Regulatory Requirements for Medical Devices including In Vitro Diagnostics in India (Version 2.0)

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Lecture – L5
Regulatory Requirements of Biocompatibility of Medical Devices and ISO 10993

Welcome to Regulatory Requirements for Medical Devices including In Vitro Diagnostics in India version 2 lecture 5, lecture 5 that is Regulatory Requirement of the Biocompatibility of Medical Devices as per ISO 10993.

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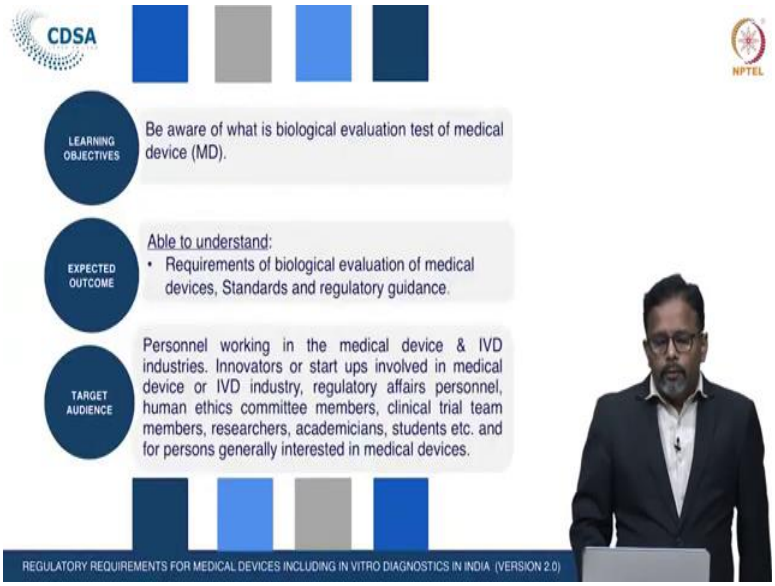

Learning objective this lecture, be aware what is the biological evaluation test? What is the requirement of these biological test of the medical devices? Expected outcome- the participants can able to understand, what is the requirement of the biological evaluation of the medical devices? What standards is applicable for the biological evaluation and the regulatory provisions for the requirement of biological evaluation test for medical devices?

Target audience, the personnell working in the medical devices and in vitro diagnostics industry, the startup involved in the medical devices and diagnostic industries, the regulatory affairs personnel, human ethics committee members, clinical trial team

member, researchers, students, academician and the person generally interested in the field of medical devices and in vitro diagnostics.

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What will we learn in this lecture? First we will discuss what is the biocompatibility, then bio evaluation with risk management process what are the process for risk management process for biological evaluation, then categorization of the medical devices and test selection based on the category of the medical devices which type of biological evaluation is required.

The standards, the standards applicable for conducting the biological evaluation and the general principles of the standards prescribed for biological evaluation of the medical devices.

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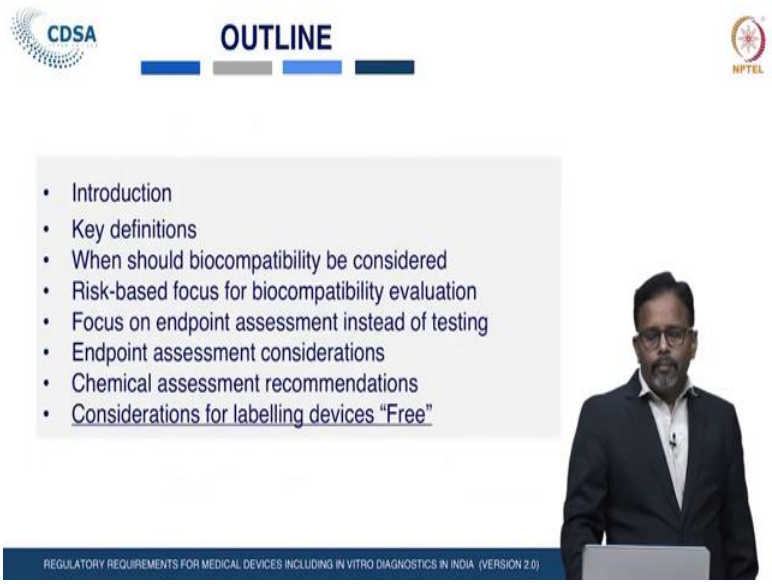

So, all topics we will discuss in this lectures and we will have detailed discussions we will have the question answer session. Now, what is the bio materials?

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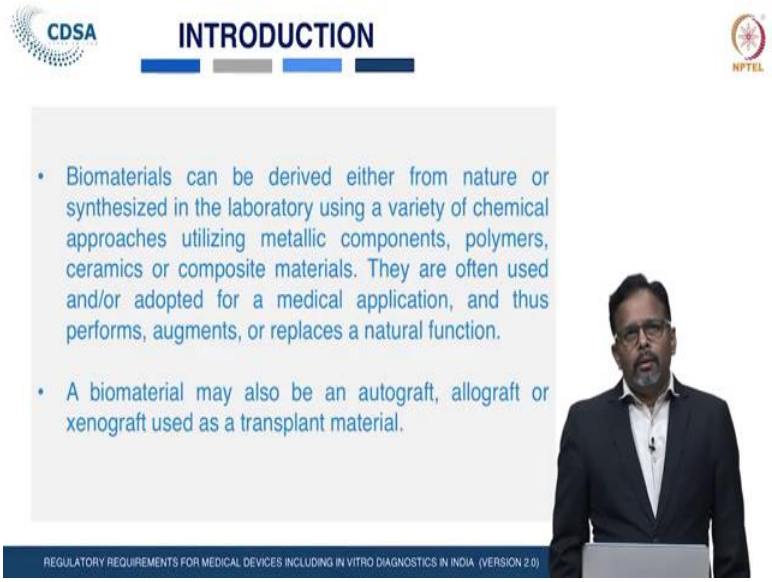

Bio materials can be derived either from the nature or synthesized in the laboratory using the variety of the chemical process variety of the approach utilizing the metallic component, polymers, ceramics or composite materials. They are often used and adopted for a medical application and perform and replace the natural functions of the human body

This bio material may also be an autograft, allograft, xenograft used as a transplant material.

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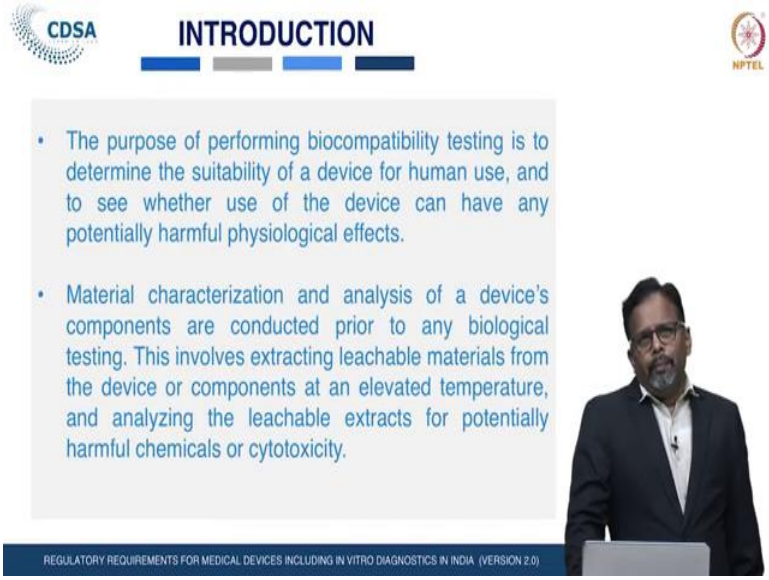

The purpose of performing biocompatibility testing of these biomaterials is to determine whether the suitability of the devices for human use and to see whether use of the devices can have any potential harmful physiological effect on the human body. So, this is the purpose of the biocompatibility. The material characterization and analysis of the devices components are conducted prior to conduct of any biological evaluation, it is not that once the bio material is developed immediately the biological evaluation or bio compatibility test can be performed.

Prior to conduct of the biological evaluation the material characterizations and analysis of the devices is compulsory. This material characterization includes extracting leachable materials from the devices or the component at the elevated temperature and analyzing leachable extract for potential harmful chemicals or cytotoxicity.

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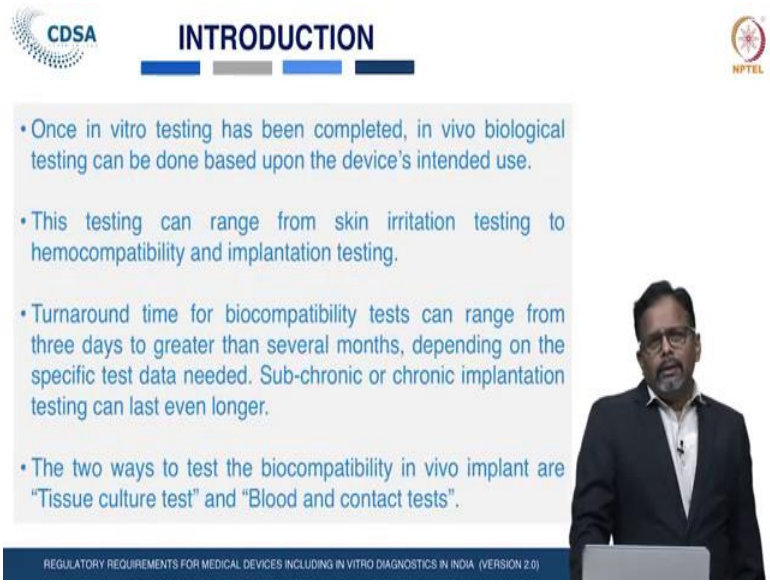

Once this in vitro testing has completed the in-vivo biological test can be done based on the device intended use. The biological evaluation testing can be ranges from the skin irritation test to hemocompatibility test, implantation test etc.

The turnaround time for biocompatibility test can ranges from 3 days to greater than the several months, depending on the specific test data needed for the materials. The sub-chronic or chronic implantation test can last even longer period. The two ways to test the biocompatibility in vivo implants are "tissue culture test" and "blood and contact test".

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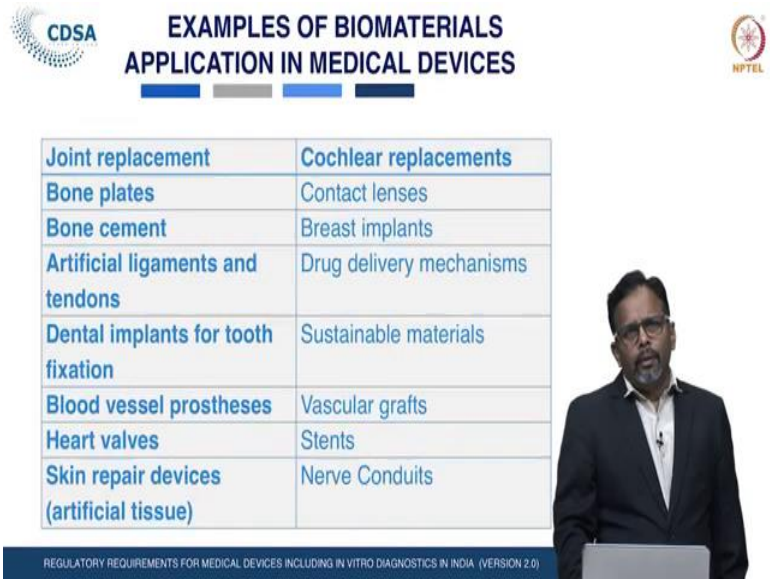

The example we have discussed what is the biomaterials and the applications of the biomaterials. These biomaterials applications is meant for manufacturing of that joint replacement, bone plates, bone cements, artificial ligaments and tendons, heart valves, skin repair devices, breast implants, vascular grafts, stents, nerve conduits, contact lens these are the applications of the bio materials.

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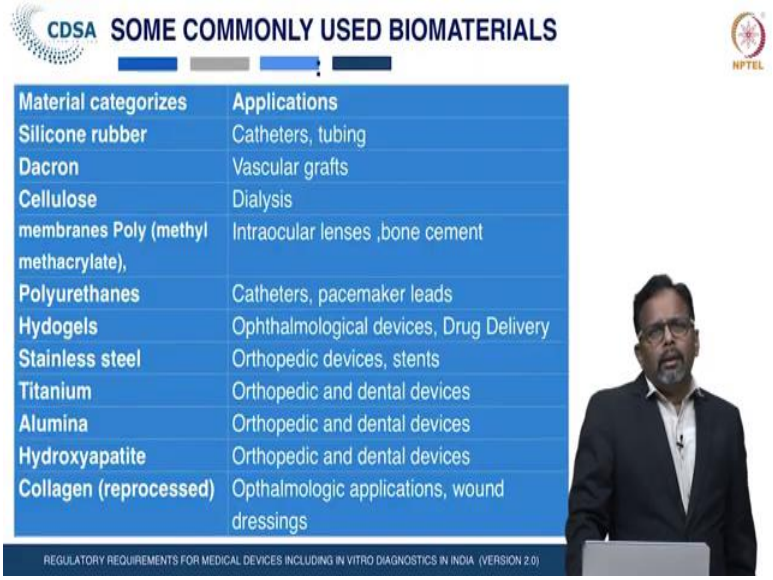

And which biomaterials are generally used for which applications we can discuss that, the various biomaterials are available like silicon rubbers. This material is to be generally used in the manufacturing of the catheters or tubes. Cellulose that is for the dialysis devices, polyurethanes that is used in the manufacturing of catheters, pacemaker leads. A stainless steel metals if you talk about the metals, the stainless steel that used in the orthopedic devices or cardiac stent, titanium that is also used in the orthopedic implants and also in the dental devices.

Alumina orthopedic and dental devices, hydroxyapatite that is also used in the orthopedic and dental implants, collagens ophthalmological applications or various wound dressing the collagens are to be used. So, these are the applications of the certain biomaterials which is used for applications of the manufacturing of these types of the medical devices. Now come to the definitions, certain definitions that related to the biocompatibility.

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First of all what is the biocompatibility? Biocompatibility is the measurement of how a compatible a device is with the biological system. Another way we can say it is the ability of the device material to perform with an appropriate host response in a specific situation.

Now, the other definition, that is direct contact or indirect contact, what is the indirect contact? Indirect contact is defined as the term that used for the devices or device component that comes into physical contact with the body tissue. If it is a physical contact with the body tissue it is considered as a direct contact.

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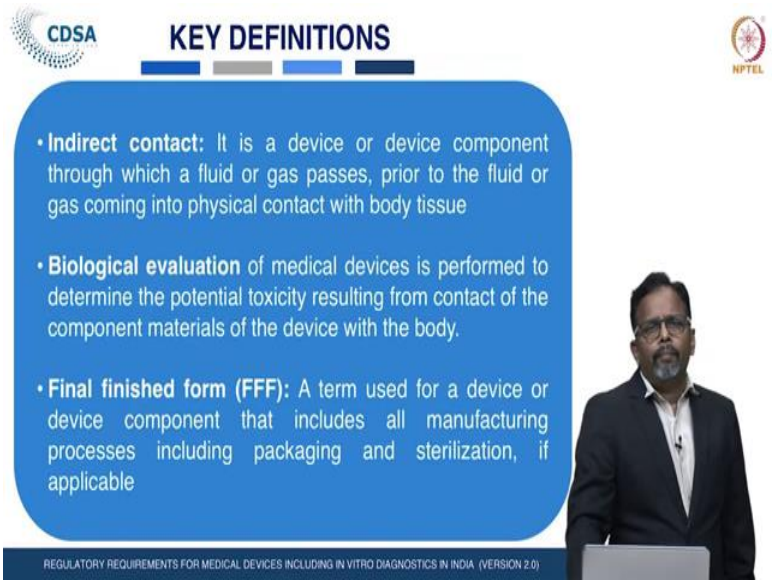

What is indirect contact? The device or device component through which a fluid or gas passes prior to the fluid or gas coming into physical contact with the body or body tissue. So, it such type of that devices or the device component through which a fluid or the gas passes prior to the fluid or gas coming into the physical contact with the body tissue that can be considered as indirect contact.

Now, biological evaluation it is also known as the biocompatibility the biologic biological evaluation of the medical device is performed to determine the potential toxicity resulting from the contact of the component material of the device with the body, this is the biological evaluation. Now, finished form of the devices that is the final finished form this term used for the devices or device component that includes all manufacturing process including packaging crystallizations if applicable.

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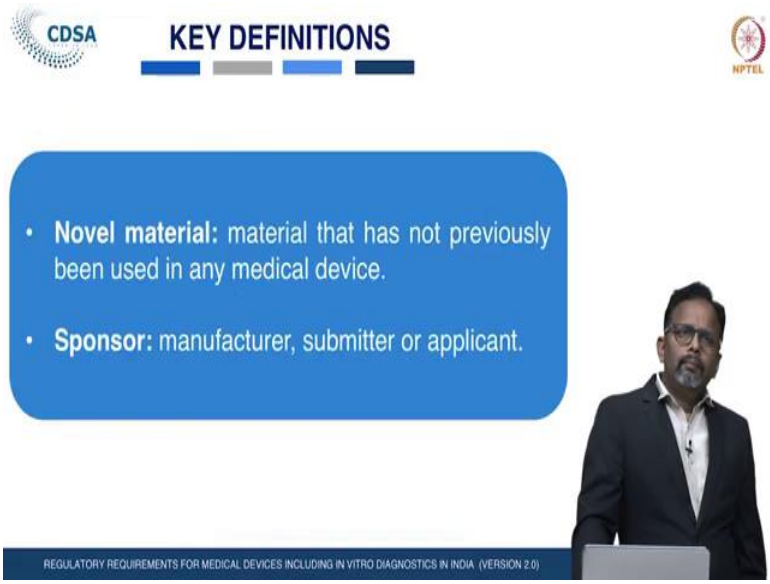

Novel materials this term can be defined as the materials that has not previously being used in any medical devices new materials which is yet to be used in their particular applications. So, any new material that has not previously used in any medical devices is known as is termed as novel materials. A sponsor, means manufacturer, applications submitters, who will submit the application for regulatory approval or any purpose to the authorities that is done by a sponsor.

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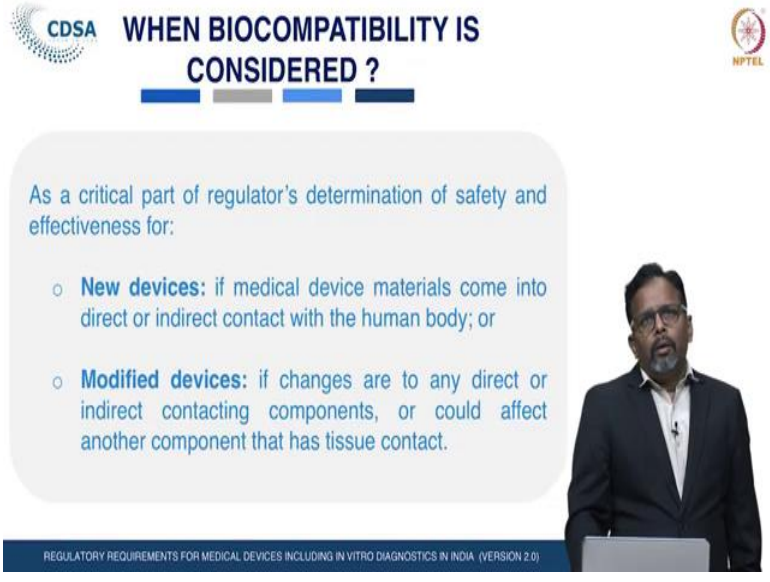

Now, come to the biocompatibility, given biocompatibility is considered we have to understand in which cases this biocompatibility test or the biological evaluation test can be considers. It is a critical part for the regulators determination of the safety and effectiveness of the new medical devices of the modified medical devices.

So, for any new devices if the medical devices, material come direct or indirect contact with the human body. Then the biological evaluation can be considers or if the particular changes have been made in the devices which affect another component which has come to the tissue contact in such cases this biological evaluation or bio compatibility test is also required.

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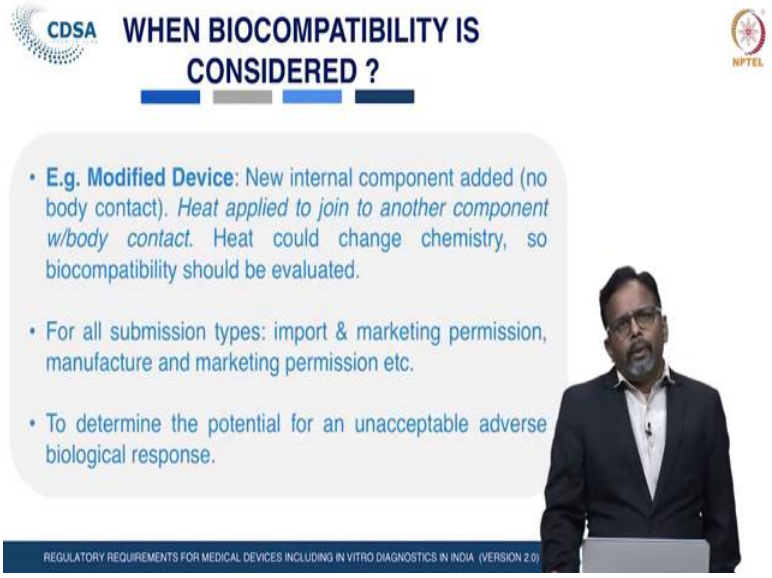

Modified devices why it is required, because in certain cases if the new internal component is added on the particular medical devices that added through some heat, heat is to be applied to join the another component with the main device. The heat could change the chemistry of the biomaterials so; in such cases the biocompatibility test is required.

This bio biological evaluation or the biocompatibility test is also required for submission of regulatory approval for import or the marketing permissions or manufacture and marketing permissions. Sometimes this study is required to determine the potential for unacceptable adverse biological response. So, in such cases this biological evaluation test can be performed on the medical devices or the component of the medical devices.

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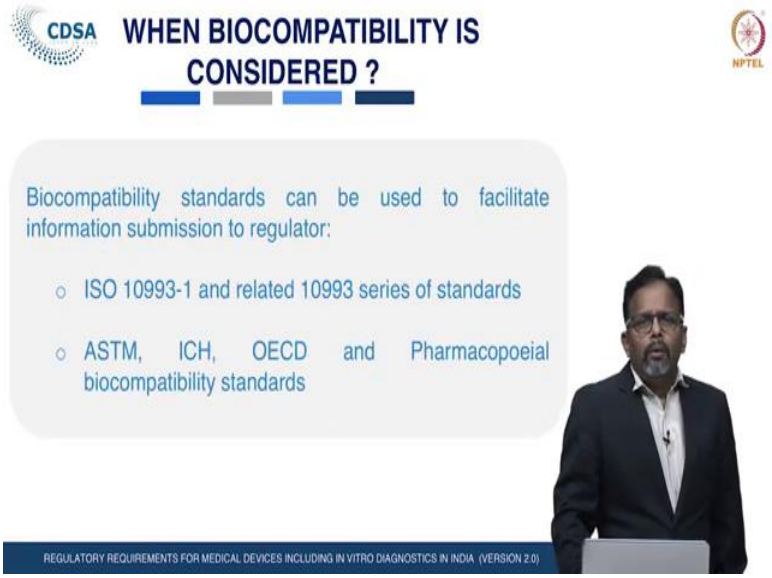

Now, the biocompatibility test It should be carried out as per applicable standards some biological evaluation test the standards have been prescribed in pharmacopoeia, some have been described certain guidelines or the standards have been describing other standards.

But the ISO 10993 that is the standards developed by ISO for biological evaluation of medical devices, various series of this standards are available and each series have different standards, guidance, principles that is included in the various series of the ISO 10993 also some ASTM or ICH or OECD guidelines are standards are also applicable and that is adopted by the other regulators.

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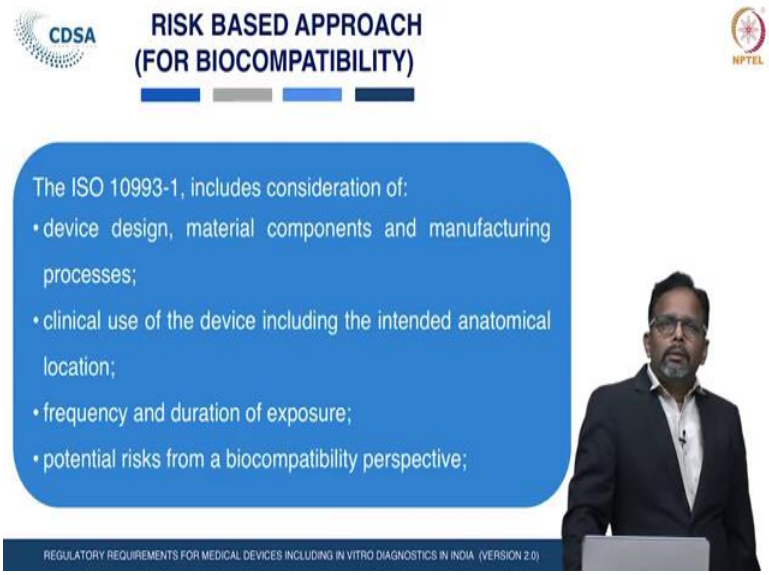

We will discuss that the standards ISO 10993 which is applicable for determination of the biological evaluation of the medical devices as per our Medical Device Rule 2017. So, in India these standards it is in the law it is clearly defined that ISO 10993 where the biological evaluation has been prescribed that should be applicable for conduct of the conduct of this test.

So, what are the main component, principles, guidance and approach for conduct of the biological evaluation, we will have some brief discussion on thisstandards. What is the standards this ISO 10993, this standards include consideration of the design devices material component and manufacturing process. This also includes the clinical use of the medical devices including the intended anatomical locations where it is to be implanted or used.

The frequency and duration of the exposure, if the device if certain time it has to be exposed to the human body so, based on the frequency and duration of the devices the test can be decided. Potential risk from the biocompatibility perspective, if there any potential risk is there in such cases also this standards this includes the consideration of such cases also.

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If certain information is available to address the identify the risk any other risk and then information needed to address any remaining knowledge gaps certain gaps are there in particular materials such as the new biocompatibility testing or other evaluation that appropriately address the risks. In such cases what type of that evaluation is required to carry out on the biomaterials or the component of the medical devices or the medical devices all those parameters, that standards includes.

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The biocompatibility test may not be needed, if the device is made of the material that has been well characterized chemically and the physically and also there is a lot of published literature is available and have long history of safe use, in such cases the bio evaluation test cannot be required or cannot be considered, provided the adequate literature and the data on the product or the biomaterial has to be produced by the manufacturers to justify whether this is required or not.

If the material or the manufacturing information is provided to demonstrate that no biocompatibility concerned is exist on the medical devices. So, in such cases it is not necessary to carry out the biological evaluation test.

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If you see the risk based approach the bio evaluation biological evaluation may be possible to leverage the previously conducted biocompatibility formations. If the previously tested device have similar indication, similar type and also the duration of the contact of the device is the same, in such case also there is the compatibility study is not necessary.

The information provided by the manufacturer to explain why differences are not expected to impact the Biocompatibility. It meets the manufacturer has to justify properly adequately by way of the published literatures the study already performed earlier and the safe views history of the safe use of that devices. They can justify who are

not performing the biological evaluation with a particular medical devices or component of the medical devices.

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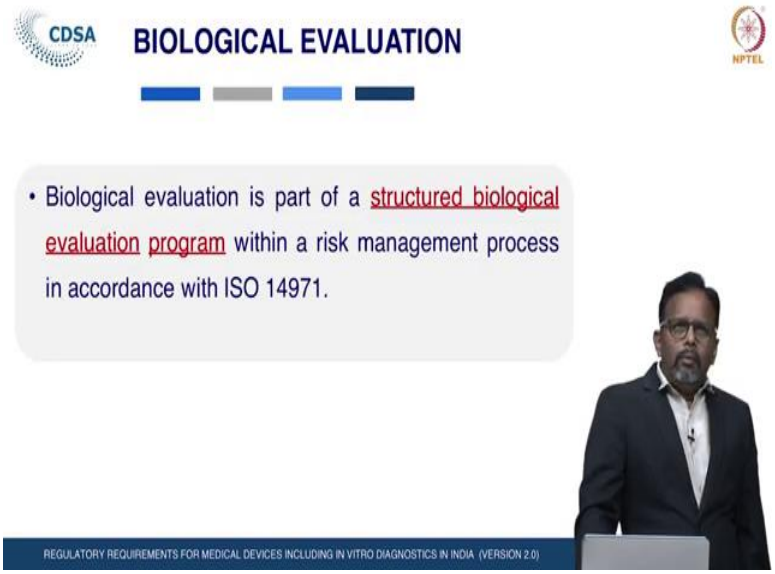

Now, come to the biological evolution, we have already discussed what is the biological evaluation, it is a part of a structure biological evaluation program within the risk management process in accordance with the ISO 14971 Risk Management Process(RMP) that ISO 14971 is applicable for all the medical devices and in vitro diagnostics. So, this biological evaluation study is the part of the risk management process in accordance with the 14971 ISO.

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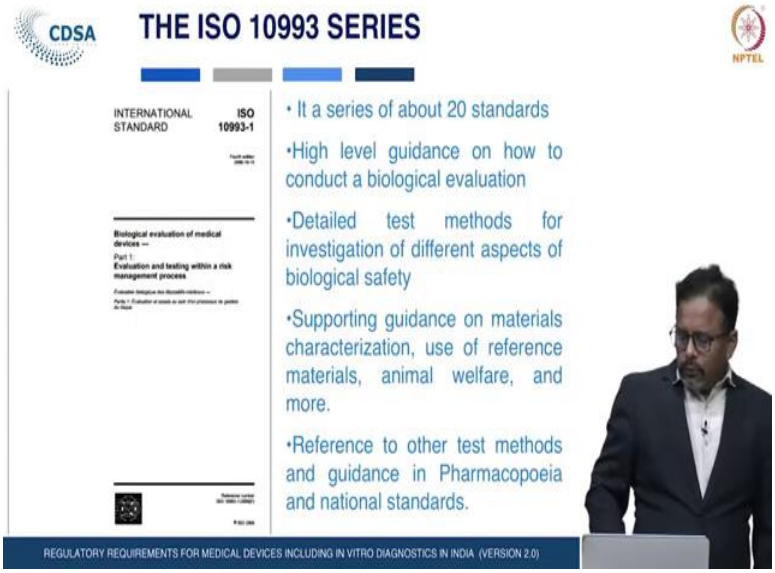

This ISO 10993 series we have discussed that it has various series and approximate 20 series of the standards is applicable 20 -22 standards are presently applicable for the biological evaluation. It is a high level guidance and how to conduct the biological evaluation, various types of the biological evaluation that procedure methods or guidance has been given in this standards. If you see the series 1, series 1 that is the general biological evaluation standards here are the details of the test method for the investigation of the disk different aspect of the biological safety.

That is given the annexures. it has 3 annexures and annexure A, annexure B and annexure C. Annexure A the matrix is available is given based on the categorization of the medical devices which test are required to conduct and which are not required that annexure A is there. Annexure B in which cases how to approach the risk based analysis of the devices and based on that what the study is required that manufacture can decide.

Annexure C that is the published literatures and the data review how to review that available data with respect to the biocompatibility of the particular biomaterials of the medical devices. So, this annexures provided in this ISO 10993 series we will discuss that.

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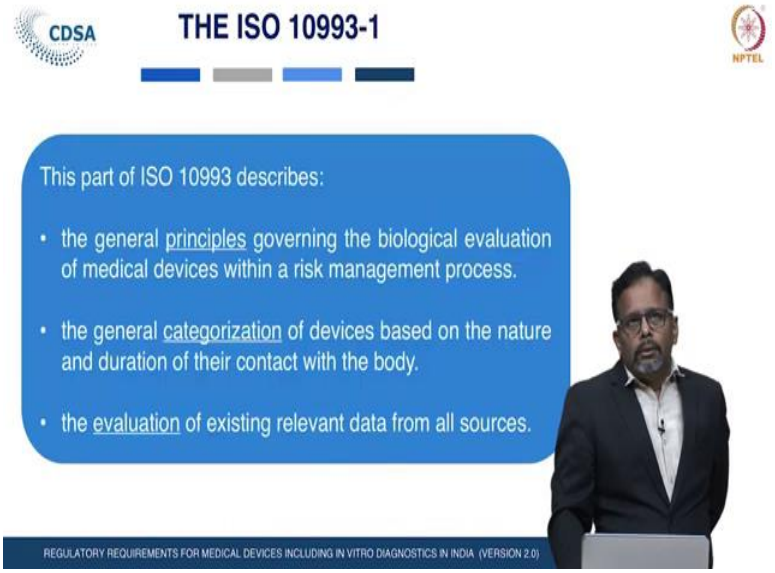

We have discussed that the 10993 series 1 that is the general standards which describes the general principles of the biological evaluation. The categorization of the medical devices based on the nature and the duration of their contact with the body. this categorization is given in this ISO 10993 part 1.

The evaluation of the existing relevant data from all the sources, this describe the identification of the gap that based on the standards that based on the available information.

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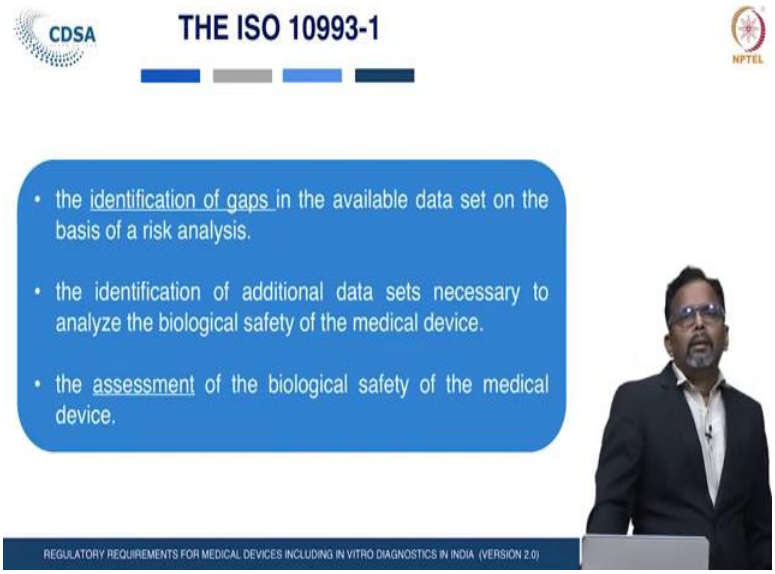

The identification of gaps in the available data set on the basis of the risk analysis that can be carried out. The identification of the additional data set necessary to analyze the biological safety of the medical devices and the assessment of the biological safety of the medical devices. These component has been described in this first series of the standards annexure A already we have discussed .

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Annexure A contains the informative tables it is applicable that in general helpful for identify the biological data sets recommended for evaluation of the medical devices; according to the category of the body and the duration of the exposure of the devices to the human body.

The appendix B that is the guidance for the application of the risk management process, how the risk management process is supplied the biological evolutions shall be planned, carried out and documented by the knowledgeable and experienced professionals.

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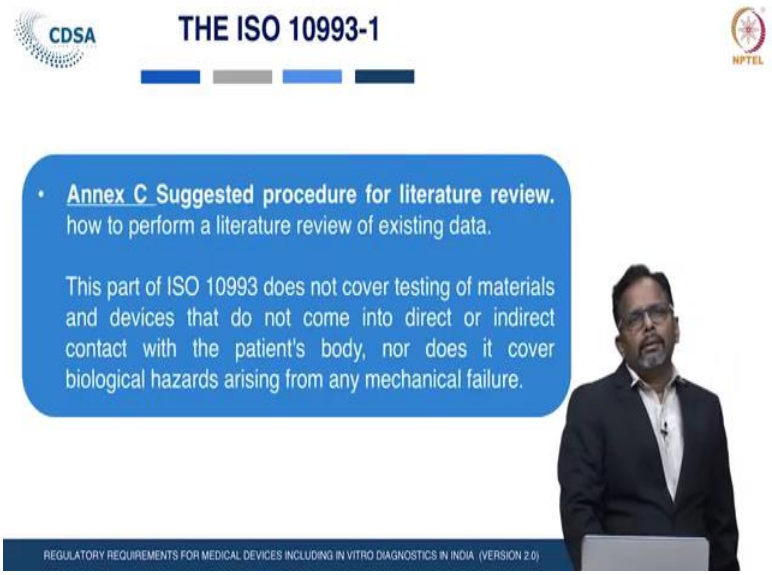

Annexure C that is the suggested procedure for the literature review, how to perform the literature review for the existing data, these are given in this annexure C of this standards. This ISO 10993 does not cover the testing of the materials or the devices which do not come into contact or indirect contact with the patient body, nor does it cover the biological hazards arising from any mechanical failure.

It means this standards, this biological evaluation test is only applicable to those devices which are direct or indirect contact with the patient body.

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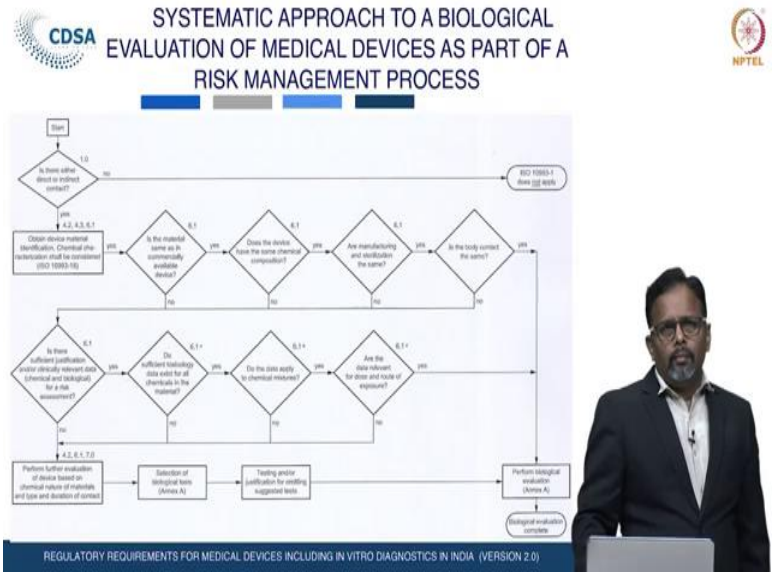

Now, the risk approach to the biological evaluation of the medical devices as a risk management process we can discuss this, this flowchart you just see in this flowchart it is clearly mentioned that risk management process has been applied which cases this biological evaluation is required.

In which cases this it is not required and where the all the biological evaluation is required in which cases the it is not required and where the al the biological evaluation is required to be carried out this flowchart gives that detail idea. If you see the devices the manufacture can decide if the devices have direct or indirect contact with the human body or not.

If it is in direct contact or indirect contact with the human body then this standards is applicable and the biological evaluation can be carried out on such type of the devices. If it is not in direct contact or indirect contact with the human body the scope of this standard is not apply, that is in such type of devices this biological evaluation test is not required to be carried out.

If that biological evaluation that bio materials is direct or indirect contact with the human body, then the device identifications chemical and physical categorization of the devices shall be carried out by the manufacturers and also after carrying out the chemical categorization the requirement of the biological evaluation that can be decided.

We have discussed in the previous slides prior to conduct of the biological evaluation these chemical categorization of the medical devices or the biomaterials is required to be carried out to prove the safety, safety of the devices So, once it is conducted then the manufacturer has to see whether the biomaterials is the same which is commercially available in the market.

If it is commercially available then whether the devices have the same chemical component, if it is a same chemical component then also he has to see whether the manufacturing or the sterlization, the manufacturing of the devices the method applied for the manufacturing and the sterilization is the same which is already available medical devices.

If it is same then whether the body contact is also the same, if the commercially available device have the same sterilization process, same chemical composition, same body

contact in such cases the manufacturer has to perform the biological evaluation assessment as described in annex B of the standards.

They will carry out risk management process based on the data available and after that they have to decide whether which test is required and whether the test is carried out by the firm is sufficient to decide to whether the product is safe for use in the particular applications or the device is safe for use in the particular intended purpose.

If the manufacturing process commercially available devices, sterilization process or body contact is not the same as available in the market in such cases again they have to determine whether the sufficient data is available, sufficient justification is available, relevant data is there, the chemical and the biological detail of the medical devices or the bio material used in the medical devices is there.

If it is there that is sufficient for the risk assessment, if it is sufficient for the risk assessment then they have to see whether sufficient toxicology data exists for all the chemicals or the materials used in the biomaterials or the medical devices. If it is there then the data whatever the data that is applied to the chemical mixtures used in the biomaterials.

If the relevance data are there so, the does so, the data is also same to justify that it is based on this data the assessment can be determined and if all such data is available then they have to perform the biological risk assessment as per the annexure B of this standards. And, particular test based on the biological risk assessment the manufacture can perform and submit to the authority for the regulatory approvals or to establish the safety of the material or the medical devices being manufactured by the firm.

If there is no sufficient justifications or the relevant data of the chemical or the biological data of the medical devices is not available, then the manufacturer has to carry out the biological evaluation. They have to select the biological evaluation test as per the annexure A of these standards, annexure A which gives the details of the biological evaluation test carried out based on the categorization of the medical devices.

So, that matrix can be adopted by the manufacturers and based on that matrix the test prescribed in the annexures can be performed the ISO 10993 annexure A. That is the minimum test required to carry out the devices or the biomaterial for which there is a no

sufficient justifications or the relevant data with respect to the chemical or the biological information is available, but other test also can be carried out based on the nature of the devices.

So, that is the minimum test that has to be performed by the manufacturer in case there is a no adequate justification relevant data regarding the chemical or the biological is available with respect to the medical devices or biomaterials. And, after carrying out the biological evaluation as per the annexure A of the standards they have to justify in based on the data generated on the medical devices.

The product can be safe for use in the particular applications or used for the particular intended use of the devices and they have to submit the data to the authority for regulatory approvals or regulatory compliance.

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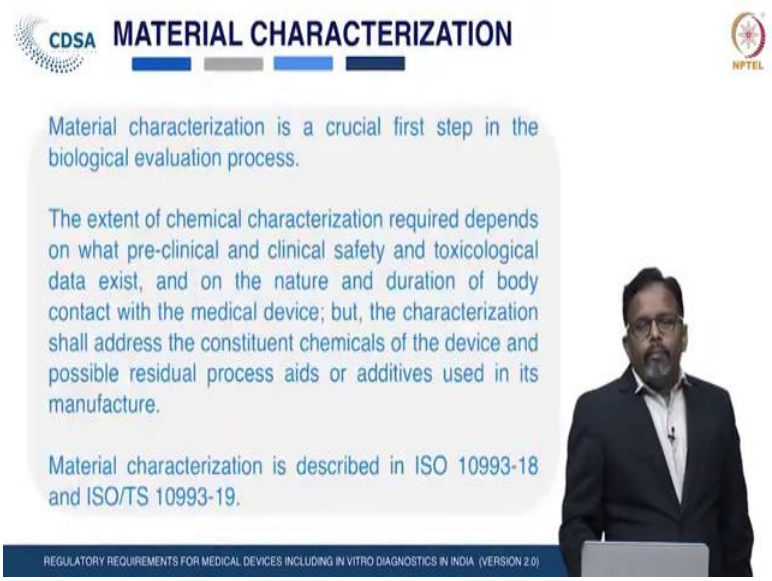

These are the principle or approach for conducting the biological evaluation and it is clearly mentioned in the standards, this is the standard that is 10993-1. And, this standards also recommended that the material characterization , material categorization are very important steps prior to conduct of the biological evaluation of the medical devices or the biomaterials.

And, the material categorization is the is carried out that is based on the standards of the ISO 10993 that is series 18 and series 19 of the ISO standard 10993 describes the details

of the material characterization process methods. it is clearly mentioned in the this series 18 and 19 of the standards.

So, based on the that standards the material categorization is to be carried out to prior to conduct of the biological evaluation and based on this material categorization the data they can use for the for the biological evaluation test for the medical devices. The extent of the chemical categorization or the material categorization depends on what preclinical or the clinical safety and toxicological data exist on the devices or the materials.

The nature and duration of the body contact with the medical devices or the material but this categorization shall address the constituent chemicals of the devices and possible residual process aid or residual process aids or additives used in the manufacturing. And the details of the material categorization is prescribed in the series 18 or 18 and 19 of the ISO 10993.

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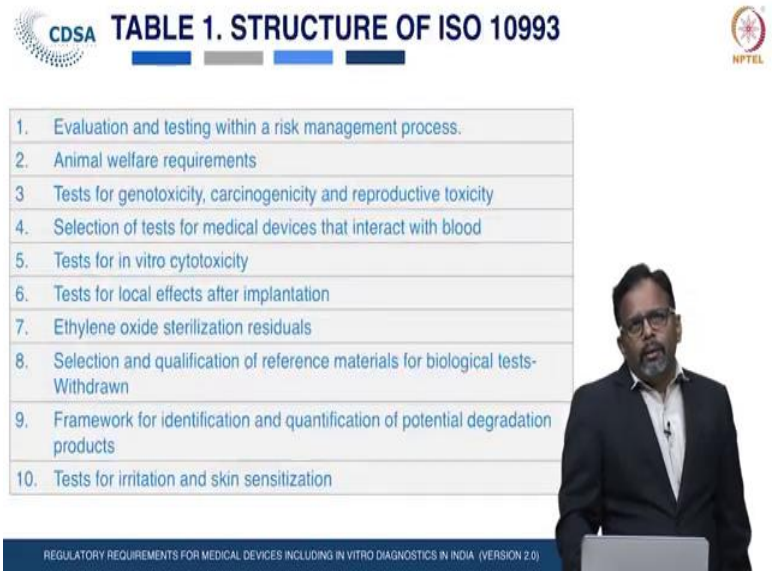

The various series of the biological evaluation is available so far published this there are approximate 22 standards series are there ISO 10993. The series 1 that we have discussed in detail that is for the evaluation in testing within the risk management process this is the general series. Series 2 of this standard that is, animal welfare requirement. Series 3 that is the, test for the genotoxicity causes genocity and productive toxicity. Series 4: that describes, the selection of the test of the medical devices that

interact with the blood. Series 5 describe the, test for the in vitro toxicity, how to conduct the in vitro cytotoxicity test, the methods have been described in this standards.

Series 6: that is the, test for local effects after implantation of the devices. Series 7 that is standards relates to the ethylene oxide sterilization residuals. Series 8 it is the selection and qualification of the reference materials for the biological test; however, the series has been withdrawn by the agency it is no more is applicable. Series 9: that describe the framework for identification and quantification of the potential degradation products. Series 10 that describes the test for irritation or the skin sensitization test.

Series 11 of this standard that describe the test for the systematic toxic case study, series 12 describes the sample preparation and the reference materials, series 13 that is the identification and quantification of the degradation product from the polymeric medical devices. Series 14 that is identification quantification of degradation product from the ceramics, series 15 that is identification and quantification of the degradation product from the metal and alloy, series 16 that describe the toxico kinetic study design for degradation product and leachables.

Series 17 that is that describes the establishment of allowable limits for the leachable substance, series 18 chemical characterization of the materials we have discussed that this series 18 and 19 that describes the chemical categorization of the materials physicochemical, morphological or topographical `categorization of the materials. Series 20: that is the principles and method for immunotoxicology testing of the medical devices.

These are the series of their standards which describes different that component in different test that is required to be carried out as a part of the biological evaluation of the medical devices. Now, we will discuss the categorization of the medical devices and the tessellation. We have discussed earlier that categorization of the medical devices as per the standard ISO 10993 that is based on the contact of the devices or the duration of the devices with the human body and based on this categorization which test is required to be carried out for biological evaluation of the biomaterial or bio compatibility that can be determined.

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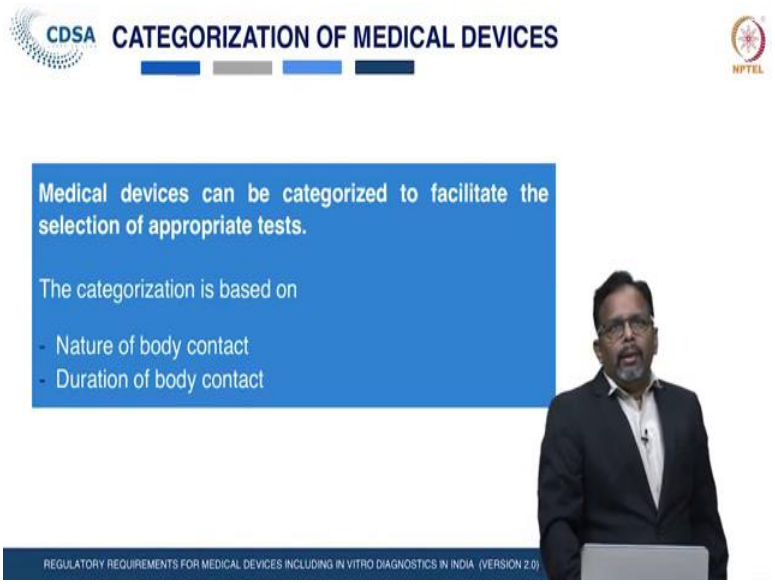

So, categorization of the medical devices already we have discussed that medical devices can be categorized to facilitate the selection of the appropriate biological test based on the nature of the body contact and duration of the body contact.

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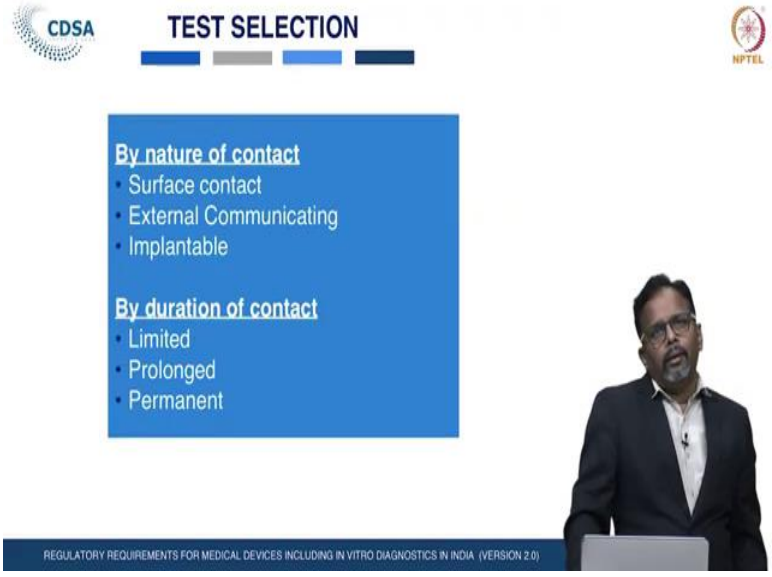

If you see the nature of the body contact the nature of the body contact that device can contact with the surface of the body, certain devices that contact that external communicating devices and certain devices that is implantable devices. So, 3 different nature of the contact of the devices that is the surface contact, external communicating

and then implantable devices And, duration of the contact that is defined as a limited duration of the contact, prolong duration of the contract or permanent duration of the contact.

So, limited contact, prolonged contact and permanent contact duration that is defined in terms of the duration then if it is in body contact up to 24 hours it can be consider as a limited contact, 24 hours to 30 days can be categorized as prolonged contact and the permanent beyond 30 days. If the, particular device is implanted or in contact with human body, that can be considered as a permanent contact devices.

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So, let us discuss the surface contact devices the devices which in contact with the skin that example of such type of devices are surgical tapes, bandages, probes, probes that is used in the certain devices, then external orthopedic braces. So, such type of devices can be which can be contact with this can is considered as a skin contact devices. Mucous membrane devices, the devices that contact intact with mucous membranes that is endoscopic, endotracheal tubes, oral swabs or the intrauterine devices.

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Compromises surfaces or breached surfaces, the devices that contact, breaches or otherwise compromised body surfaces that dressings or the bandages for wounds or ulcers or the burns such devices which is in contact with such conditions that can be classified or considered as a breached or compromised surface contact devices.

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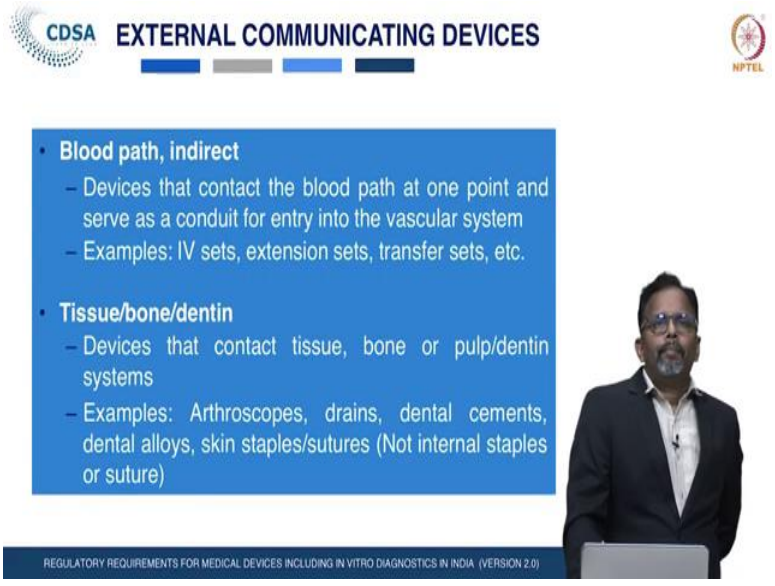

External communicating devices this also further divided into the nature of the contact if the devices that contact the blood path at one point and serve as the conduits for entry into the vascular system like intravascular sets, extension tubes, transfer sets, etc..

The devices that contact the tissue, bone or dentine systems that is considered as a tissue, bound dentine devices.

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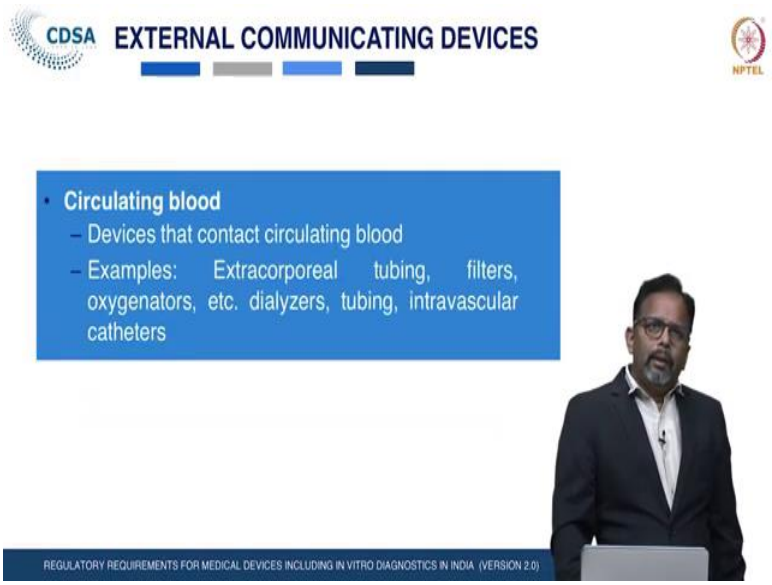

Or the circulating blood devices that devices that contact the circulating bloods example of these devices are oxygenator and intravascular catheters, dialyzers.

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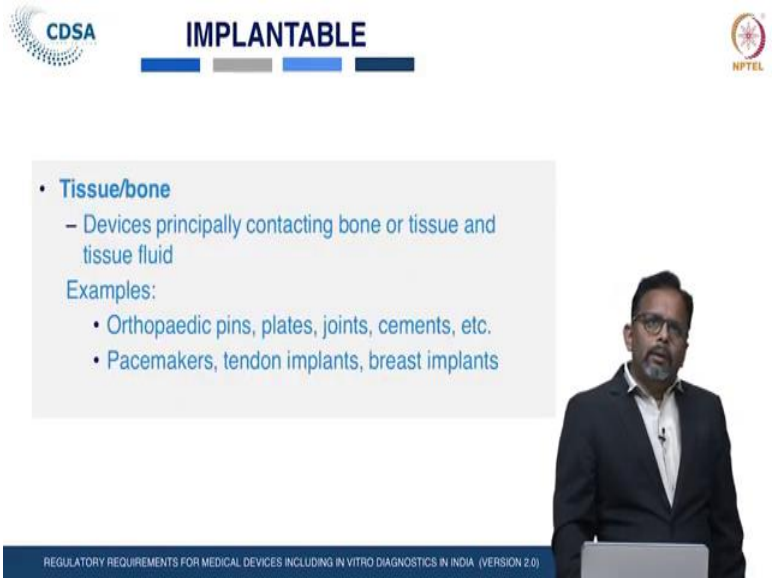

Implantable devices, the devices contacting the bone or the tissue and tissue fluids examples are the pacemakers, breast implants, orthopaedic implants.

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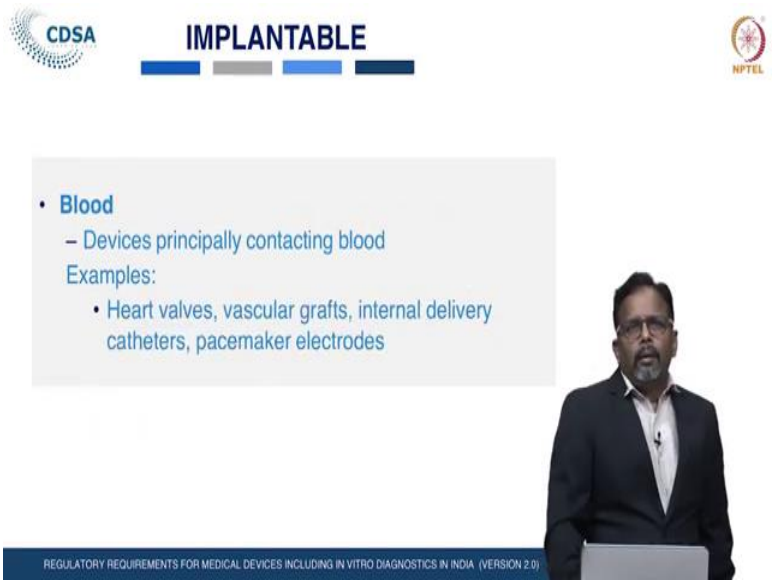

The blood implantable devices, the devices principally contacting the bloods example of such type of devices are the heart valves is one of the example, vascular grafts, the pacemaker electrodes. So, these are the various types of the medical devices based on the types or the Category of the contact of the medical device with the human body.

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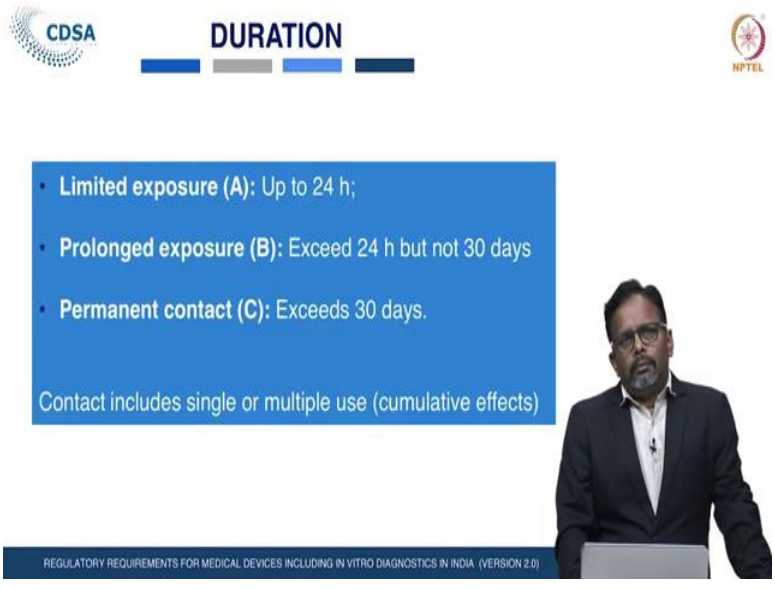

That can be categorized into 3 main parts and the duration; duration of the contact that we have discussed , 3 types of the duration is prescribed in the standards. So, limited exposures that is the devices is in contact with the human body up to 24 hours Prolonged

exposure that is defined as the devices which in contact with the human body for 24 hours to 30 days. And, the permanent contact devices that can be categorized if the device is in contact with the human body which exceeded 30 days.

The contact includes the single or multiple uses the cumulative effect of the devices can also be considered as a based on the use of the devices that also be considered as a permanent contact devices, if it can be used multiple times beyond 30 days.

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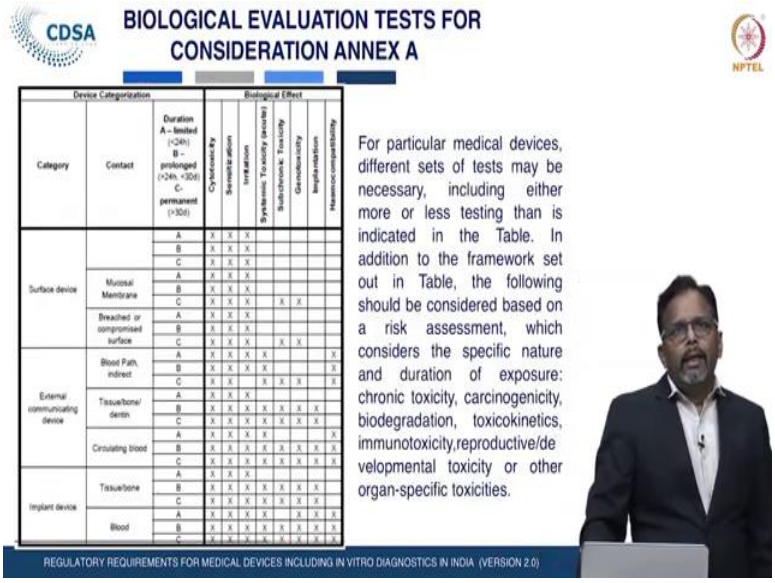

This is the appendix A that is the matrix based on the device categorization, we have discussed that device categorization is based on the category of the devices with the contact of the human body and the duration of the contact. This table gives which mandatory tests are required for the medical devices where there is a no biological evaluation data or the toxicity data are available.

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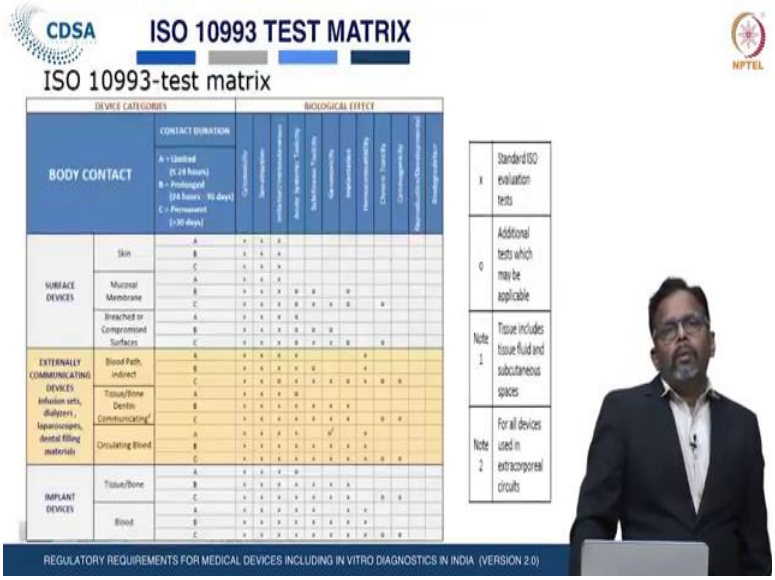

The device is noble in nature or the biomaterial is used first time in such cases based on their category, the duration of the contact and the nature of the contact of the devices. These certain test that is prescribed in the standards, that is the cytotoxicity, sensitization test, irritation test, systematic toxicity test, subchronic toxicity studies, genotoxicity, implantation test, hemocompatibility test.

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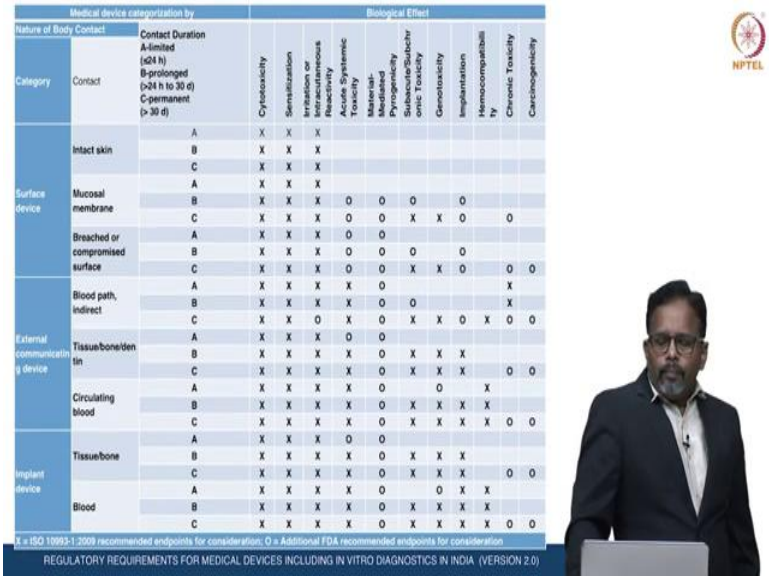

These are the minimum test that is required to be carried out by the manufacturers. If you see these standards ISO 10993 if you compare with the US guidelines in USA certain additional test is also required to be carried out.

And, this table shows which are the additional test is required to be carried out on the particular devices based on the categorization of the devices, certain additional test is performed, but this test is as per the requirement of US FDAand however, the manufacturer can do the test based on the available standards and they can justify after carrying out the risk base assessment of the particular medical devices.

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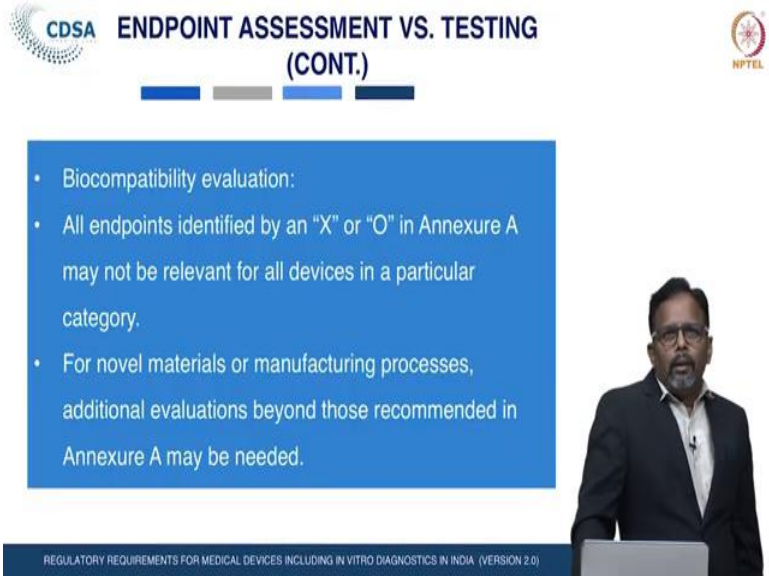

The end point identified by "X" or the "0" in annexure A may not be relevant for all the devices in particular category. We have discussed that it is only applicable for the devices where the there is no data is available with respect to the material chemical data or the biological evaluation data or the toxicity data in such cases these test can be, the test prescribing the annexure A can be carried out.

And this is the minimum test already I have explained that the additional test that as per the US FDA what are the additional test that is also mentioned in the another table which is given in the slides and although these test which is given in the table is not the complete test. It is the minimum test beyond those recommended that annexure A other test as appropriate that can also be performed by the manufacturers and also that can be

recommended by the regulators to perform that particular additional test which is not mention in the annexure A of the annexure A of this table.

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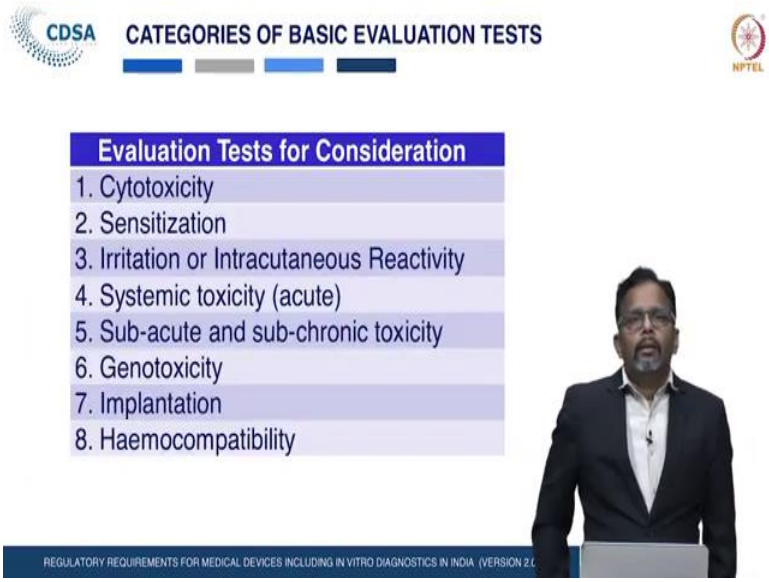

Now, the basic evaluation test we have discussed that is a cytotoxicity test, sensitization test, irritation or intracutaneous activity test, systemic toxicity, sub-acute or sub-chronic toxicity test, genotoxicity test, implantation test and haemocompatibility test.

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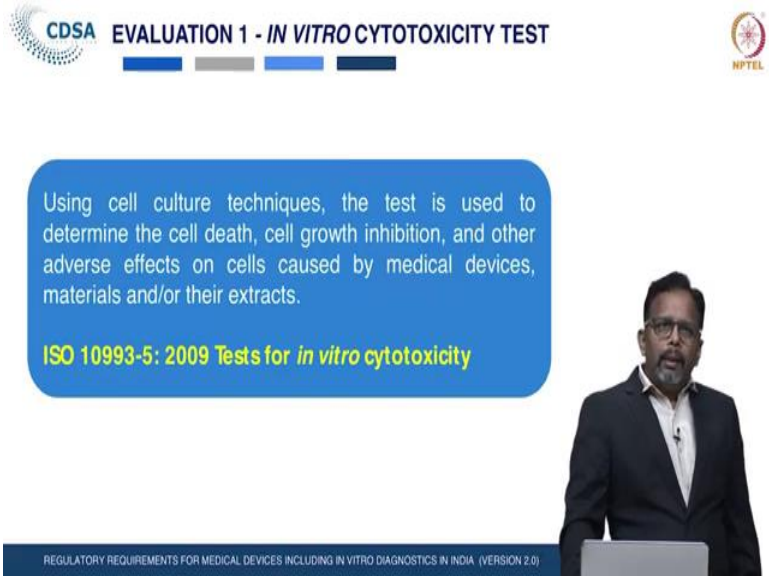

The general purpose for conducting these test we can just have look the cytotoxicity test that is performed to determine the cell death or the cell growth inhibition. And, another

adverse event on the cells caused by the medical devices or materials or their extract and the details of the test to be performed by the manufacturers is given in the ISO 10993 series 5.

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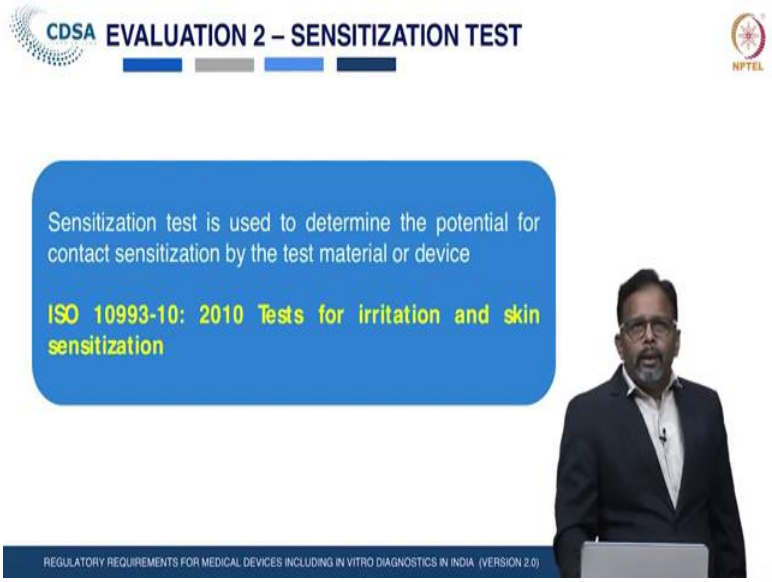

Sensitization test, this test is to be used to determine the potential for contact sensitization by the test material or the devices the standards ISO 10993 series 10 which gives the details of the test which is to be performed.

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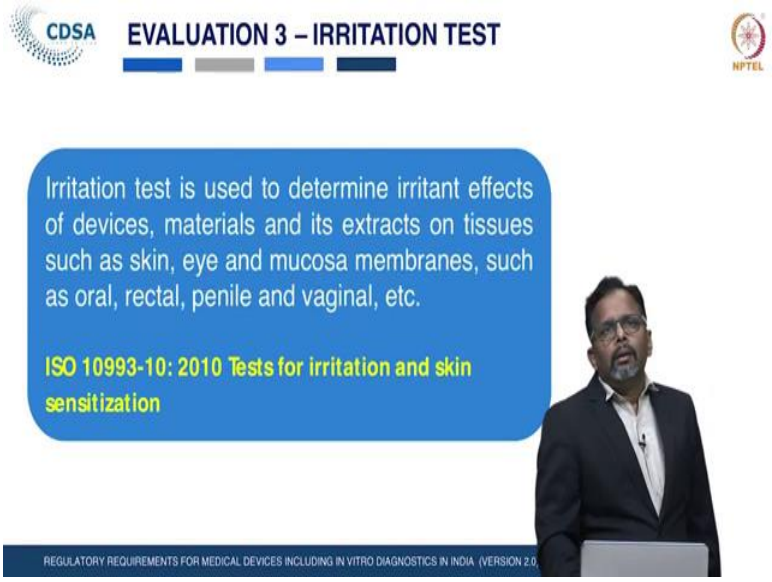

Series 10 also includes the test for irritation this irritation test is used to determine the irritant effect of the medical devices or material or is extracted or the tissues such as the skin, eye or the mucous membrane.

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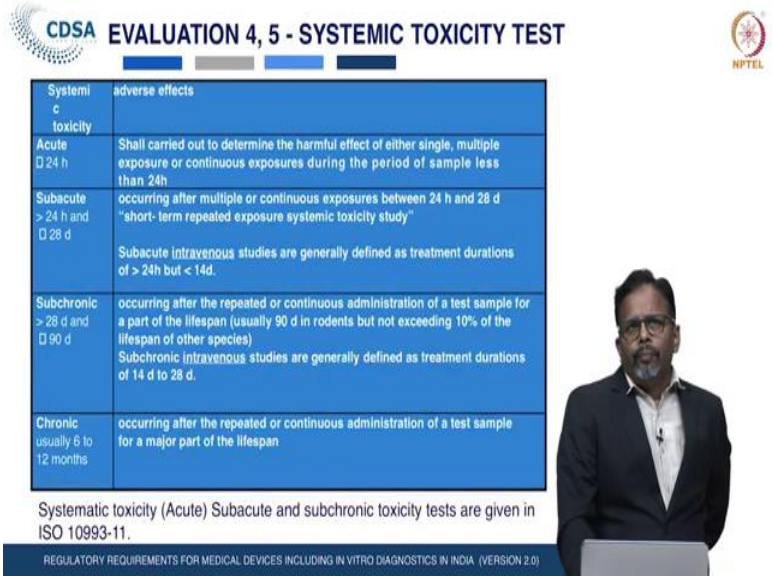

The main series 11 of ISO 10993 that describes the detail of the systematic toxicity study, under this study the acute toxicity study, sub acute toxicity study, subchronic and the chronic study that how to perform, how long that test can be performed that is given.

For acute toxicity that is to determine the harmful effect of the devices either by single or multiple exposure during the period of the sample, less than 24 hours. If the duration is between 24 to 28 days that sub acute toxicity is required to be carried out, if it is 28 days to 90 days then sub chronic and beyond 90 days that is chronic study is required to be carried and the duration of the chronic studies shall be carried out up to 6 month to 12 months and series 11 describes the details.

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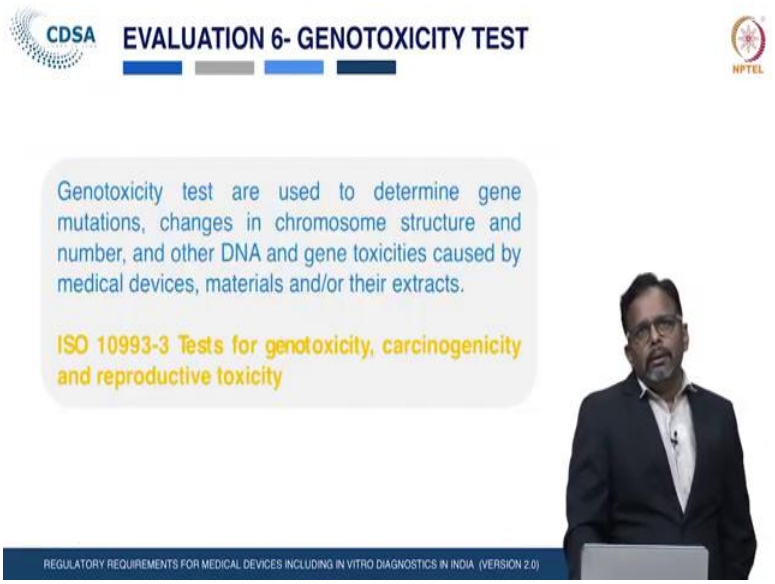

Genotoxicity test: ISO 10993 series 3 that gives the details about the genotoxicity test, this test are used to determine the gene mutations, changes in the chromosome structures and the number and other DNA and gene toxicity caused by the medical devices or materials and or their extracts.

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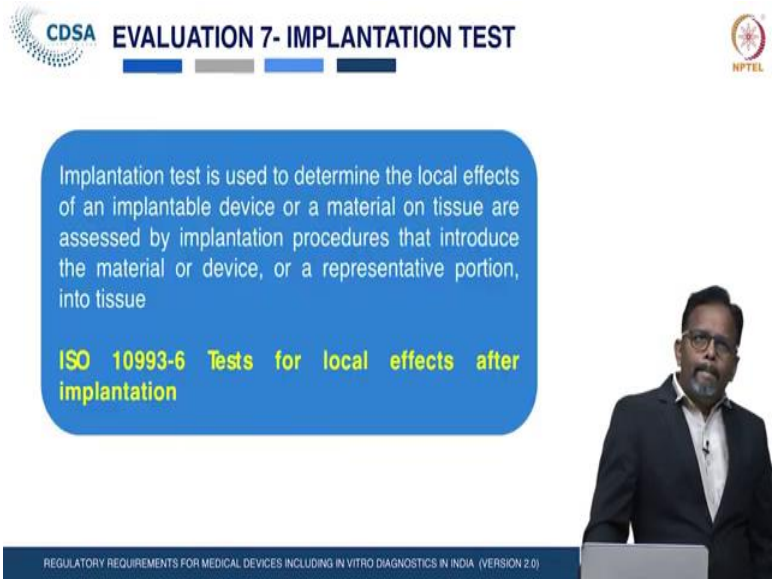

Implantation test: This test is used to determine the local effect of an implantable device or the material or the tissue by implantation procedure that introduced the material or the

devices into the tissue of the animals and series 10993-6 that gives the details of the implantation test.

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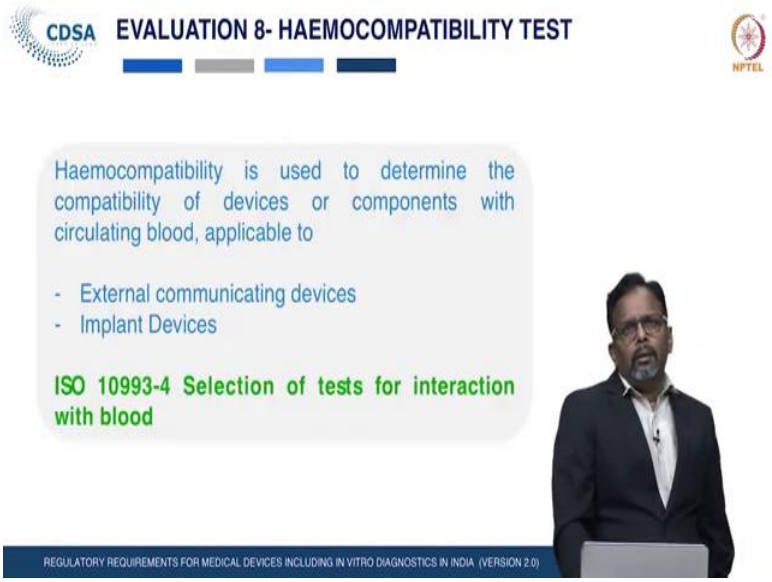

Hemocompatibility test that is required to use the to determine the compatibility of the devices or the component with the circulating blood. And the series 10993 series 4 that gives the details of the haemocompatibility test study.

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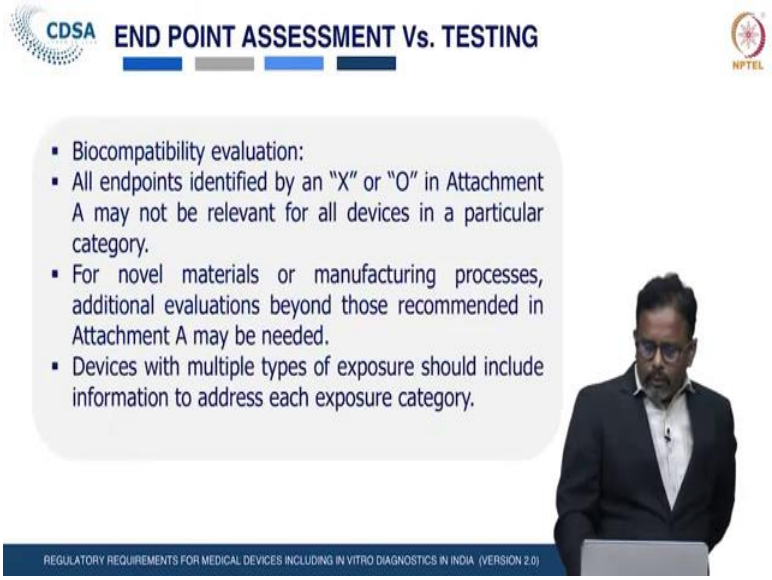

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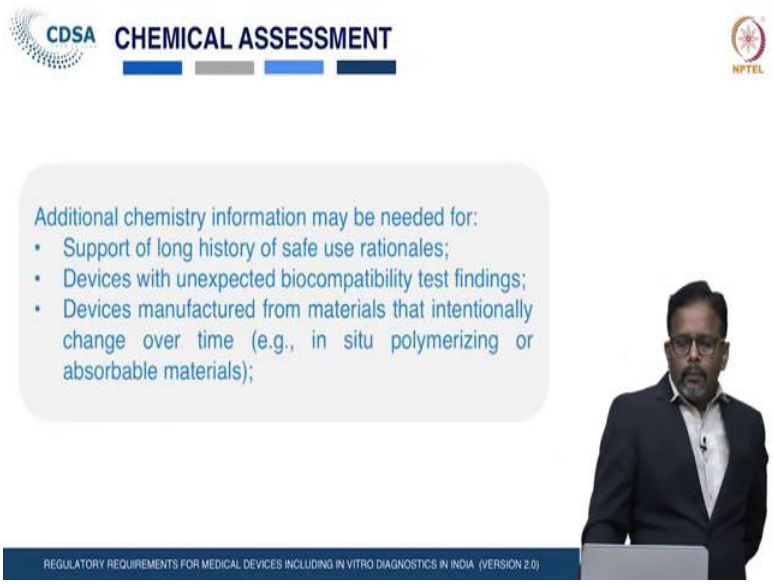

Chemical assessment of the devices, we have already discussed that additional chemistry information also required to be carried out by the manufacturer to support the long history of the safe and use the rationales. These chemical assessment is also needed the devices with unexpected biocompatibility test findings. The device manufacturer from the material that intentionally change over a time, in such cases these chemical assessment is also required to be carried out by auto initiate the biological evaluation study.

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Some devices including the chemical with the known toxicity, where the new biologics testing is really conducted in such cases this chemical assessment is mandatory. New chemical entity used first time or modified material that formulation in such cases or the novel materials if it is used, then chemical assessment is mandatory prior to conduct the biological evaluation test of the medical devices or the material.

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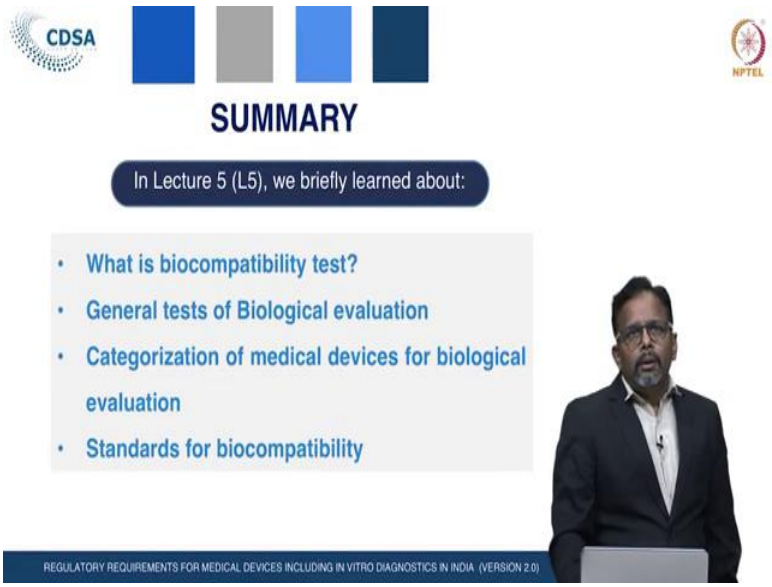

So, friends this is all about the biological evaluation, I hope you have now got the general idea about the biological evaluation test or biocompatibility test, what are the standards applicable for this, what is the guidelines, what is the risk based approach for selection of the biological evaluation test, categorization of the medical devices for the biological evaluation, how to categorize and the standards the main standards which is applicable for conducting the biological evaluation.

So, this is all about this lectures and before concluding this lectures let us have some question answer session question.

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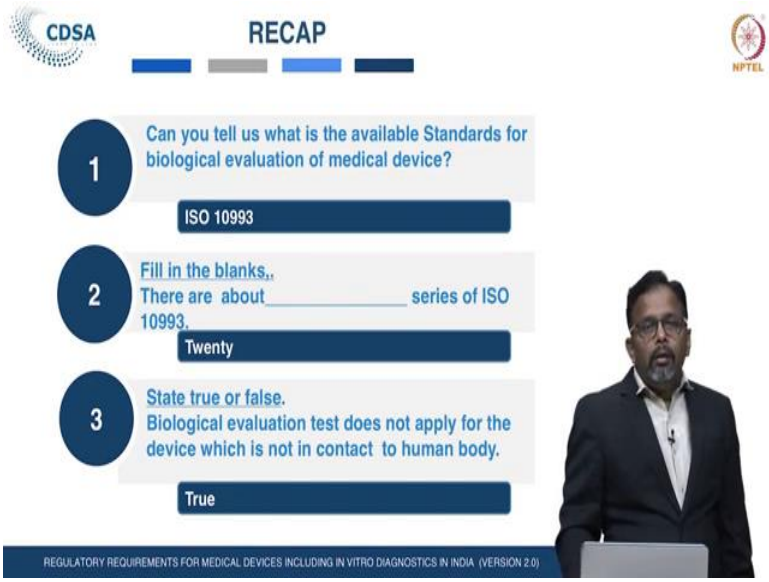

Now, the first question can you explain what is the applicable standards for conducting the biological evaluation of the medical devices as per Medical Device Rule 2017? Yeah, in the correct answer that we have long discussion on the standard that is ISO 10993. Now another that question key that, how many series of the ISO 10993 is there? Approximate we have discussed.

Student: (Refer Time: 60:01)

That more than 20 standards 20 series of the standards is available which covers the biological evaluation. Now, the last question, whether the biological evaluation test that is not under the purview of this ISO standards which type of the devices that cannot be in which the biological evaluation test is not applicable.

Yes devices which is not in contact to the human body in such type of the devices this biological evaluation test is not required that is ISO 10993 is not applicable for such type of devices. So, this is all about this biological evaluation test. Thank you very much and another topic we will discuss in subsequent lectures.

Thank you very much.