means, you have to verify that a particular item is 6 6 inches long at a particular process. It you have to verify that it is 6 inches long; in that process which is been verified by process validation.

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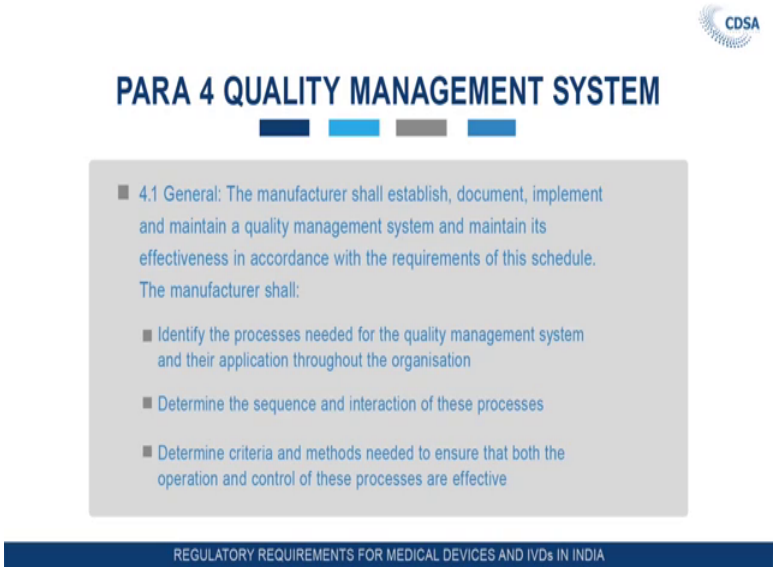

Para 4 quality management system; general, the manufacture shall establish document, implement and maintain a quality management system that and maintain its effectiveness in accordance with the requirement of the schedule; that means, he shall establish a QMS initial document everything that is done over there in the QMS. And implement that in the plant to maintain the quality management system.

The manufacture shall; I will define the process needed for quality management system and their application throughout the organisation. He has to identify the processes, the small process that I mentioned earlier. Those processes have to be identified by the management. And they have to be put forward for as a part of the validation system. b, determination; determine the sequence and interaction of these processes. That mean one process; process a will precede process b and process b will precede process c; you cannot process a and then, process f and come back to process b. The sequence I have to established and the interaction of these processor.

One process will follow the next process, the sequence and the interaction with these processes have to be established. Determined criteria and methods literature that both the operation and control of this f processes are effective. You have to have a criteria and a system by which you have to ensure that both the operations and control. Operations means you are doing it regularly a process and control mean that that regular process that you having doing its controlled by way of a method.

So, these have to be effective and this management has to establish; d, ensure the availability of resources and information necessary to support and the operation and monitoring these process; remember resources means not only money. Resources means manpower; resources mean machinery; resources means areal thing is required to monitor of the process. So, the management should ensure the availability of everything that is required to ensure the QMS system. Management should monitor measure and analyze that these processes.

You have seen that this is this is part of the validation and verification process. Implement action necessary to achieve planned results and maintain the effectiveness of these processes. Implement actions necessary to achieve planned results; that means, in case if a result that you are getting is not what you have required. Then, to implement the change that method; so, that the end result remains the same year after year, month after month.

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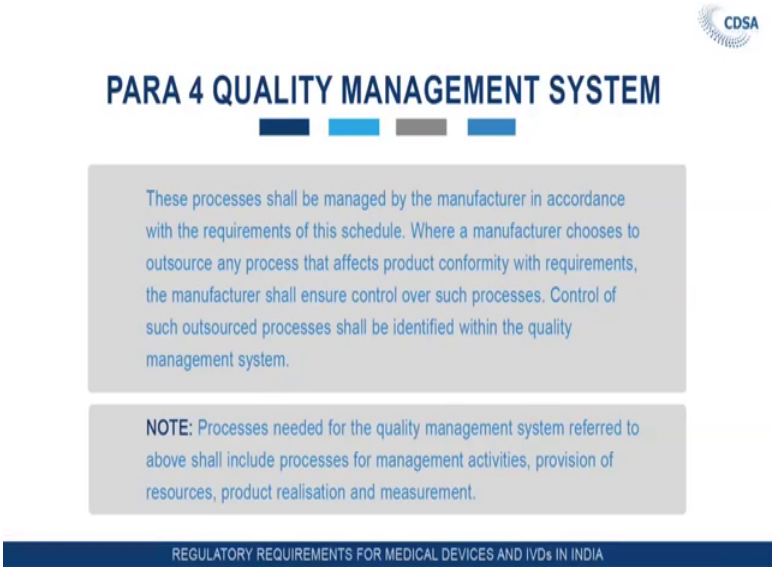

These processes shall be managed by the manufacturer in accordance with the requirements of the schedule; where a manufacturer chooses to outsource any process that affects product conformity with requirements.

The manufacturer shall ensure control over such processes; control of such outsourced process shall be identified within the quality management system. Note is that processes needed for the quality management system referred to above shall include process of

management activities, provision of resources product realization and measurement. second line is very important; it says that when a manufacturer chooses to outsource any process that affects the product conformity with requirement.

That means I manufacture a medical device; a part of it or a component of it is been manufacture by somebody else under my contract. Now, in that case I am responsible for the QMS of that contract manufacturer process also. So, I have; I am have a added resourceability for that.

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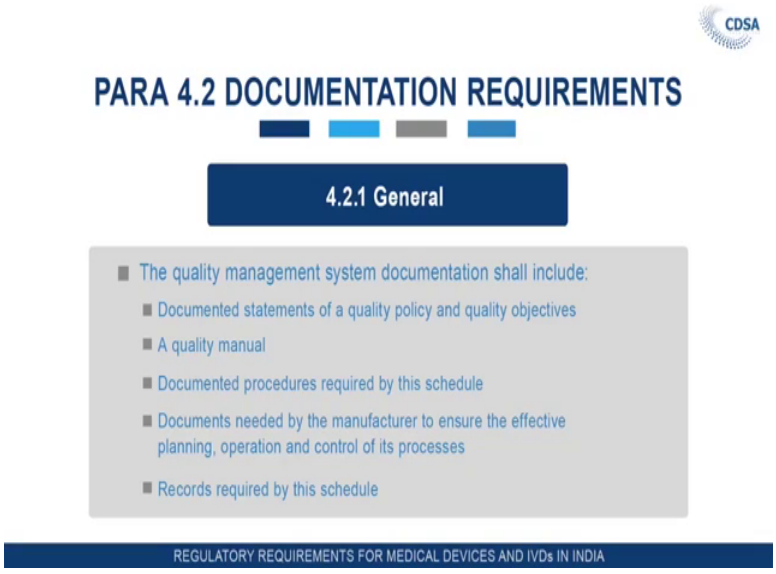

Part 4.2 is documentation requirement; this is extremely important, extremely important. Generally is a quality management system documentation shall include. Documented statements of quality policy and quality objectives; a quality manual; documented procedures required by the schedule. Document needed by the manufacturer to ensure the effective planning operation and control processes. Records, records required by this schedule. Remember a document which is not just statement of quality and quality objective.

That is of course, over there we find them framed them put on the walls in the company. That is very important to remind the people working over there the quality policy and the systems; however, each activity that is carried out in the plant. Each, when I say each activity; I mean each activity right from the way the personal or recruited, trained, put into operation, how I switch in a machineries operated; all these have to be documented

and each one of the action that is taken care of is again documented that process has been done.

So, documentation is extremely important objective of QMS. In case of documentation the benefits are that in case something goes wrong somewhere, we can trace to source of that problem with the help of documents. Documents are interlinked and you can go down to the source of the problem and rectify that.

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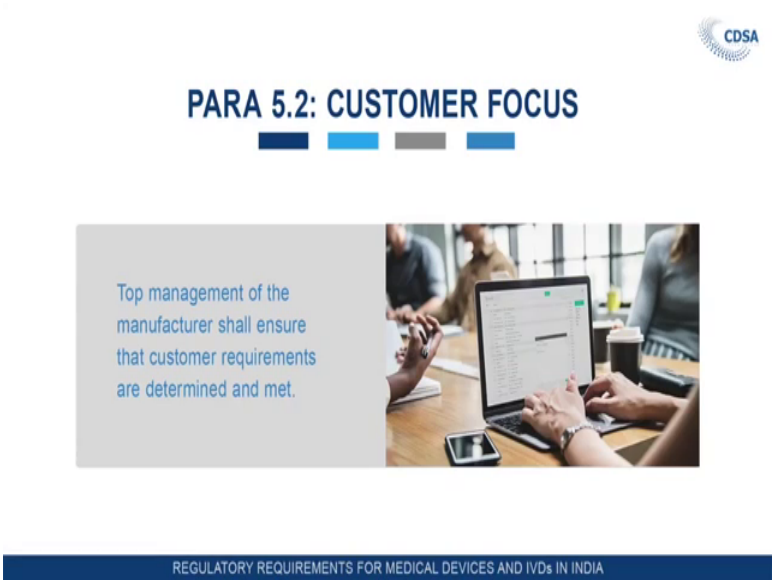

Customer focus; this is we know need to emphasize that customer requirements are determined and I met management of the manufacturers are ensure; that means, if I manufacture something a ten or a whatever it has to be to the satisfaction of the ultimate end user who is the customer. So, our production should be customer focused.

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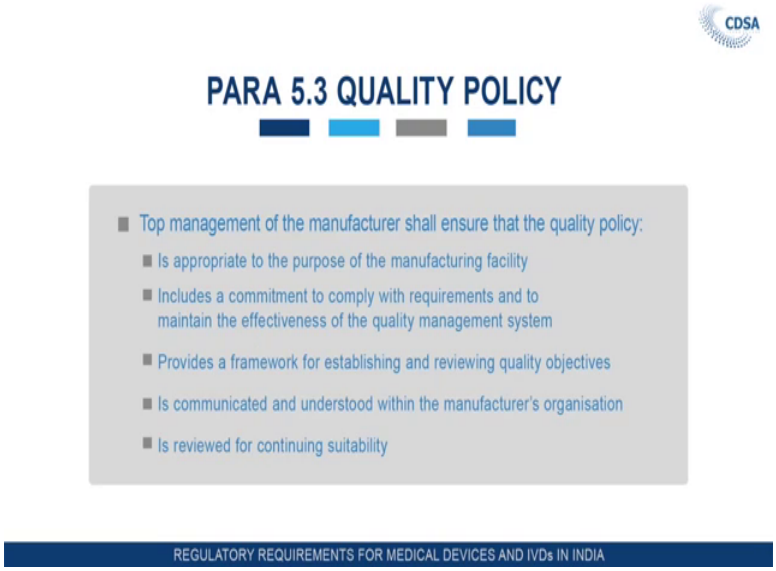

5.3 is quality policy; what is the quality policy of a plant? Quality policy is top management of the manufacturer shall ensure that the quality policy is appropriate to the purpose of the manufacturing facility. You cannot of a quality policy of something else applied to your plant; it should be appropriate to the purpose of the manufacturing the time to way.

Include a commitment to comply with the management requirements and to maintain the effectiveness of quality management system; provides a framework for establishing a reviewing quality objective is communicated and understood within the manufacturers organisation and is reviewed for continuing suitability. These each of these lines of self exploratory and they do not need to be elaborated further.

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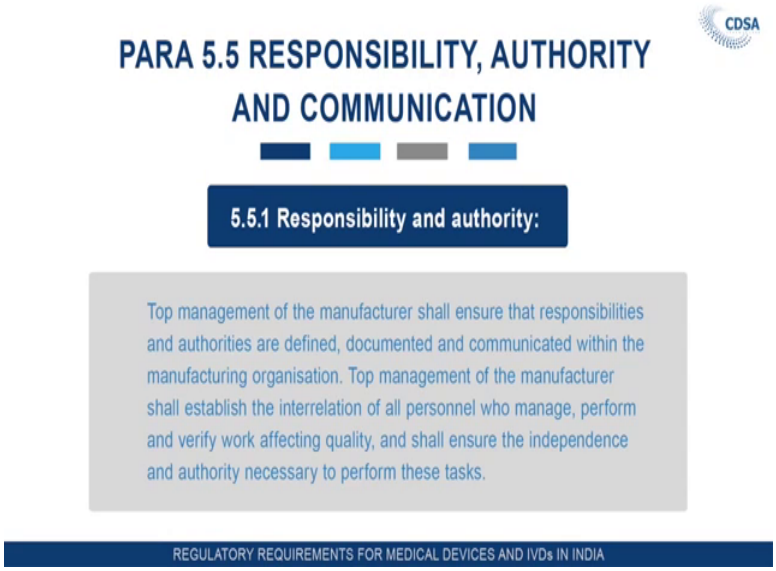

Responsibility authority and communication 5.5.1; responsibility and authority top management of the manufacturer shall ensure that the responsibilities and authorities are defined, documented and communicated within the manufacturing organisation. Top management of the manufacturer shall establish the interrelation of all personal who manage perform and verify work affecting quality and shall ensure to independence and authority necessary to perform these tasks.

We must ensure; we must emphasize over here other that in this case the ISO or QMS has roped in or the top management of the company. The directors or whoever the owners they are also responsible for quality. It is not only the shop floor people or the technical people; the top management shall ensure the necessary resources and facilities are provided and they shall be held responsible if it is not there.

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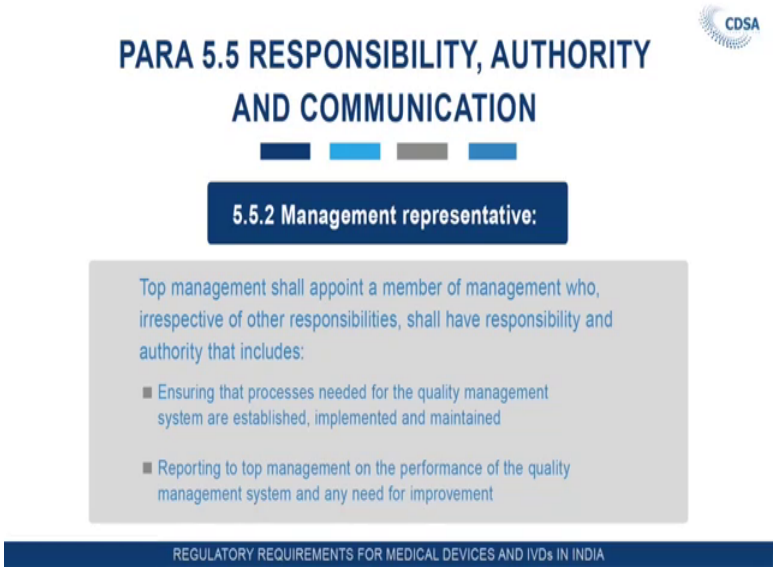

Management representative; who is the management representative? This is a management representative you can find a ISO 9000 also. Now, that is a replica; this is replica of that only. Top management shall appoint a member of management; who, irrespective of other responsibilities shall have responsibility and authority to that include ensuring that a process needed for the quality management system are established implemented and maintained.

Reporting to top management on the performance of the quality management system and any need for improvement and ensuring the promotion of awareness of regulatory and customer requirement in forth manufacturing organisation; that means, top management shall appoint a member of management; that means, top management system, directors who will appoint a person as a management there their representative for overseeing the whole process of QMS. These shall be responsible for as a communicating being between the top management and the plant to pass on the messages and improve things.

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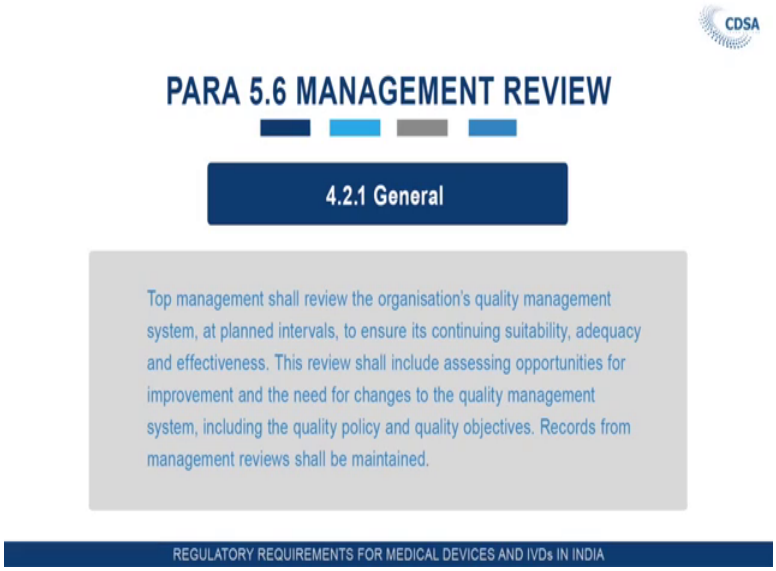

Management review; general, top management shall review the organisations quality management system at planned intervals to ensure its continuing suitabilities, adequacy and effectiveness. This is also the responsibility given to the top management. The top management cannot say that since I am a top management, I am a director of the company or we are the directors of the company. So, we are not responsible for this. They are fully responsible as per this para 5.6.1.

This review shall include assessing opportunities for improvement and the need for changes to the quality management system, including the quality policy and quality objective records from management review shall be maintained. It does not mean that the top management can be an expert or should be an expert in a particular medical device. He has to sit down with the management representative and the technical persons and discuss and decide for going forward further.

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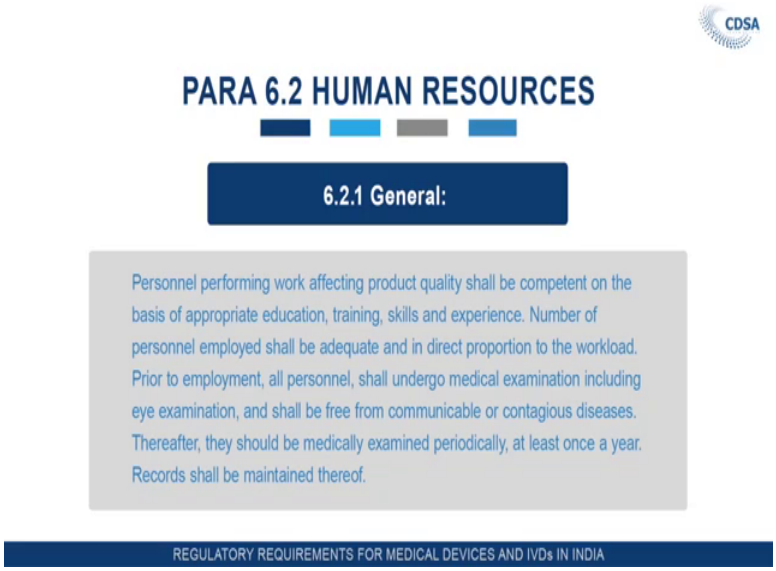

Human resources; general, human resources means people working in the plant, anybody; it can be the guard of the gate to the technical person who is actually overseeing the production; personnel's performing work affecting product quality shall be competent on the basis of appropriate education, training, skills and experience. Number of personnel employed shall be adequate and in direct proportion to the workload. These are all simple easy to understand sentences. Prior to employment all personal shall undergo medical examination including eye examination and shall be free from communicable or contagious diseases.

Thereafter, they shall be medically examined periodically at least once a year records shall be maintained thereof. Personnel performing work affecting, the first line affective product quality shall be component on the basis of appropriate education training, skills and experience. Now, as I get the example of a gate the guard over there may allow a truck containing material to come inside the plant after examining the suitable, suitability of documents to show that the plant requires that and then, verify then allows. So, everybody that is working in a plant has some sort of responsibility under the QMS and he has to follow that.

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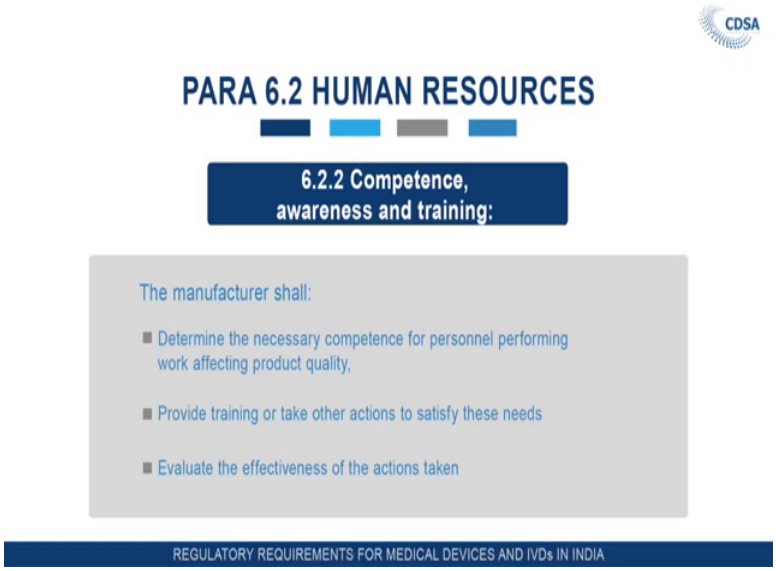

6.2.2 competence awareness and training; the manufacturer shall determine the necessary competence for personal performing work affecting product quality; provide training or take other actions to satisfy these needs. Evaluate the effectiveness of the actions taken; ensure that its personnel or aware of the relevance and importance of the activities and how they contribute to the achievement of the quality objective. Maintain appropriate records of education, training, skills are required experience. And establish documented procedures for identifying training needs and ensure that all personnel train that adequately perform their assign.

These all this provisions were there in Schedule M III in a different language. So, this is not something new for any manufacturer; training is very important and we know that training is actually improves quality. So, they have to be trained the evaluation of the training has to be done of the people who are taking the training. Then, they should be made aware of what they are doing. These are all records have to be maintained of the training. These all are Schedule M III, but in this it is a language of ISO basically, which expressed them.

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Infrastructure; we come to the breaker motor. Now, the organisation shall determine provide and maintain the infrastructure needed to achieve confirmatory to the product requirement. Infrastructure includes as applicable; buildings, 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 maintenance activities including their frequency; when such activities or lack thereof can affect product quality, record of such maintenance shall be maintained.

Now, this is very easy to understand. When they say that in such a means building, workspace and associated utilities it does not simply mean the (Refer Time: 30:46) the building and any workspace. Building or workspace are again control by distilled paragraph; what kind of building you required? What is infrastructure you required? The workspace, process equipment those are covered elsewhere, but this actually tells you that all these have to be controlled under the infrastructure 6.3.

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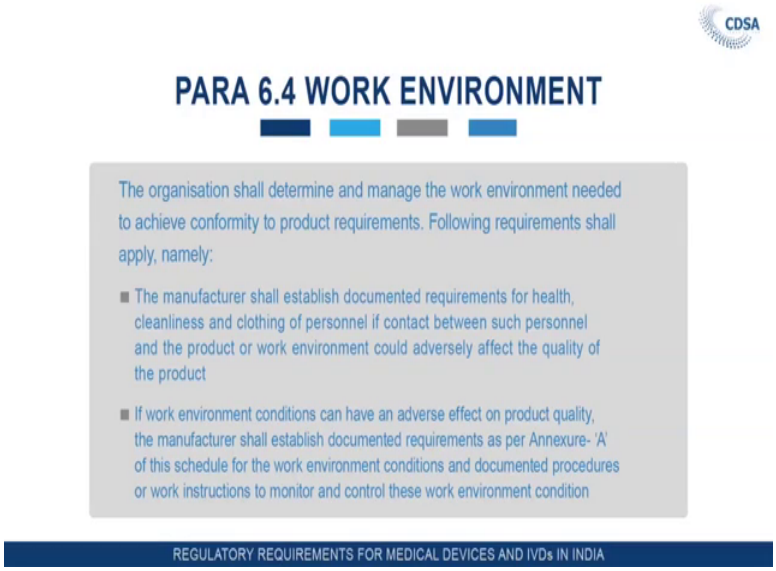

Working environment; the organisation shall determine the and manage the work environment needed to achieve conformity to product requirements. So, the environment that this used for the manufacture of these products should conform to the product requirement. Remember, the product should not conform to the environment, but the environment should be design for whatever the product a finally, is following requirement shall be, shall apply namely.

The manufacturer shall establish document requirements for health cleanliness and clothing of all personnel. If contact between such personnel and the product or work environment could adversely affect the quality of the product; that means, in simple language, if a operation requires that the personnel shall wear gloves and full body suit that is part of it. If they required to wash your hands and feet before entering the area that, forms part of the environment.

B says if work environment conditions can have an adverse effect on the product quality; the manufacturer shall establish documented provision requirement as per Annexure A, which is later on of the schedule for the work environment conditions and documented procedures for work instruction to monitor and control these work environment condition.

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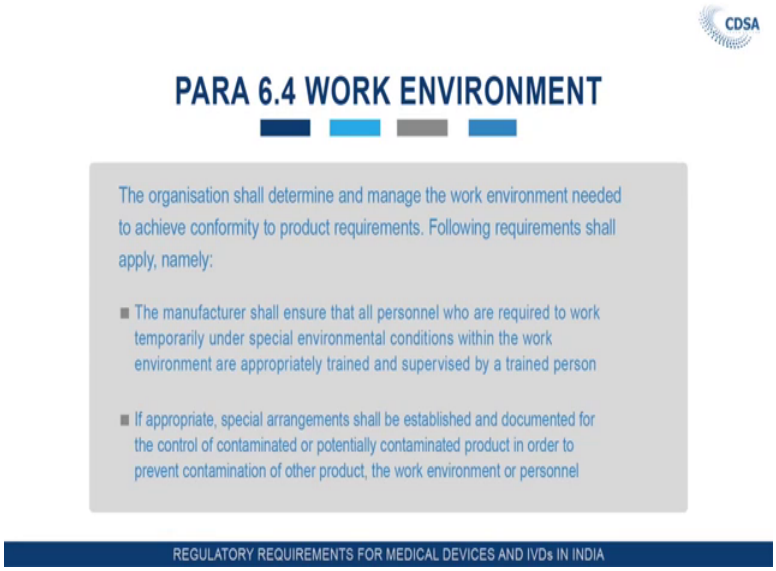

The manufacturer shall ensure that all personnel who are required to work temporarily. And the special environmental conditions within the work environment are appropriately trained and supervised by trained person. What does it mean? What does the C mean? C simply means in our layman's term that were required to work temporally; means either there temporally appointed of a short term basis to work in their environment. Or if I take it to a different level all together; if a machine in a special environment is broken down and the maintenance people have to enter the premises he works there a temporarily.

So, he shall be trained for that environment property; is appropriate. General, special arrangement shall be established and documented for the control of contaminated or potentially contaminated products. In order to prevent contamination of the product; the work environment or personnel; so, if a product has to be sterile, we have to have documented and established control of such product manufacturing. Special arrangement means it should have a clean room, clean air supply and all those stuff. So, the product personnel as well as the product is saved from contamination.

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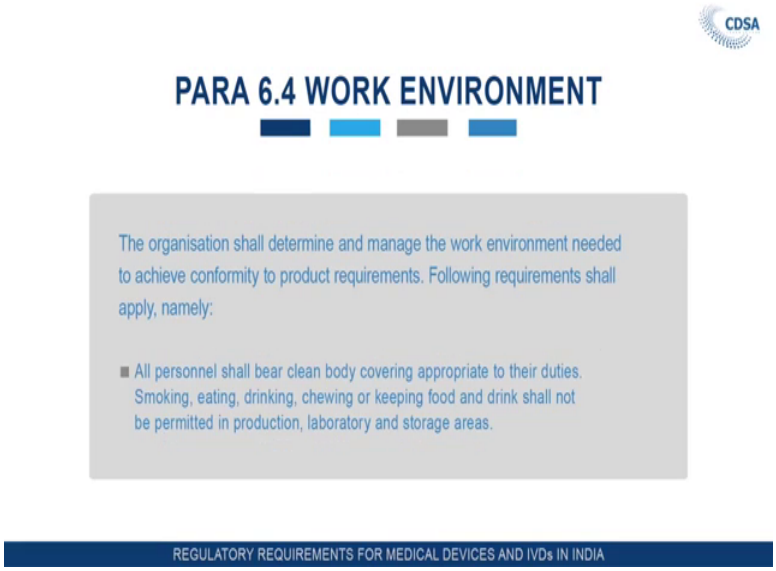

All personnel shall bear clean body appropriate to their duties. Smoking, eating, drinking, chewing or keeping food and drink shall not be permitted in production laboratory and storage areas. This is part of the length three which very clearly says these things.

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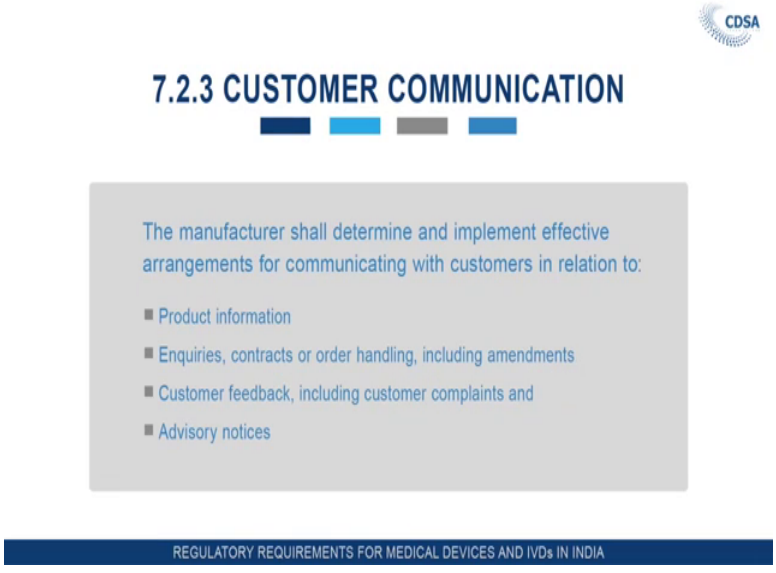

Customer communication; the manufacturer shall determine and implement effective arrangements for communicating with the customer in relation to product information; enquiries contract or other order handling including amendments; customer feedback,

including customer complaints and advisory notes. So, a manufacturer is not only the product of the manufacturer; should not only be oriented towards the physician or the personnel who is going to apply those products on a human body, but even the customer himself in case it is a patient, the patient has to have the product information to.

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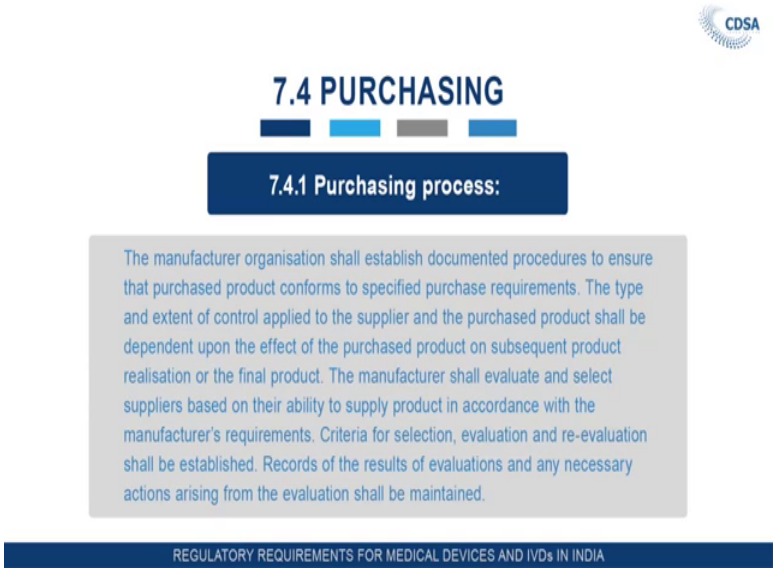

Purchasing process 7.4.1; the manufacturer organisation shall establish documented procedures to ensure that purchased product conforms to specified purchase requirement. The type and extent and control applied to the supplier and the purchase product shall be dependent upon the effect of the purchased product on subsequent product realization or the final product. The manufacturer shall evaluate and select suppliers based on their ability; this paragraph basically is vender evaluation in a common GMP terms.

Whenever you want to purchase a particular item from outside; you have to evaluate that product that it that the product that you purchasing is conforming to your final product and it is useful in that case. The vender there is supplying to you is confirms to quality management system and he is able to supplying with that product of consistent quality time after time. So, it is vender selection evaluation and revaluation shall be carried out.

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Verification of purchased product; this is basically in common term phase, this is testing of the raw materials purchased, but in this case in medical devices it may well go beyond the verification that is required for drugs. The manufacturer shall establish and implement the inspection or other activities necessary for ensuring that purchased product meets specified purchase requirements.

You may have to visit the venders premises to inspected or carry out anything else to ensure that the purchase product meets the specified purchase requirements. You have certain criteria for that purchase, purchase product and by way of any means including inspection you have to ensure that the manufacturer of that product can supply you that product as per your requirements. Where the manufacturer intends to perform verification at the supplier's premises; the manufacturer shall state the intended verification arrangements and methods of product release in the manufacturing, purchasing information.

Records of the verification shall be maintained; that means, you are also responsible for the products quality at the suppliers premises also. Paragraph related to GMP. Now, GMP forms a part of QMS. So, these are some of the paragraph which will actually related to GMP. Some of the paragraph that I mentioned earlier also conforms to GMP requirement; these are specific that I picked up for our understanding.

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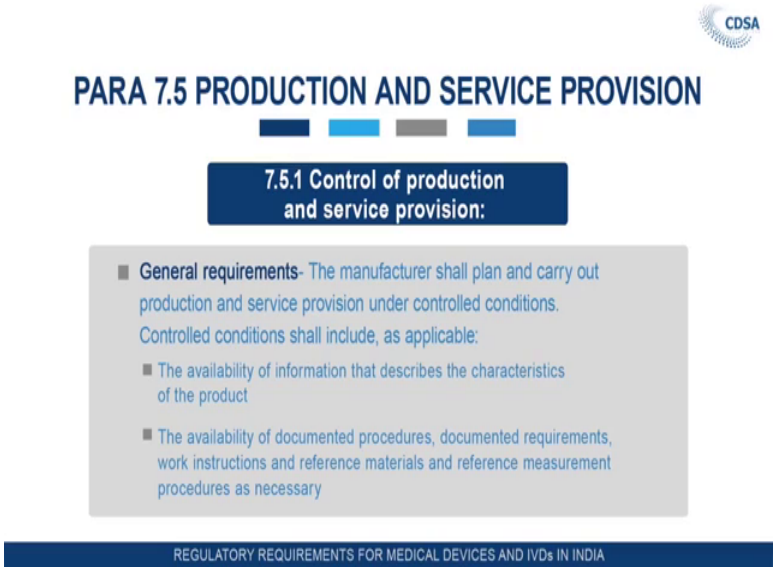

Production and service provisions; 7.5.1 control of production and service provisions; 7.5.1.1 under this para say general requirement, the manufacturer shall plan and carry out production and service provision under controlled conditions. Controlled conditions shall include as applicable wherever required. The availability of information that describes the characteristic of the product. The availability of documented procedures, documented requirements, work instructions and reference material and reference measurement procedures are necessary.

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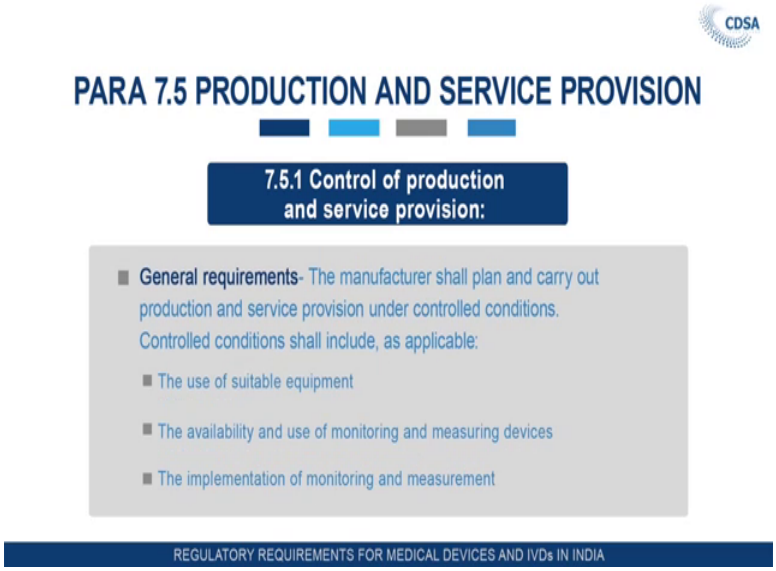

The use of suitable equipment, use the availability and use of monitoring and measurement devices. So, this is the general requirement of a manufacturing process as required.

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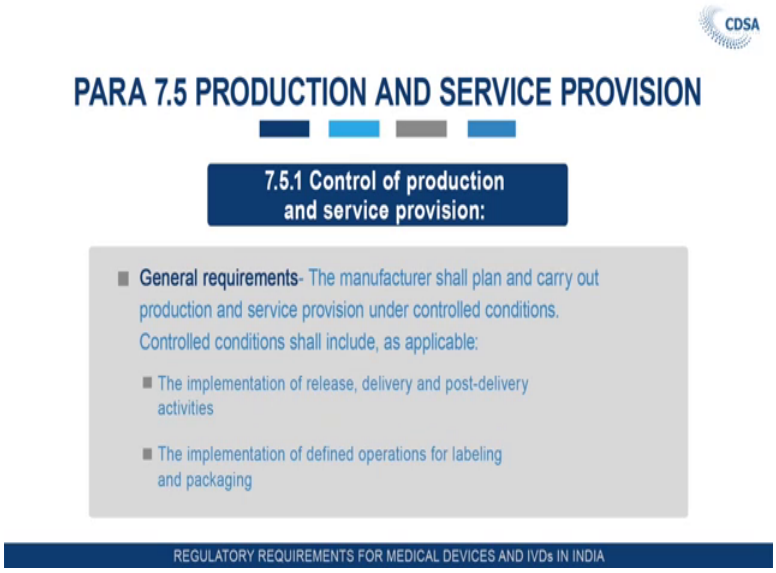

Followed by the implementation of monitoring and measuring equipment is the implementation of release delivery and post delivery activities; that means, not only you release the product and deliver it. Even post delivery activities you have to implement as per the requirement of that particular product. The package, the implementation of define operations for labeling and packaging.

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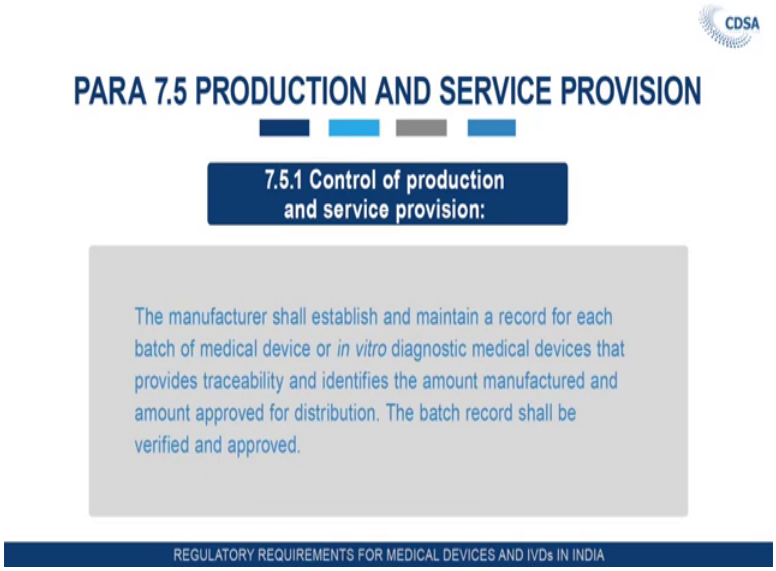

The manufacturer shall establish and maintain a record of each batch of medical device or in vitro diagnostic medical devices that provides traceability and identifies the amount manufactured and amount approved for distribution. The batch record shall be verified and approved. The last para is very important and. so well known in the manufacturing circles of pharma.

We have to have a batch record; that means, we are manufacturing in a batch of say 20 products, 20 medical devices then, that 20 batch record shall be their; giving all details of that the raw material the manufacturing process, the release distribution, documents etcetera. And, these shall be verified by somebody over in the personal who is preparing these and approved.

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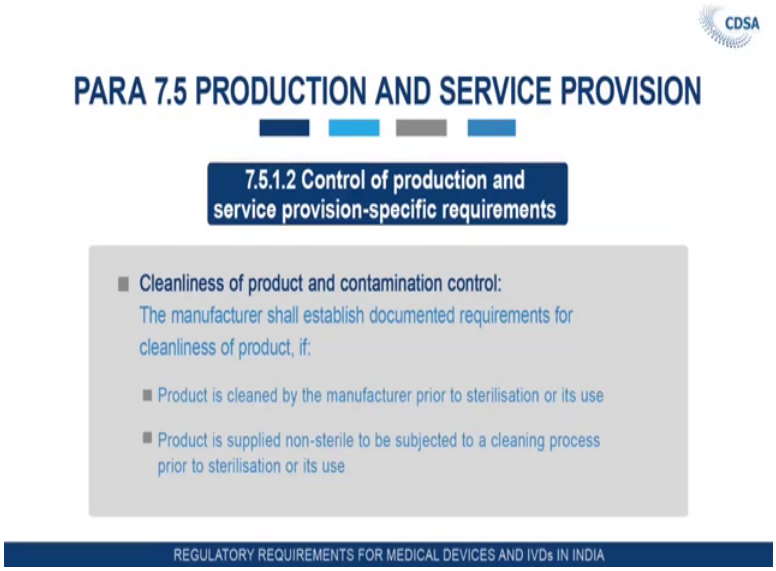

7.5.1.2 Control of production and service provisions specific requirements; one of that is cleanliness of production contamination control; the manufacturer shall established documented requirement for cleanliness of the product; if product is cleaned by the manufacturer prior to sterilization or its use.

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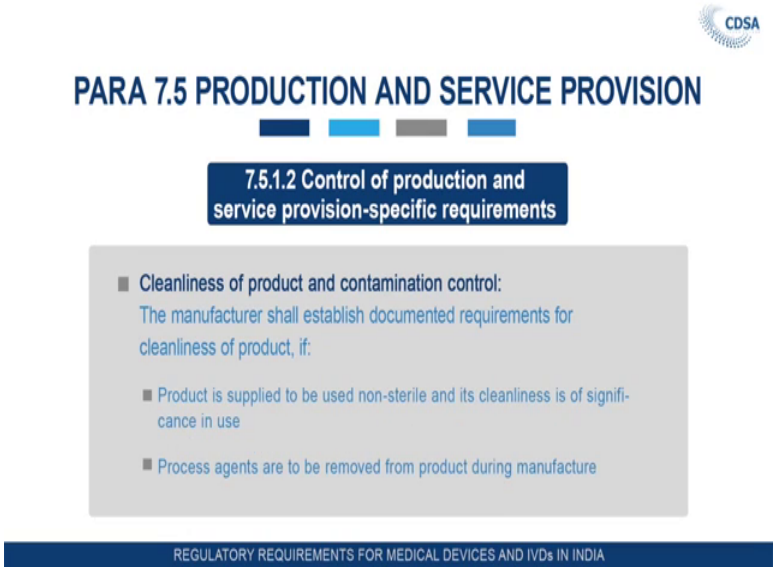

Or product is supplied non sterile to be the subjected to a cleaning process prior to sterilization. Or its use or product is supplied to be used non sterile and its cleanliness is of significance in use. Or process agents are to be removed from the product during

manufacture. Now, this is this is this is something which we treat between the lines actually. The product is to be cleaned we understand that it has to be clean. Now, the level of cleanliness depends on it is use; it can be manufacture by you ah.

And made sterile by sterilization process and packaged and sold. It can be sterilized before used by the user or it can be sold non sterile too. Sometimes what happened is process the agents are to be removed from the product; in case of, I can give you a very simple example of a process agents; in case of ethylene oxide sterilization, we find that the ethylene oxide gas it use for sterilization of certain eye times like syringes or tyvek paper packed products. Now, in case you want to sell that product we must ensure that ethylene oxide is 0 in the product after it is sterilized. So, anything that is used in the process has to be removed which we are not required in the final product.

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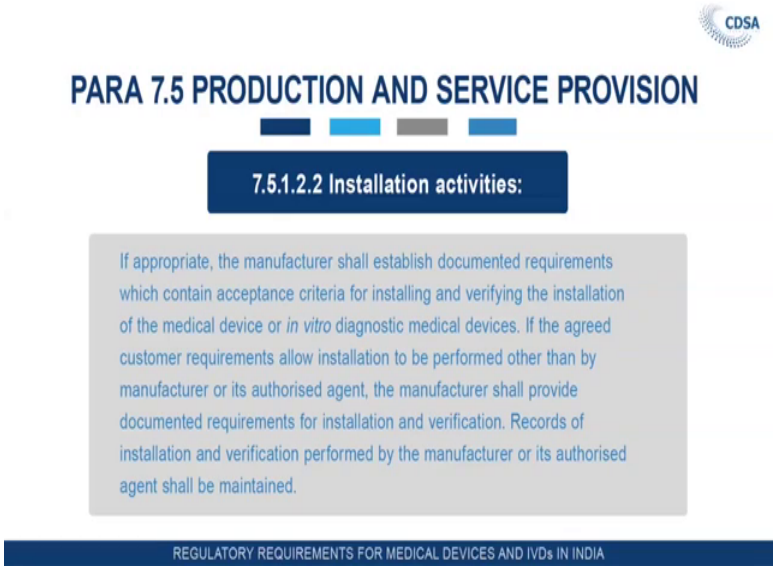

Installation activities, if appropriate the manufacturer shall establish documented requirement; which contain acceptance criteria for installing and verifying the installation of the medical device in or in vitro diagnostic medical device.

If the agreed customer requirement allow installation to be performed other than by the manufacturer authorized agent; the manufacturer shall provide documented requirements for installation and verification. Records of installation verification performed by the manufacturer or its authorized agent shall be maintained. Now, we are the bit confused in this; we all are because how do you install a medical device? This is not for the medical

devices, which are notified at the moment. These are for both medical devices whichever large for it is of MRI machine or X ray machine which are actually installed in a manufacturing premises. In such cases, the manufacturer shall provide the necessary know how and the man pot install that the premises if they cannot; they must provide the necessary documents for a third party to install that machine in the premises.

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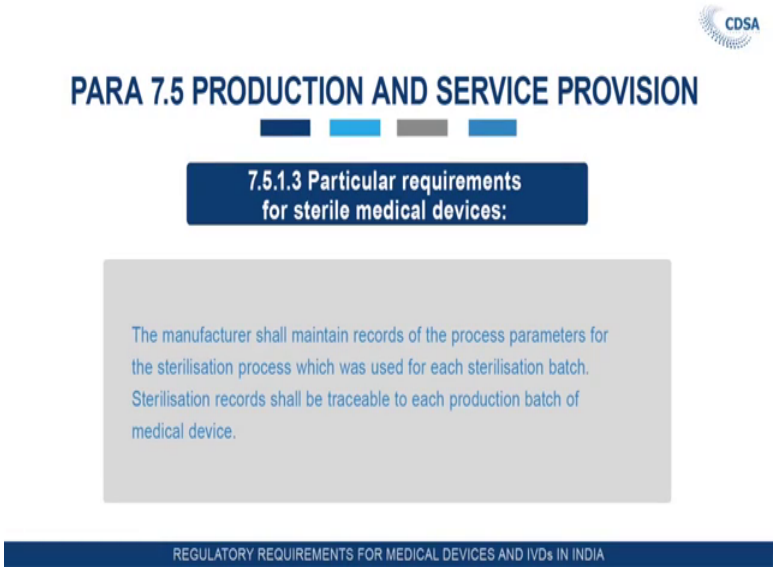

Particular requirements for sterile medical devices, this is very important because lot of medical devices in the market which are high and class t risky medical devices are sold sterile. These medical devices either usually go into the human body for use or cultural human body for used. The manufacturer shall maintain records of the process parameters for sterilization process, which was used for each sterilization batch.

Sterilization records shall be traceable to each product batch of the production batch of the medical device. This is very simple; we know that whenever you have to sterilize something the parameters of the sterilization are to be maintain. What kind of sterilization with a steam, dry heat, and ethylene oxide or gamma radiation each batch that goes through it has to be documented and record in the manufacturing records.

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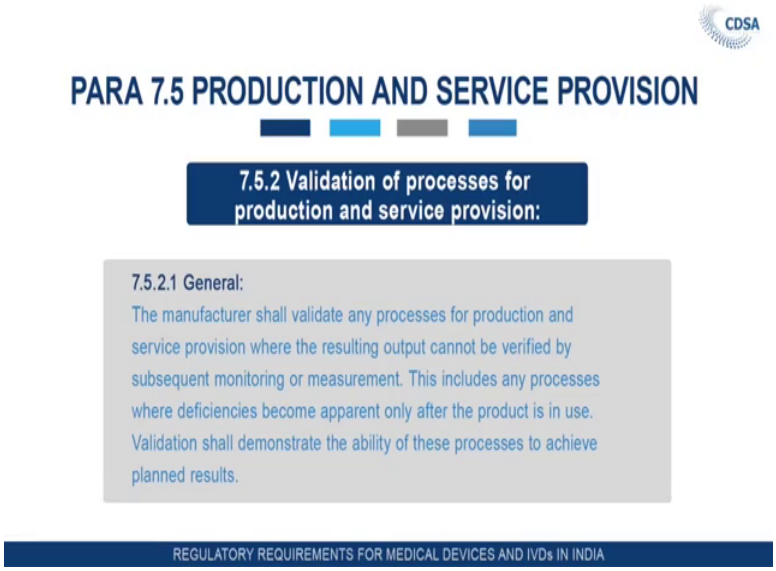

7.5.2 Validation of process for production and service provision, we had a glimpse of validation earlier. Now, in this its mark for in detail; 7.5.2.1 says in general, the manufacturer shall validate any process or production and service provision where, the resulting output cannot be verified by subsequent monitoring or measurement. This includes any processes where, deficiencies become apparent only after the product is in use.

Validation shall demonstrate the ability of these processes to achieve planned result. There are lot of medical devices; we know very well that what are medical devices; they which cannot be the usage of that product cannot be validated by way of end product testing, at the end of the production cycle. So, in that case the manufacture has to validate each process that is going on in the manufacturing, that which is of course, designed carefully for that particular process. So, that at the end of the day even if the product is not tested it complies with their standards.

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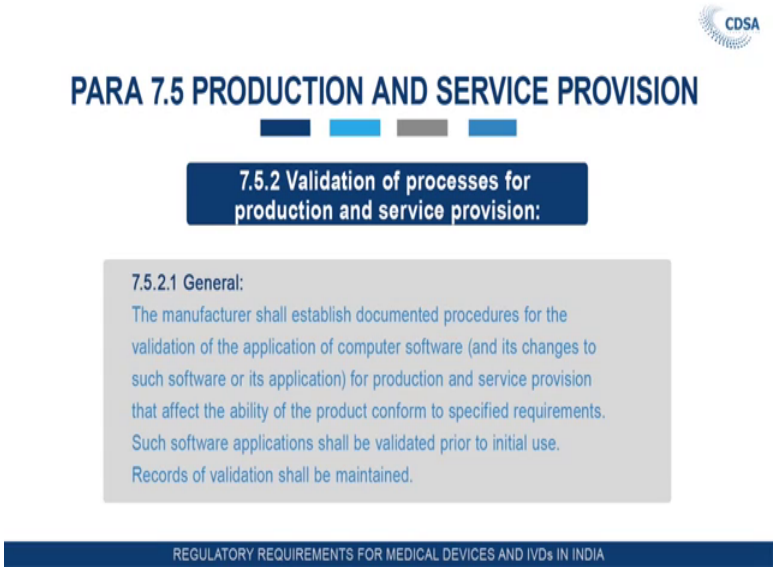

Manufacturer shall establish documented procedures for the validation of the application of computer software and its changes to such software. Now, in this case it is a computer software validation in the devices that are notified at the moment do not require any computer or software for they running; these are required in high end medical devices, which are actually of the range of say MRI, X-ray machines and all those equipment which required a software for its running in application. So, that software or computer system has to validated again.

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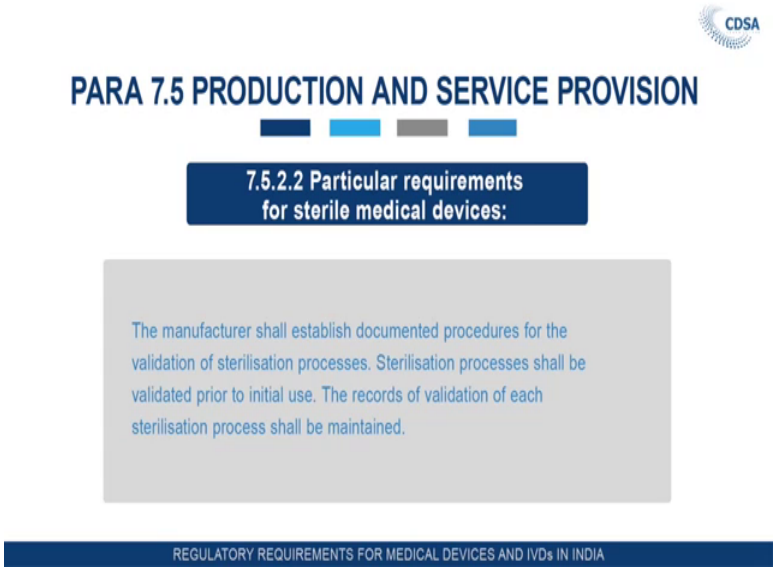

Particular requirements for sterile medical devices; it is 7.5.2.2 is extension of 7.5.2. Manufacturer shall establish documented procedures for the validation of sterilization process. Sterilization process shall be validated prior to initial use; the records of validation of each sterilization process shall be maintained. We already saw that as I as I batch we saw that; that each batch has to be validated. In this case each production cycle of a sterilization process has to be again validated and recorded.

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Traceability 7.5.3.2.1 is general; the manufacturer shall establish documented procedures for traceability. Such procedures shall define the extent of product traceability and the records required. Where traceability is requirement; the manufacturer shall control and record the unique identification of the product; that means, what happens is once the product goes on the market in used and it means it malfunctions.

We have to back trace from the product to the manufacturer, to the production cycle, to the batch. So, this is actually traceability and in case of intra plant traceability, we can trace a particular process to a batch to a person who made that; who activated that process and who responsible. Traceability of an action: in a manufacturing plant each extremely important to troubleshoot problems later on.

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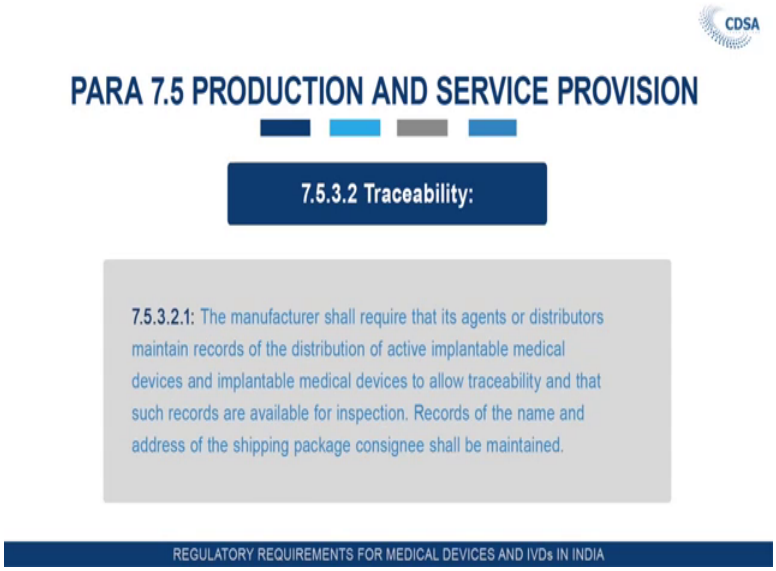

Manufacturer shall require that it is agent or distributions maintain record of the distribution of active implantable medical devices. And implantable medical device to allow traceability and that such record are available for inspection. Records of the name, address of the shipping, package, consignee shall also be maintained. So, it is a comprehensive record keeping of the whole product.

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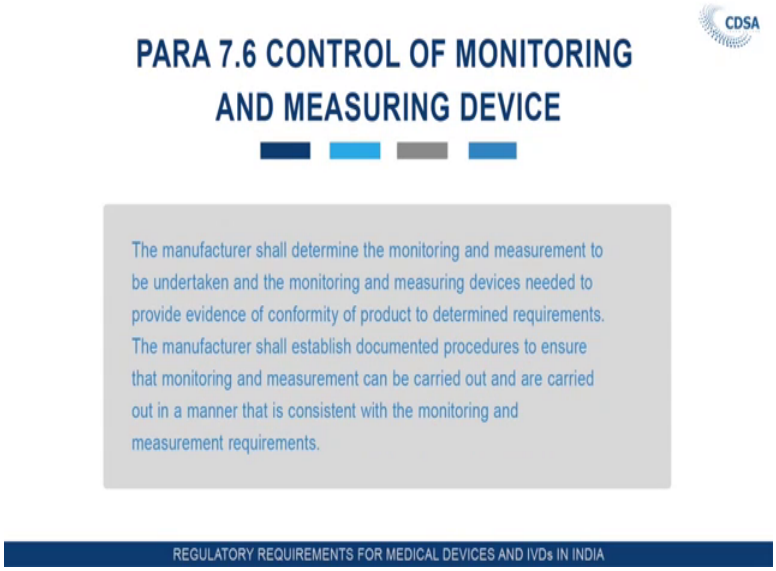

7.6 Control monitoring and measuring devices; these are devices which actually control and record and measure unit quantities of anything. For instance, it can be temperature

pressure relating humidity or length breath which is, which has a quantifiable value. The manufacturer shall determine the monitoring and measurement to be undertaken and the monitoring and measuring devices needed to provide evidence of conformity of the product to determined requirements. The manufacturer shall establish documented procedures to ensure that monitoring and measurement. And measurement can be carried out and are carried out in a manner that is consistent with the monitoring and measurement requirements.

So, the monitoring in measurement requirements are control by monitoring and measurement equipments; which are again depended on what is the requirement of the product. The product requires a length of 6.5 inches. The instrument require for that measurement should be calibrated; for that particular item now and then we calibrated. So, that anything that is going on in the plant, which can be identified by a value, has a machinery or equipment or instrument which is actually proper calibrated and use regularly.

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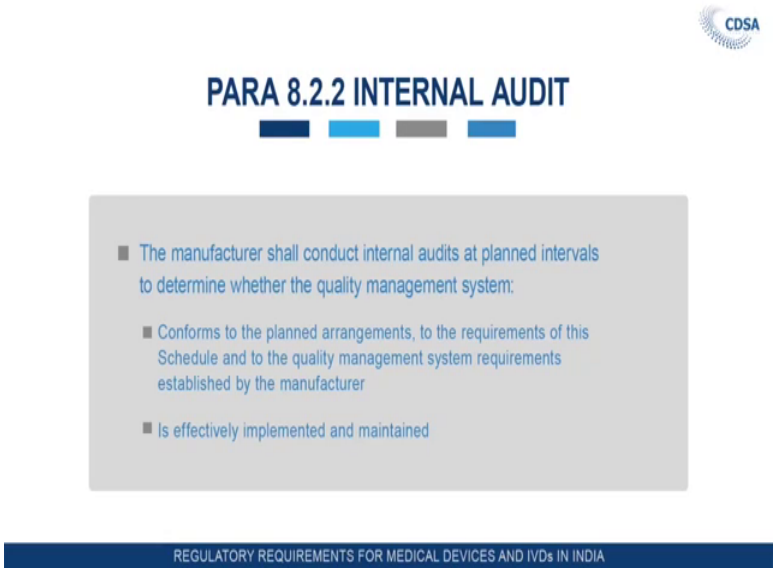

Internal audit; now, what is an internal audit? The manufacturer shall conduct internal audits at planned intervals to determine whether the quality management system; conforms to the planned arrangement to the maintenance to the requirements of this schedule and to the quality management system requirements established by the manufacturer and is effectively implemented and maintained.

What is internal audit? Internal audit is basically a self infection of the plant by its own. Internal audit is different from external audit in which an external agency carry out, carries out an audit. For the regulator to carry out a inspection it is an external audit, but internal audit carry out. It is internal inspection sort of we can say in which selected personal for the plant carry out the audit of the plant as per the requirement a thorough honest audit to find out the requirements that are actually out of specifications or improvement that are required to be done and records of such have to be maintained properly.

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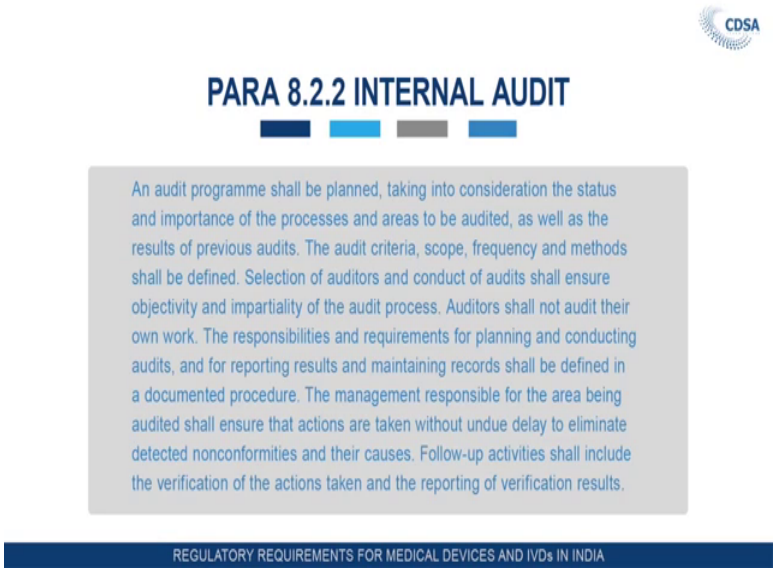

And audit programme shall be planned; now, this internal audit programme shall be planned taking into consideration the status and importance of the processes and area is to be audited, as well as the pre results of previous audits; that means, if this is the simple process you need not do the audit internal audit or the regular basis. But it is a critical process that internal audit has to be done properly and documented. The audit criteria, scope, frequency and methods shall be defined.

Selection of auditors and conduct of audits shall be ensure the objectivity and impartiality of the audit; I mean it is needed to say that audit has to be extremely impartial; you cannot be partial to a particular area within the order because that particular area has one of the persons whom you like. So, it has to be impartial and it is best to avoid auditing those areas by interested people of the plant have neutral impartial

people audit in those areas. Original shall not audit their own work; very important as I mention a laboratory audit cannot be done by personnel for the laboratory. It has to be from somebody other than the laboratory area.

The responsibilities and requirements for planning in conducting audits and for reporting results and maintaining records shall be defined in a documented procedure. The management responsible for the area being audited shall ensure that the actions are taken without undue delay and eliminate detected conform conformities and their causes follow up activities shall include the verification of the actions taken and the reporting of the verification result.

After now, I already have to prepare a nonconformity report or the audit report in which it has to be mentioned and highlighted the short comings and in the action taken to be time to be given. And, the conformities have to be the deficiencies have to be conform to the requirements within that particular time period.

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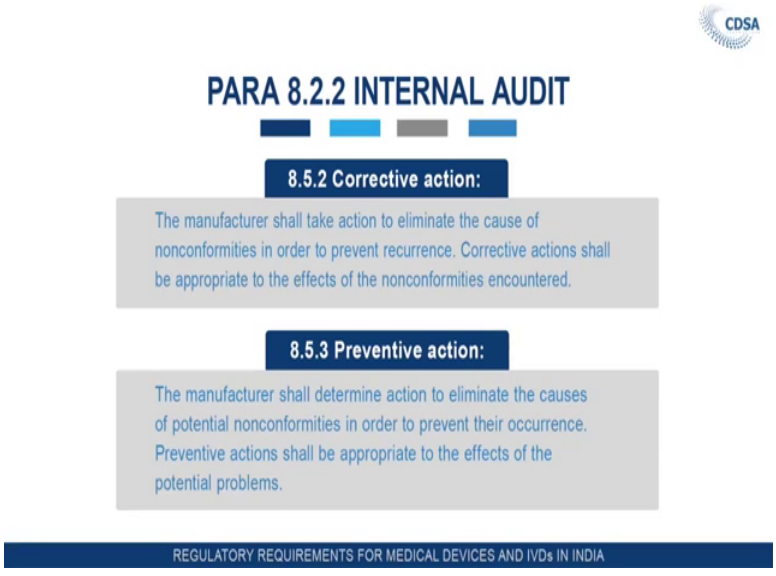

Corrective action; manufacturer shall take in, take action to eliminate the cause of nonconformities in order to prevent. Recurrence; corrective action shall be appropriate to the effective to the effects of nonconformities encountered; explain in earlier also. Corrective action is simply removing the defects and recording it. Preventive action, the manufacturer determined action to eliminate the cause of the potential conformities.

In order to prevent their occurrence; preventive action shall be appropriate to the effects of the potential problems. Preventive action is basically, preventing maintenance is one can be preventive action; likewise.

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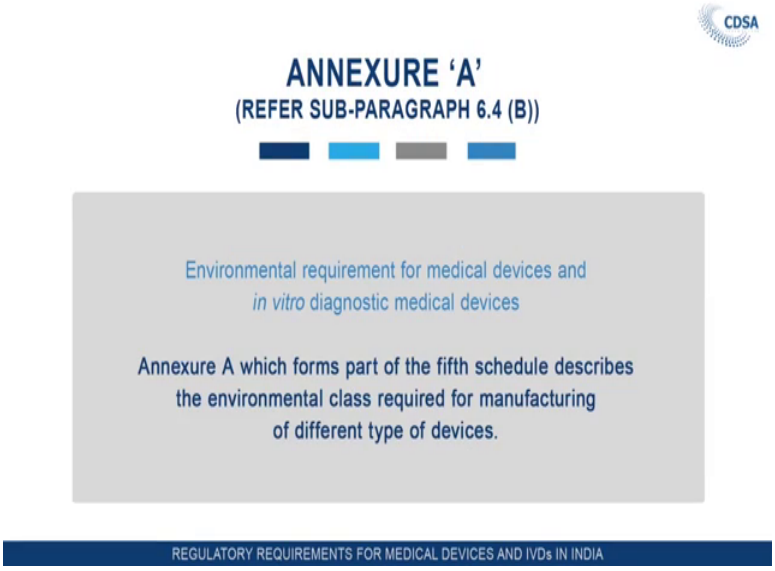

Annexure A refer to sub paragraph 6.4 B; environment requirement for medical devices and in vitro diagnostic medical devices. Annexure A which forms part of the fifth schedule describes the environmental class requirement for manufacturing of different type of devices. We have different classification Class A, B, C, D, E particle count grade a, grade A, grade C the all this requirements will conform to the requirement of a product.

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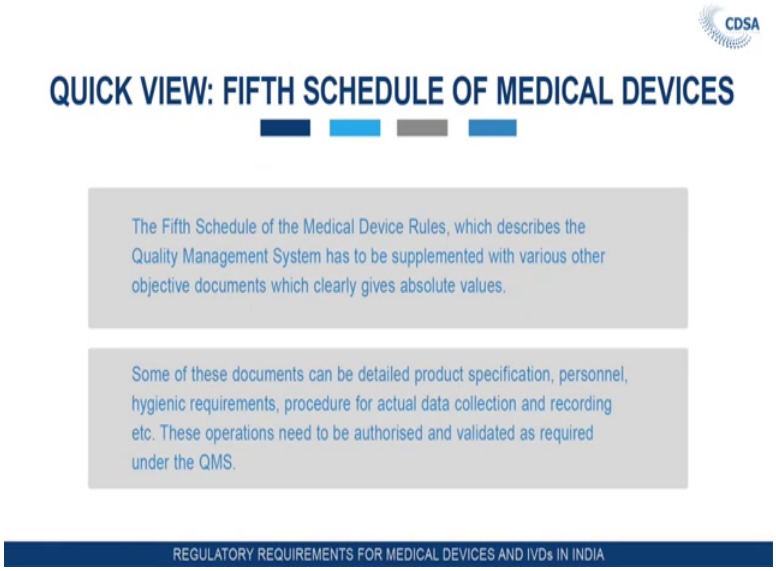

The fifth schedule of medical device rule, which describes the quality management system, has to be supplemented with various other objective material which clearly gives absolute values. Some of these documents can be detailed products specification, personnel, hygienic requirements, procedure for actual data collection and recording etcetera. The operation need to be authorized.

And validated as required under the QMS; that friends, in the actual is Quality Management System, if you have any queries you can get back to us and we shall make a every effort to answer your queries and remove your doubts.

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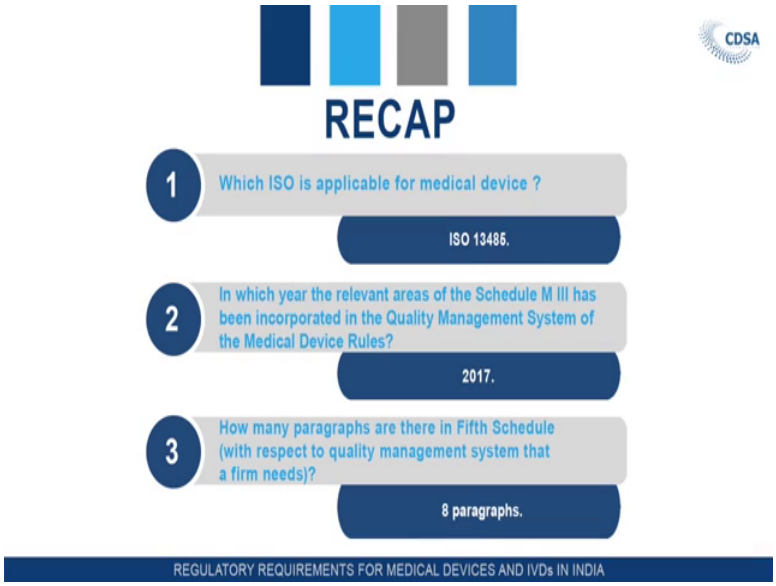

Now, some of the question and answers over are over here; very simple one. However, you will be getting much more question and answers, we have to submit later on for assessment.

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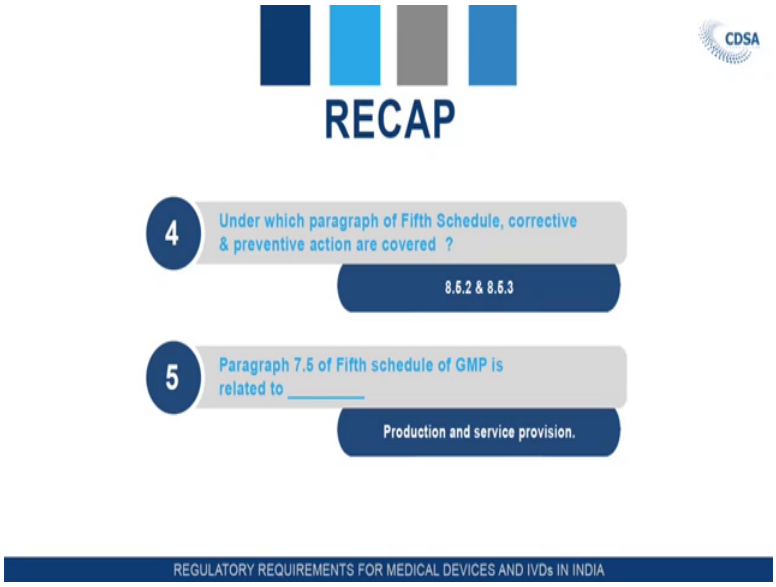

Thank you very much.