Legal and Regulatory Issues in Biotechnology
Prof. Niharika Sahoo Bhattacharya
Rajiv Gandhi School of Intellectual Property Law
Indian Institute of Technology, Kharagpur

Module - 03
Biotech Product commercialization: Regulatory Approval Process
Lecture - 15
Data exclusivity and Patent term extension

Hello all. So, in the previous classes like I have been telling about certain incentives which are given for the biopharmaceutical manufacturers as well as biosimilar or bio generic manufacturers, which is known as the data exclusivity or patent term extension. So, in this lecture, I would like you to give certain more information regarding these beneficial provisions of with respect to the biopharmaceutical.

So, here in this lecture we will cover the terms like data exclusivity, patent term extension, and supplementary protection certifications. And we will see how these are helping this biopharmaceutical industry to grow further.

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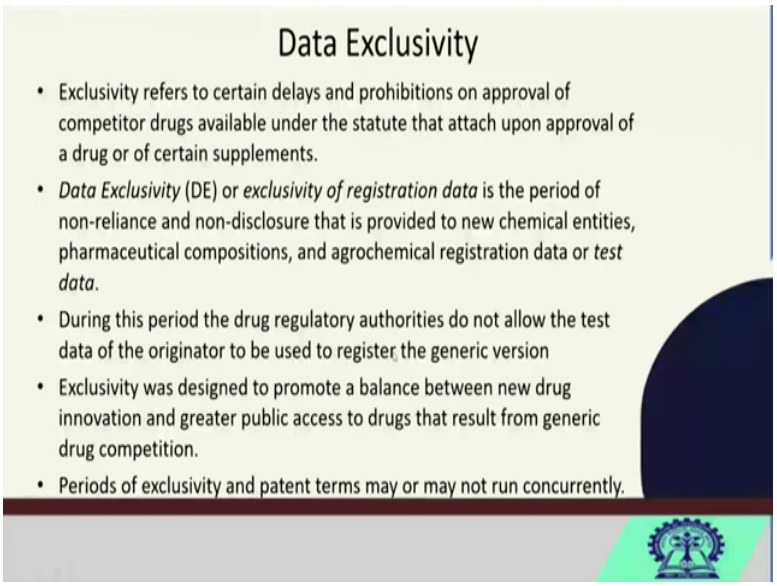

So, in earlier classes also I mentioned for the biopharmaceuticals as well as for the new drug molecules data exclusivity. So, what is this data exclusivity, how it is relevant for the biopharmaceutical industry or any industry per say? So, if you see data exclusivity or

exclusivity is generally something which basically refers to delays in approval or certain prohibition for the approval of a competitor drug product which is available under the statute.

And basically when the approval of a drug product is dependent on certain prior information or prior data submitted by another original drug product develop; original drug developer, then there is a certain time period or limitation between which it may not be allowed. So, if we go by the definition, the data exclusivity or exclusivity of the registration of the data is the period of the non-reliance and non-disclosure which is provided to the new chemical entities, or any pharmaceutical compositions, or any agronomical registration or any test data.

So, this test or the data generated for the submission procedure or approval procedure are regarded as very critical information and they are a part of intellectual property law. Like the TRIPs agreement under Article 37, this undisclosed information is a kind of a trade secret, because it said this undisclosed information which keeps certain commercial advantage to the competitors or rivals may be regarded as a trade secret which is of high value.

So, what happens in the pharmaceutical segment or even in the agro chemical segment or normal chemical segment, because the test data is essential for giving the marketing approval for such products to access their safety. So, the manufacturer has to submit those test data. And based on the test data, the drug regulator or the other agencies they generally approve those substances. And unless and until it is a public emergency, they are not supposed to reveal this test information, test data.

And this test data is now covered by various provisions as per the different countries legislation. But in the developing country by understanding the importance of such test data or the clinical submission in case of the drug substances they have given certain exclusive period during which those test data cannot be rebuilt to the competitors.

Because I said the generic companies can use the original company in clinical trial data and they have to prove the bio equivalency only, and they can apply for the abbreviated new drug application. Even in the biopharmaceutical also biosimilar company can take use certain reference data, and then give the application. But again, because high cost is involved, time is involved, and the manufacturer, original manufacturer has to get certain incentive to again get

back those costs incurred as well as to have some profit, so these provision has been introduced.

So, basically what happens; during the data exclusivity period the drug regulatory authorities do not allow the test data of the original company to be used by the genetic company. And this is a provision by which there is a endeavour to create a balance between the new drug innovation and the greater public access to the drugs that is resulting from the generic drug competition. So, in both means you are also giving certain incentive to the innovator by giving them the exclusivity period. And after that also you are allowing the genetic companies to proliferate. So, both the way it is trying to create a balance.

And this data exclusivity should not be confused with any of the intellectual property right, like patents or other things. It is definitely the test data is a confidential information and may be regarded as an asset or a trade secret. But again, it should not be confused with something which is related to the patenting of the drugs. And the drug exclusivity, data exclusivity period as well as the patent term of the drug product may run differently as well as concurrent. So, there is no correlation between these two concepts as such.

Like, a patent is generally filed at the initial stage like suppose when a company is already having certain clue regarding certain entities which can be used for certain indications. In that case, when they have some information on some R and D data, so they can go for they can file for the patent application. And it is generally advisable that the patent application must be filed as early as possible.

Once they are convinced that, now this drug product is going to have this is the new invention for the treatment of certain disease or indication. And the patent tenure starts from the date of filing to the 20 years, time period; next 20 years time periods once it is granted.

But what happens many a time as I said it is a long process, biopharmaceutical development is a long process. So, even though you have a patent from 10 years, last 10 years it possible that your drug product is still not have not entered into the market; because you know development, the clinical trials, then the regulatory approval all these processes takes certain time period. So, it may vary from 10 to 12 years.

So, the effective time period which remains after the drug approval or after the marketing authorization is sometimes very less; maybe 7 years, maybe 5 years or sometimes like maybe 10 years. So, sometimes the, so it is believed that because the complexity of the process the patent monopoly right is not that effective or not enjoyed to the full extent by the innovators.

So therefore, other provisions are there which again links the patent as well as the drug marketing authorization or we will see all these things.

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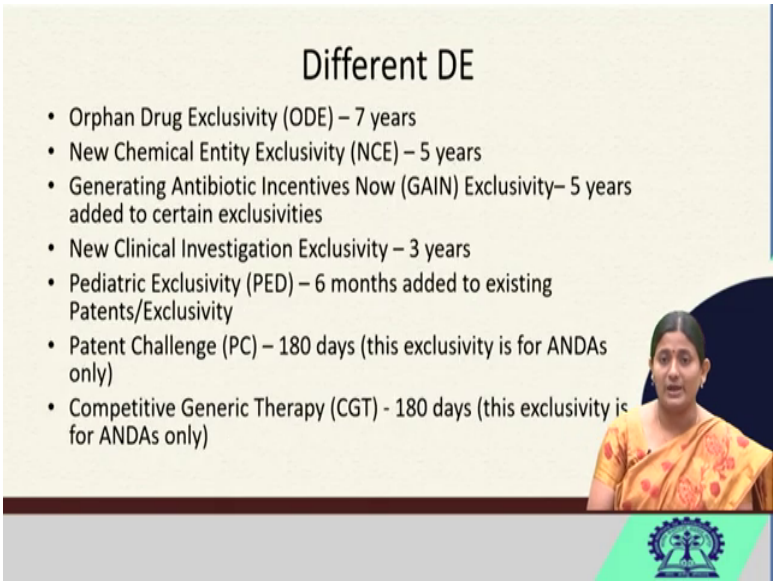

So, coming back to the again drug exclusive data exclusivity. They are different exclusivity period for different kinds of the drug. For example, there is a category of the drug known as the orphan drug like a drug which is generally developed for a rare disease; again, the definition of the rare disease varies like it may be one patient in per 5 lakhs of population.

So, depending on the country the definition of the orphan drug changes. And if any company develops any orphan drug, so 7 years of data exclusive period is given; means within that 7 years, no competitor company would be allowed to use those information.

Again, we have this New Chemical entity Exclusivity for 5 years as we saw in Hatch-Waxman Act. Then we have Generating Antibiotic Incentive that is a gain exclusivity

for 5 years, then New Clinical Investigation exclusivity for 3 years, Pediatric Exclusivity means it is again 6 months are added to the existing exclusivity.

Suppose, a medicine is generally available for any indication, and we have given a 5 year exclusivity; and further it has been proved found to be effective against in case of pediatric patients, then 6 months are also extra is added means 5 plus 6 months. If it is a new chemical entity and then it is again used for certain pediatrics purpose then 6 months exclusivity is added.

Like we saw Para IV certification or in abbreviated new drug application 180 days of exclusivity is given for the first company who has applied for this ANDA after, and that starts from the date on which it gets the marketing. Then competitive generic therapy again 180 days of exclusivity is given.

So, depending on the nature of the drug molecule, different drug exclusivity period has been mentioned in the United States. And again in India, we really do not have any formal drug exclusivity period, but for the first 4 years generally no generic companies are allowed to use the test data. So that 4 years may be considered as an exclusive period for the manufacturers, but we do not have any co-regulation upon that.

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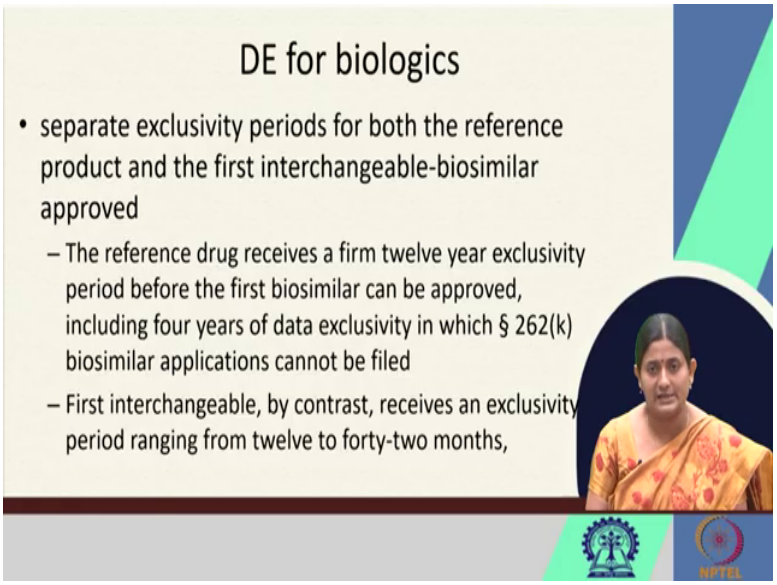

And coming to the data exclusivity of the biologicals. So, we saw under the Public Health Safety Act, United states, they have provided certain data exclusivity for the biologics. For example, the reference drug receives twelve years of exclusivity period before the first biosimilar can be approved; means the first drug gets twelve years of exclusivity. So, that is quite a long than compared to the generic versus like 5 years and this is twelve years.

And in the twelve years, first four years of data exclusivity in which the biosimilar applications cannot be filed. And the first interchangeable receives an exclusivity period ranging from the twelve to forty-two months. So, this is given in the different legislation of the corresponding countries.

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So, now as I mentioned this data exclusivity and other terms are not specific or are not common for all the countries. Developed nations have adopted those principles to promote more innovation in this area of drug development or biopharmaceutical development. So, they are known by different terminologies in different countries.

So, we now talked about the data exclusivity there is something called the market exclusivity; Data exclusivity is like that information of the test data cannot be used by the competitor. Market exclusivity is that nobody apart from the one which has been given the marketing

authorization can enter into the market. Maybe the application process is under thing they have applied, but they are not allowed to market.

So, the market exclusivity, is a term which is defined in which a biosimilar manufacturers will not receive an approval from the respective authority, even though he may have requested for such approval and presented the necessary data already and if the data has been taken from the authorization of the innovator. So, even though the application is pending, but they will not get the marketing authorization. So that period is known as the market exclusivity.

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And so, this marketing exclusive, market exclusivity is used mostly in the European Union. So, if you see in the European Union, the data exclusivity and the marketing exclusivity are to be used together. So, that is known as 8 plus 2 plus 1 formula. And this has been set under the regulation 626 upon 2004.

So, according to which an eight-years of data exclusivity term is provided, and this term begins with the marketing authorization of the original drug. So, once the marketing authorization has been given, so till next eight-years, the data exclusivity period remains. And under that condition that any new indication with the significance clinical benefit is available that will be provided.

Then additional two-years marketing exclusivity is provided if for the same product, one and more new therapeutic indications are filed during that period. And this is applicable to all the biopharmaceutical products which are approved after 31st October, 2005. And all the drug products which have been approved before 2005, a drug exclusive period of 10 years is applied. And then and a few of the European Union countries, member countries that they have been mutual recognition among themselves, and for them and it is 6 years.

So, as I said there is no fixed formula or fixed definition or a fixed rule for this marketing exclusivity or the data exclusivity under the different national legislation.

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Now, coming back to the relation of the intellectual property like patent with the drug marketing and other process or drug approval process, there are again a lot of debate. Keeping in the view like same thing, the feeling that the biological drug development is a long process and the innovators are not getting sufficient, not enjoying to the full time period of 20 years for their drug, and effective patent term remains very low for most of the biopharmaceuticals.

This provision known as the patent term extension has been introduced in many developed nations. And particularly this is known as the Patent Term Extension or the PTE. And this doctrine, PTE doctrine comes from the Title II of the Drug Price Competition and Patent

Term Restoration Act of 1984 or the Hatch-Waxman Act. And the purpose being the same that you have to encourage new drug research and you have to compensate some way by, the reduction in the effective patent term by some way.

So, like we have to understand one thing, patent approval process is a different process, it is controlled by the USPTO – United States Patent and Trademark Office. And drug approval process is guided by the USFDA – United States Food and Drug Approval Agency.

So, these are two different agencies. So, there might be; if there is no coordination between these two agencies, so there might be a chance where the, questions of patent infringement if the generic drug has been approved earlier. So, you are not effective 20 years time period has been realized by them. So, they have tried to coordinates two agencies.

So, in this patent term extension, so the information from the patent agency and information by the regulatory agency is combined together. And additional time period is given to the manufacturer company, so that they can enjoy the patent rights for a substantive time period.

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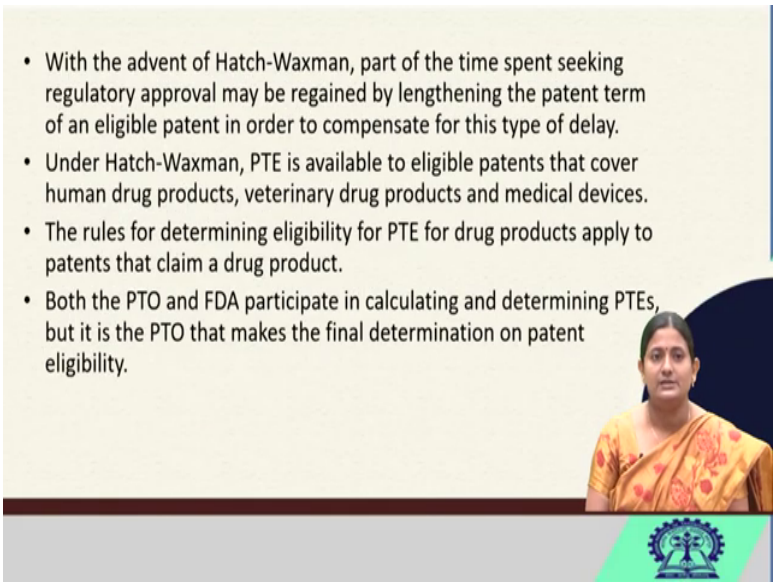

In this, under first during the Hatch-Waxman Act, the part of the time spent while seeking the regulatory approval was regained by lengthening the patent term for an eligible patent in order to compensate the type of the delay. So, not, for every patent, this can be given you

have to now cite an eligible patent; means maybe the patent over the active ingredient or the main patent related to the drug molecule.

And under this Hatch-Waxman Act, this patent term extension provisions were available to the eligible patents, and covers human drug products, veterinary drug products, and as well as the medical devices. And they have a defined set of rules which determines the eligibility for the patent term extension of the drug products. And what kind of the claims or patent can be covered under this patent term extension.

And both the Patent and Trademark Office as well as the Food Drug Agency participate in calculating and determining the patent term extensions. But again, this is the Patent Office which makes the final determination on the patent eligibility; means they have to again see which patent has to be given this extension. They cannot give, so there might be 10 patents over a single molecule – single drug product, but again one eligible patent can be given the extension.

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So, in the United States the maximum term extension is 5 years, provided the extension does not result in the total remaining patent term more than 14 years. That means, like 5 years additional patent term give, can be given that may be 20 plus 5, that means, 25 maybe; but again, we have to calculate after the marketing authorization.

Means, once the marketing authorization has been granted means it has been approved for entering into the market from that it would be calculated. So, after marketing authorization maximum 14 years should be the remaining patent term. So, accordingly maximum patent term extension is given 5 years.

For example, when a marketing authorization has been granted for a drug molecule, the remaining patent term is supposed 5 years, then additional 5 years would be given. So that means, 10 years of patent term would be the after-patent term extension the effective patent protection would be 10 years, even though it has like 15 years has been passed by.

But if the remaining term is already suppose 13 year, when the marketing authorization is granted, and they have remaining 13 years of time period to enjoy the patent then only 1 year extension might be given; because it should be maximum of 14 years after the marketing authorization. So, that is the calculation which is made by the PTO as well as the FTO.

So, the 14 year period is measured from the date of the drug product received the regulatory approval up to the date of the patent expiration. And any term extension granted under this statute is applied from the original expiration date of the patent including the patent term like PTA.

So, patent term edition; that is another patent term addition is another concept which is again individually done by the USPTO - Patent Office. Means if during the patent prosecution or the patent approval due to certain process the process has been delayed, so they adjust the term. And it is only found in the United States only.

So, if you ever get a chance to see any patent document, you might see there is a patent term adjustment. So, this PTA is Patent Term Adjustment. So, this patent term adjustment like few days or depending on the nature of the process, so that some time period has been adjusted. And accordingly, they decide the date of expiration of the patent. And that date would be taken into consideration while calculating the patent term extension.

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So again, as I mentioned there should be set of rules which guides which patent must be eligible. So, a patent will only be eligible for the extension if it includes at least one claim covering the approved drug products or its approved method of use or method of manufacturing it. So, like a patent is generally given for an invention.

So, in a patent document generally the inventor specifies certain claims means on which aspect of the patent you want to have the patent, those are known as the claims. So, claims are the basic they are the main thing of a patent. So, the claim must cover the like approved drug product, or method of use, or how they are manufacturing it.

And they have to also satisfy few conditions; like the patent should not have expired, the term of the patent has never been extended before, the patent owner or its agent submitted a complete and timely application for the extension, and the product has been subjected to the regulatory review period before it is commercial marketing or the use, and the permission for the commercial marketing or use is first permitted accepted patents claiming a method of making a product primarily using the recombinant DNA technology were different. So, these rules, are set of rules which has to be followed. And the patent has to be like found eligible for giving the patent term extension.

And this patent term extension why it is necessary, so what benefit will you give? So, it increases their profitability. Means, till the time the patent is alive nobody is allowed to copy that product. So, you have the monopoly for additional 5 years of time period in the United States. So, that is the advantage. Like there was an example of Prozac by Emily Lee. So, like when the patent for that drug molecule expired that drug Prozac; it next 5 years benefit was the highest among whole of its life term.

So, you may understand how this patent term extension gives the commercial advantage to any company who is marketing their drugs. So, that is the way the patent term extension is being helpful.

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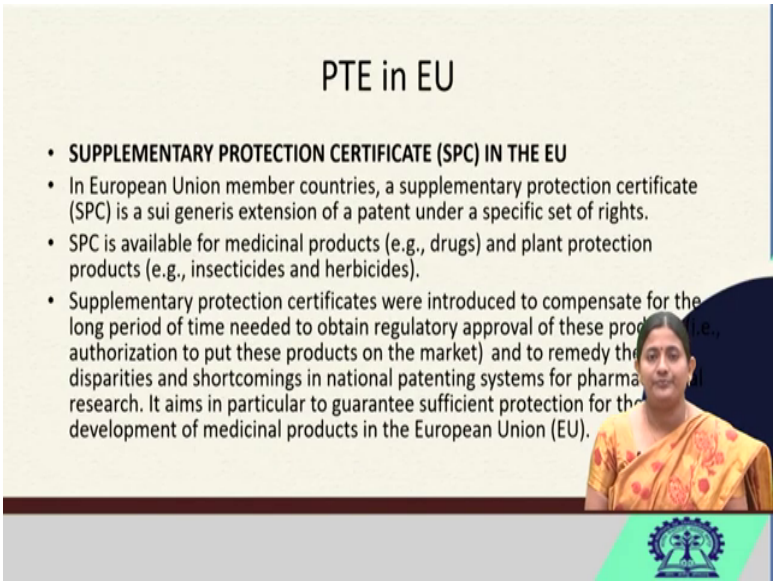

Now in the united, in the European Union, we do not call this patent term extension as PTE rather it is known as the Supplementary Protection Certificate or the SPC. So, in the EU the SPC or the supplementary protection certificate is sui generis or a specific extension of the patent under a specific set of rights. And it is available for the drug products, medicinal products, plant protection products like insecticides and herbicides as well.

And again, this is in the same way has been introduced to compensate the long time period needed to obtain the regulatory approval. And so that the profit by profit for the

manufacturers is generally higher, and they incur more profit and the loss is compensated in some way.

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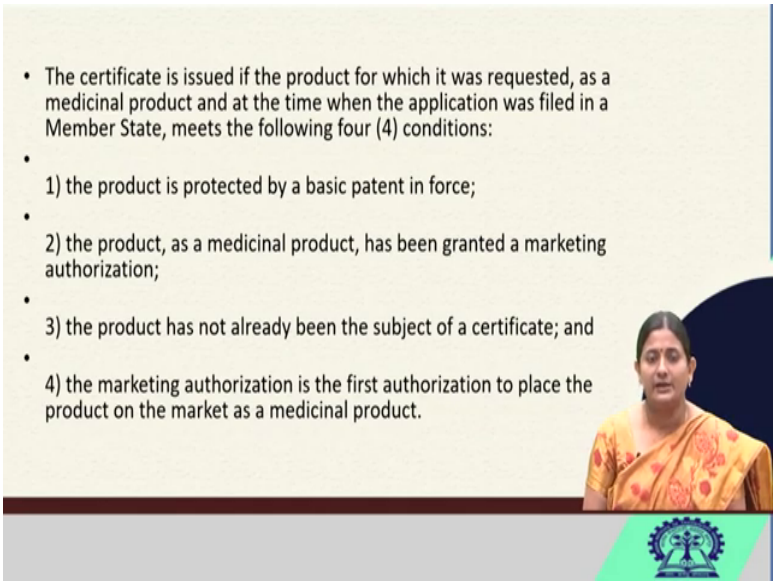

And again, the product again has to satisfy few conditions like; first for which you are giving a patent extension or the SPC. The product is protected by a basic patent which is in force, the product should be a medicinal product which has been granted the marketing authorization, and the product has not already been subjected to certificates, and the marketing authorization is the first authorization to place the product on the market as a medicinal product.

So, there are a few conditions which has to be met in European Union as well so that the supplementary protection certificate can be granted.

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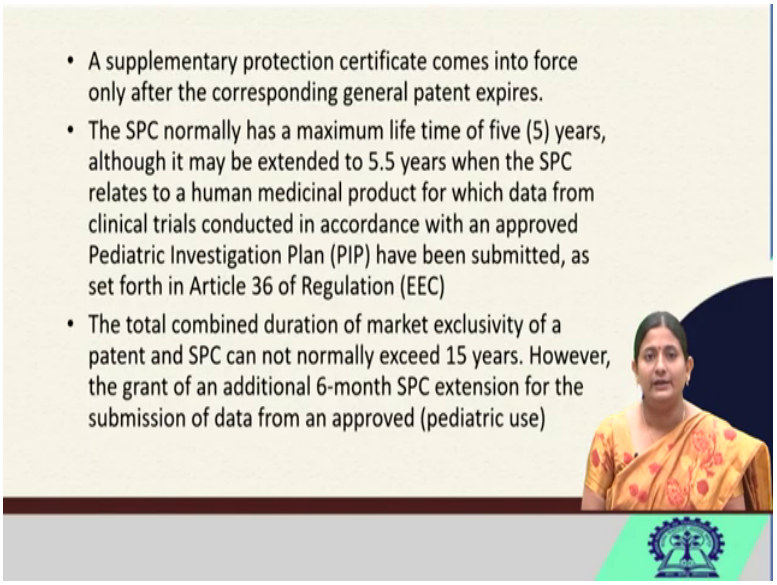

And this supplementary protection certificate again it is not related to patent directly in European Union, it is a supplementary certificate. So, it starts only after the patent expires. And as in the same way like United States, the supplementary protection certificate has a maximum life of 5 years. And in some cases, it is extendable to 5.5 years when it is related to the human medicinal product for which the data from the clinical trials are conducted under the approved pediatric investigation plant. Means, if it is a pediatric indication in that case the exclusive, the extension may be for 5.5years.

But similarly, like United States the duration of the total market exclusivity of the patent and the SPC should not exceed 15 years; in United States that is 14 years and here it is 15 years. And however, the grant of this additional 6 months of SPC for the pediatric thing, is again allowed 15.5 years that may be in some cases.

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And so they have specific regulations that is regulation number 1768 of 92, and 1610 of 96. So, these are the various regulation which is related to the supplementary protection certificate. And this is one way through which the companies tried to maximize their profit and monopoly over the market that is why patent or intellectual property also plays a crucial role in case of the pharmaceutical industry, because through which they are getting to or they can extend their life of the market or they get market exclusivity, they get other benefits from the same.

But again, in India things are a little bit different, we do not have any patent linkage provision or patent term extension per say and that is not been recognized in India. But in other countries that is one of the way incentives has been given to the pharmaceutical companies. So, these are the few concepts with respect to pharmaceutical as well as the biopharmaceutical in specific which as a student all of us should know. And the provisions are also like new things are coming up as complexity of the molecule is being resolved the data requirement are also being developed.

So, if you see the United States FDA, you will see lot of guidance document for monoclonal antibody, for normal protein, for any recombinant DNA product, or gene therapy product, or

blood transfusion product. So, because it is so complex, we need to have a specific set for the different set of molecules.

In India, of course, we are trying to get our regulation in place at par with the other, but still there are a lot many scopes for improvement. And also, there is one good thing is that there are certain international standards. So, we have again ICH – International Standard Council for Harmonization, so that also gives certain guidelines regarding this product development, purity safety, and efficacy study.

So, those are the international standards which can also be adopted by different country for making their product at par or of better quality. So, these are all different provisions. I hope this would be some informative to you all. So, keep exploring and keep reading more about this.

So, that is all for this session. So, thank you for being with me. So, we will meet in the next module.

Thank you so much.