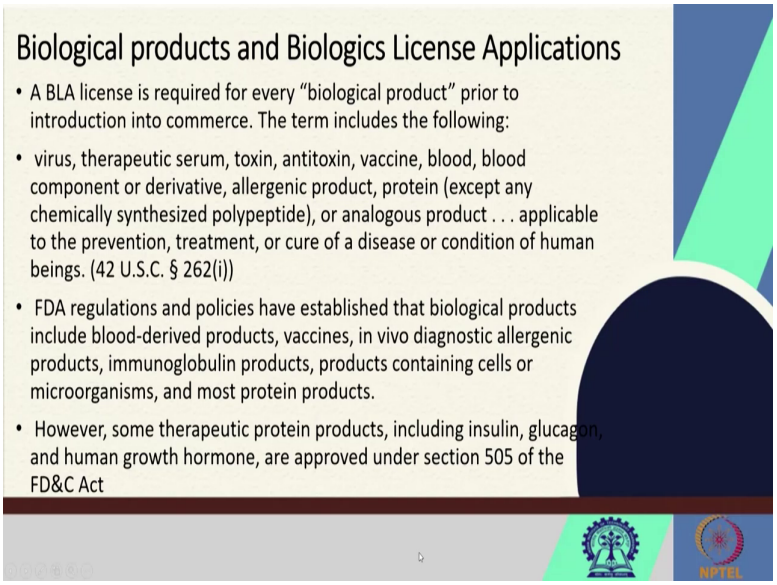
Legal and Regulatory Issues in Biotechnology
Prof. Niharika Sahoo Bhattacharya
Rajiv Gandhi School of Intellectual Property Law
Indian Institute of Technology, Kharagpur

Module - 03
Biotech Product commercialization: Regulatory Approval Process
Lecture - 14
Regulatory approval process for Biopharmaceuticals and Biosimilars in US

Hello all. So, in this lecture today, I will explain some basic details about the Regulatory Approvals for the Biopharmaceutical and the Regulatory Pathway for the Biosimilars in the United States.

(Refer Slide Time: 00:44)



So, in the United States, actually the US FDA or United States Food and Drug Administration is the nodal agency or the apex body which basically takes care of the drug approval process like various drugs, including the chemical as well as the biological.

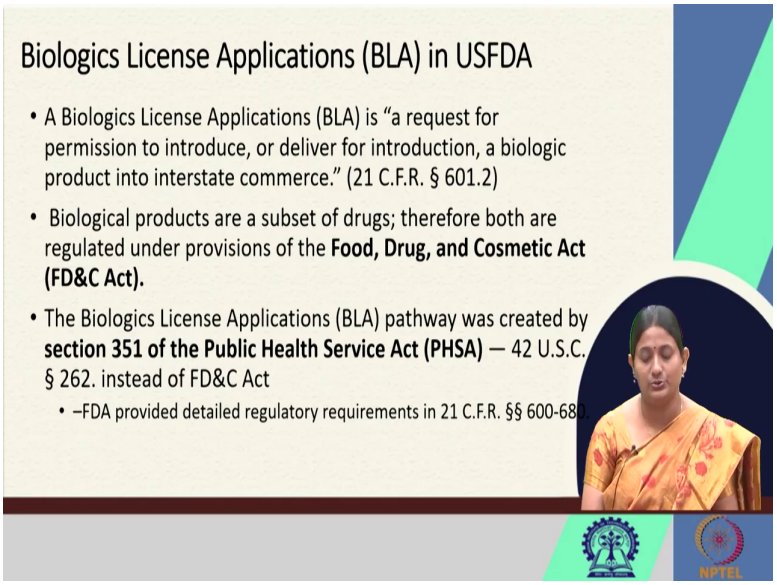
So, in United States for the biological product, basically they need a license known as the biological license approval or Biological License Application BLA. So, this BLA license is required for every biological product prior to which the product is introduced into the market or introduced into commerce.

And the biological products include a whole range of compounds including the virus, therapeutics serums, toxin, antitoxin, vaccines, blood, blood component derivatives, allergenic products, proteins, etc. some chemically synthesize polypeptides or analogous product. And those products are applicable to the prevention, treatment, or cure of the disease or any condition in the human being.

So, basically, we have the Food and Drugs Cosmetic Act in United States. So, if so, that is the main act which regulates the all the drug molecule product. And they have also there are different guidelines CGMP manufacturing standards, then how the CMC protocol has to be submitted, number of guidance documents are also available.

And these FDA has a number of regulations and the policies which are there for the biological products including the blood derived product, vaccines, or in vivo diagnostic products, immunoglobulin products. So, this US FDA is considered as one of the best agency where the manufacturers and the authority has tried to adopt a high standard for the preparation of the safe and effective medication.

(Refer Slide Time: 02:53)



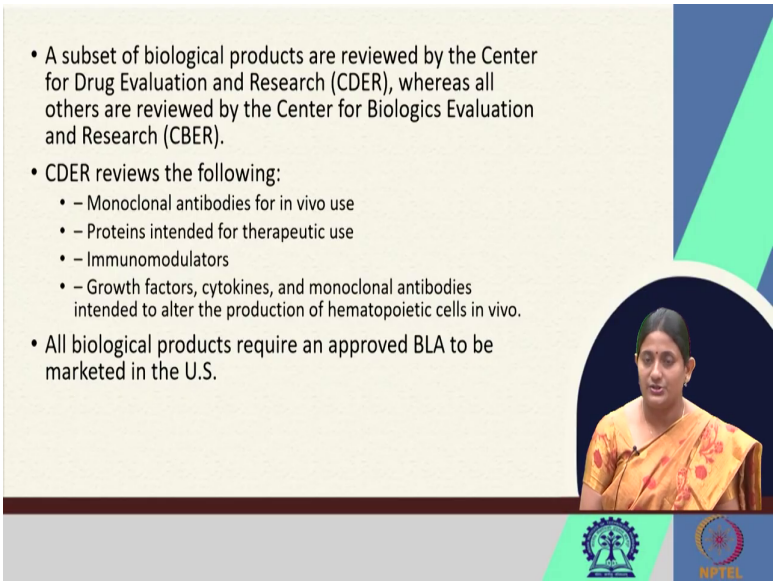
So, if we see the biological license application which pertains to the biologic molecule is basically the request for the permission to introduce or deliver for introduction, a biological

product into the interstate commerce as per the 21 code for federal regulation of number 601.2.

And if we see the biologics, are also drugs. So, these are basically a subset of the drugs therefore, the biologics are, not that it is immune from the Food and Drugs and Cosmetic Act. So, the biologics are also regulated under the Food and Drugs and Cosmetic Act or majorly regulated under this act, but for the simplification of the process of approval the biological license application pathway were created under another act which is known as the Public Health Service Act, PHSA Act.

So, the section 351 of this Public Health Service Act has introduced the provision for the biological license pathway and other regulatory requirements are given in the Food and Drugs of Cosmetic Act. So, basically under 21 CFR 600 to 680, other regulations are also there. So, both the Act are again applicable to this biological molecule.

(Refer Slide Time: 04:20)



So, if you see the structure of the US FDA, it has two agencies. One is known as the CDER and other is the CBER. So, CDER is the Centre for the Drug Evaluation and the Research which basically looks into the chemical or the normal synthesized molecules.

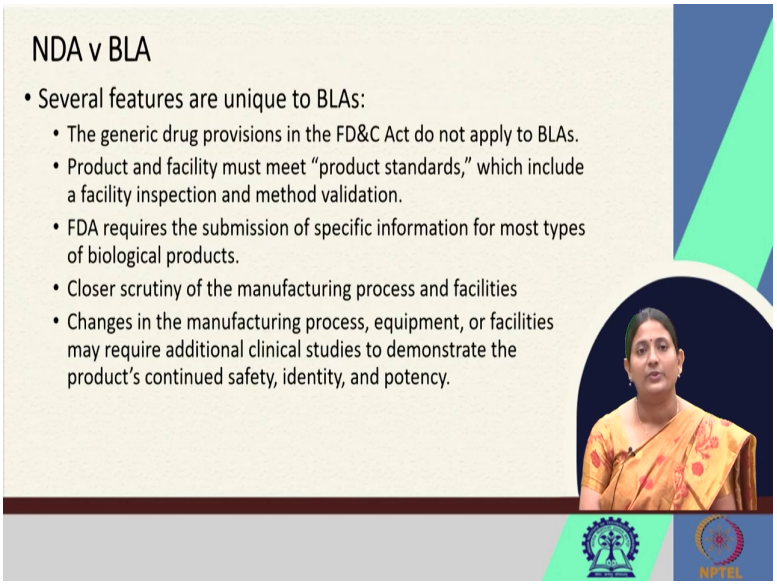
But again, it includes the monoclonal antibodies for the in vivo use, the protein intended for the therapeutic use, the immunomodulators, growth factors, cytokines, monoclonal antibodies

which is again intended to alter the production of the hematopoietic cells in vivo. So, these are also included under the CDER.

So, in the literature there are a lot of debate also like how the distinction has been made between the CDER and the CBER Centre for Biological Evolution Research and Centre for Drug Evaluation Research. So, again at the current stage there has been a demarcation where what kind of drug molecule would be controlled by whom. So, CDER takes the charge of monoclonal antibodies 14.

So, whether it is synthesized in living organism or chemically synthesized that is again a separate matter to be questioned. So, this is the current stand where CDER looks into the following matters. And as I mentioned BLA, Biological License Application is required for the marketing of the biological product approval.

(Refer Slide Time: 05:53)



So, now, similar as we have discussed in the last lecture we have two pathways, like new drug application which is basically for the chemically synthesized drugs, and we have something called the biological license application.

So, even though logically both of them are same like are directed to the application for a new drug molecule, but there are several features which are unique to the biological license

application pathway, where the generic drug provisions for the provisions as mentioned in the Food and Drugs and Cosmetic Act is not applicable to the biological license applications.

And the product and the facility must meet the product standards which includes the facility inspection and the method validation. And the FDA requires again submission of the specific information for many of the biological products which is not there in the generic product. Then, closer scrutiny of the manufacturing process and the facilities are required under the BLA.

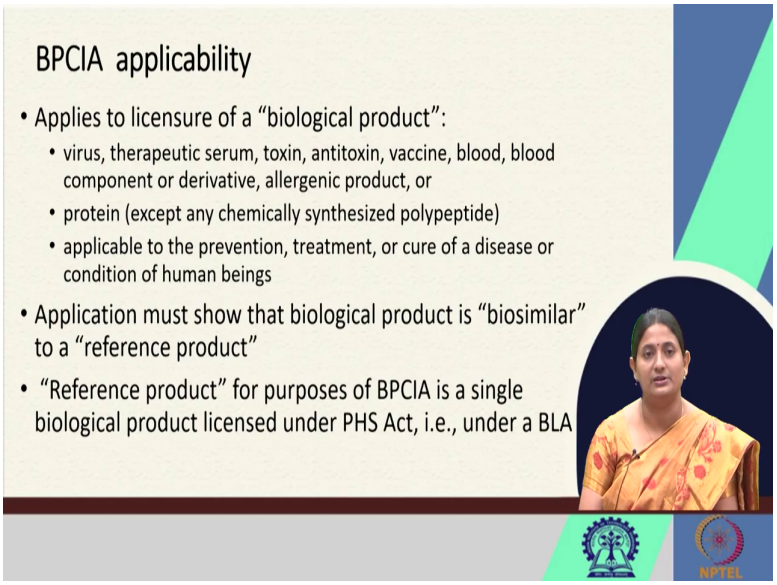
And the changes in the manufacturing process, equipments, or facilities also require additional clinical studies to demonstrate that the product is again continuing to be safe and identical and the potency is remained unchanged. So, the BLAs requirement are more stringent in compared to the requirement of a new drug applications.

(Refer Slide Time: 07:23)

And if we look into the biosimilar approval pathway, basically this pathway was first of like how the biosimilar should be approved because if device similar has to give all the data as an innovator drug molecule, so that will lend in the time as well as the financial burden on the company. So, that is why under the Patient Protection and Affordable Health Care Act, the biologics price competition and the innovation act was enacted in 2010.

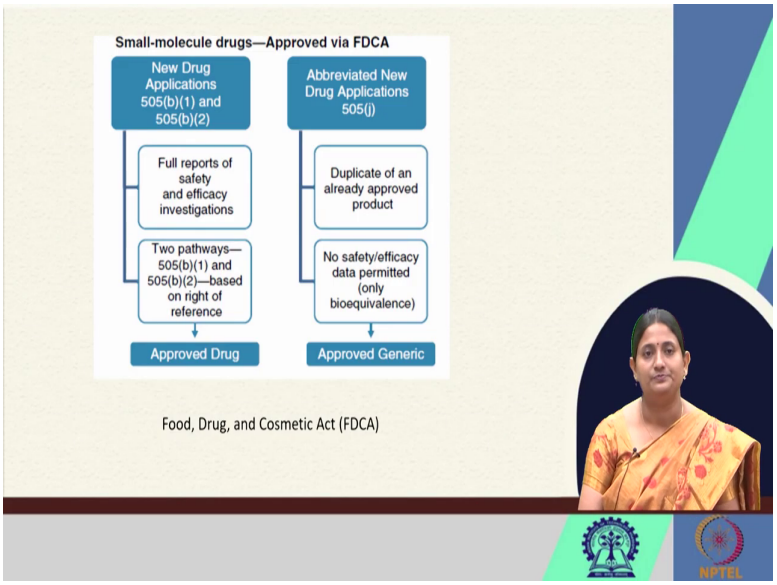
And it added a new section 351 k, under this Public Health Service Act, to create an abbreviated pathway for the biological product approval and which is known as the biosimilar or the interchangeable product in terms of US FDA. So, basically, under that pathway, it basically simplified the process of application for the biosimilar and the submission requirements for the biosimilar.

(Refer Slide Time: 08:32)



So, basically this Biological Price Competition and Innovation Act, is applicable to the biological product like same vaccines, therapeutic serums, or toxins, or proteins except any chemically synthesized proteins. And it has mandated that the application must, so that the biological product is biosimilar to the reference product and reference product is like the first application which has given for the approval.

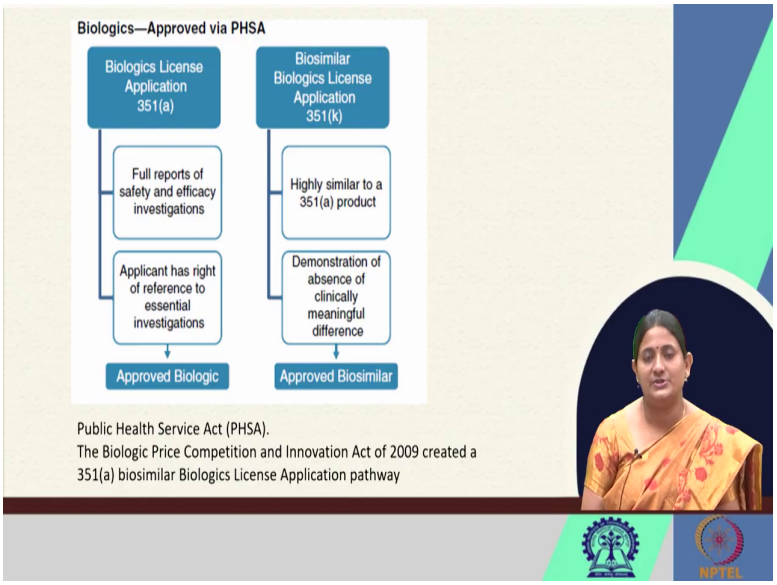
(Refer Slide Time: 09:04)



So, if you see under the food and Food, Drugs and Cosmetic Act the both the new drug application and the abbreviated new drug applications are evaluated like section 505, b 1 and b 2. So, where the new drug has to give the full reports from the safety and efficacy of the study and there are two different pathways of 505 b 1 and b 2 depending on the right of the reference.

And similarly for the generic product we had ANDA application process, where the duplicate of already which is basically a duplicate of the already approved drug molecule. Here we do not really need any safety or efficacy data, only the bioequivalence data is required for and that gives the approval for the generics, and wholly regulated by the Food, Drugs and Cosmetic Act.

(Refer Slide Time: 09:59)



But in case of the biologics, under this Public Health Service Act. So, here the biological license application for the new biological entity you need full reports of the safety and efficacy. And again, applicant has the right of reference to the essential investigations, and then that leads to the approval of the biologics.

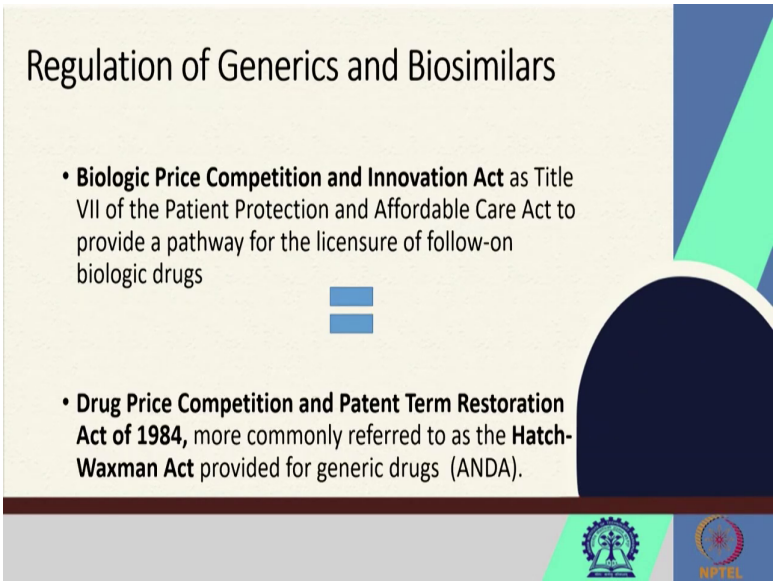
Similarly, for the biosimilars in the area of the biological product, first you have to prove that your product is highly similar to the thing and accordingly you can go through this abbreviated pathway. So, you have to demonstrate the absence of clinically meaningful differences and then it would be approved. So, this is basically governed by the Public Health Service Act and we have this BLA licensing pathway which basically governs this thing.

So, here the basically the US FDA has these two pathways which basic again differentiates between the chemical drug and the biological drug product. And number of regulatory guidelines are there, which is very helpful for the manufacturers to how for the submission of data requirement and other things.

(Refer Slide Time: 11:10)

So, this is in brief the US FDA protocols were the other requirement being the applicant information, all the product manufacturing information, preclinical studies, then clinical studies and the labelling requirements and number of guidance document has been given.

(Refer Slide Time: 11:35)



In United States, basically all the biopharmaceutical products or all the drugs are regulated by the US FDA and there are two main regulations, those are the Food, Drugs and Cosmetic Act

as well as the Public Health Safety Act. So, those two regulations are there in place to regulate the different aspects of the biologicals.

Though the food and drugs and cosmetic or FDC Act mainly pertains and related to the chemically derived drug, but there are few biologicals which are smaller in size like insulin. So, those are also regulated by the Food and Drugs Cosmetic Act under the CDER.

And however, the a PHSA along with the Food Drug Safety Act are the two important legislations. And like, we have also just briefly look into how the generic versions of the chemically derived drugs are approved under this FDC Act in United States.

So, the purpose of our separate pathway for the generic drug is that because the generic pharmaceutical does not have to submit all the necessary safety, efficacy, and clinical trial data, rather they have to establish the bio-equivalence in terms of their structure.

Then, if both of them the new drug as well as generic drug would be regulated in the same pathway, it may lead to the delayed entry of the product in the market. Further, it will also enhance the cost of production. So, as you know the brand drugs are little bit costly and generics are cheaper because they do not really need this clinical trial information for the safety and efficacy of the product.

So, now to have a streamlined pathway or have an abbreviated pathway a shorter pathway through which these generic pharmaceuticals can be approved this ANDA or ANDA application process has been enacted under the Hatch-Waxman Act which is a part of this Drug Price Competition and Patent Term Restoration Act of 1984.

In the similar way, for the biopharmaceuticals and particularly for the approval of the biosimilars the follow-on biologics under the Public Health Safety Act, which is again popularly known as the Obama Care which is enacted in 2010, which was introduced in 2010. So, we have a provision known as the Biological Price Competition and Innovation Act.

So, they are under the title 7 of the pay Patient Protection and Affordable Care Act or the Obama Care. It has introduced a shorter pathway or the abbreviated pathway for the approval

of the biosimilars. So, we can say this ANDA procedure under the Hatch-Waxman Act is equivalent to the Biological Price Competition and the Innovation Act for the biosimilars.

However, even though this biosimilar approval pathway has been introduced in the line of the Hatch-Waxman Act, but still there are lot of debate regarding the efficiency of this process. Because though these are two parallel line of approval process we may say, but still there are certain differences as we progress, we will also discuss the various differences between these two approval pathways.

(Refer Slide Time: 15:22)

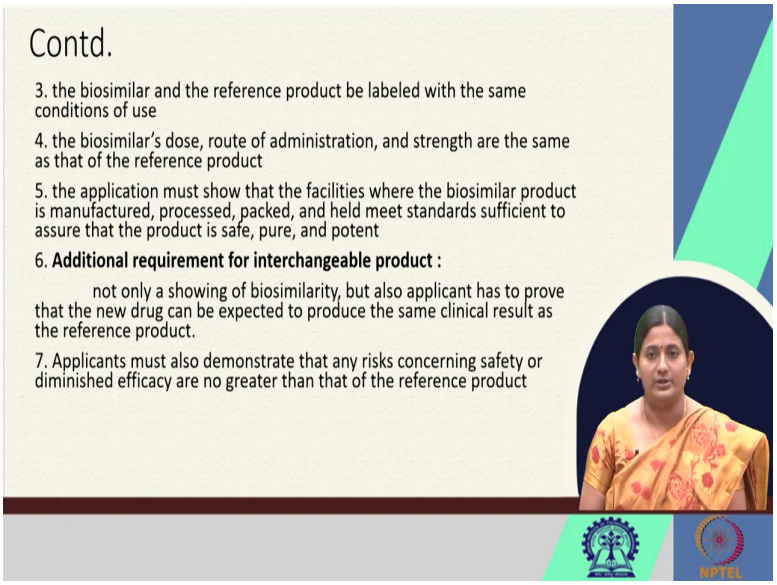
As I mentioned, generic application requires only bioequivalence data. But when it is a biosimilar or an interchangeable product, then the application requirements are far more than the bioequivalence data. If we see there are 5 main requirement and there might be certain additional requirement for the approval of the biosimilars or the interchangeable products.

For example, the biological product has to show the similarity with respect to the reference product. And this similarity must be derived from the analytical chemical studies which shows that the products are highly similar. Animal studies including the toxicity assessment, then clinical study or studies which will sufficiently demonstrate the safety, purity, and potency of the purity and the potency of the product.

So, you may see nearly we have to conduct different types of the experiment which is required for the new drug as well. But again, the quantification or the extent of different types of experimentation has been given in various guidance document depending on the nature of the product because this biological molecule may range from like few kilos Dalton to like the size varies. So, depending on the complexities of the product the data requirement might vary.

However, in case of the chemical drugs which is normally a small size molecule in compared to the biological molecule, simple structural similarity assessment or how it is acting inside this bioequivalence study is considered as sufficient. Further in this situation for the biosimilars, the biological license application is must, so that the biosimilars action or mechanism of the action is as same as the reference product. It mirrors the reference product. So, those activities or experimentation has also to be performed.

(Refer Slide Time: 17:30)



The third point or third requirement is that the biosimilar and the reference product should be labelled with the same condition of the use. So, both of the drug products should be used as the same condition because you know these are the protein molecule. So, slight variation in the temperature, slight variation in the storage condition, or even different mode of action may lead to different mechanisms. So, it has to be labelled similarly.

Then, the biosimilars dose route of administration and the strength must be same as the reference product. And also, the application must show that the facilities where the biosimilar product is manufactured, processed, packaged, and but all the production process takes place should meet the standards sufficient to assure the product safety, purity, and potency.

But in case of the generic pharmaceuticals, after you establish the bio equivalence you may not have to necessary, again suppose there is a change of production facility, then you may not have to again show all these things which is a during the manufacturing production in case of this biopharmaceuticals. The CGM, the good manufacturing compliance or the good clinical practice compliance, those things are mandatory depending on the production facility. But, the inspection mechanism and the scrutiny how these productions are taking place at different production units that is also very critical in case of the biosimilars.

And when it is an interchangeable product which we saw in the last class means a kind of biopharmaceuticals which is as same as like the normal or the first reference drug means at the prescription level it may be interchangeable. If something suppose you need a medicine, so instead of a you may get a 1, so at the prescription level.

So, here not only the requirements for the biosimilar molecules which we discussed so far, the applicant has also need to submit that the new drug can be expected to produce the same clinical result as the reference drug. And it they have to also demonstrate any risk concerning the safety or diminished efficacy and that no clinically significant differences. So, those has to be proved scientifically and experimentally.

So, if we see all these requirements and compared with the generic drug, then you see, so nearly the number of experiments which the manufacturer has to conduct or the data which is has to provide is also very critical and very lengthy. So, that is why the biosimilars even though these are the generic versions of the drugs are not that cheap.

The reference drug or the new biopharmaceuticals are always costly, you know in US it is estimated that nearly 800 billion dollars are invested for different research purposes of this biopharmaceuticals. But again, for this biosimilars there are not many biosimilars, since 2010 we may say this pathway has been approved, but the number of drug molecules approved as a

biosimilar or as a reference interchangeable products are very less because of the high cost associated with all this experiment.

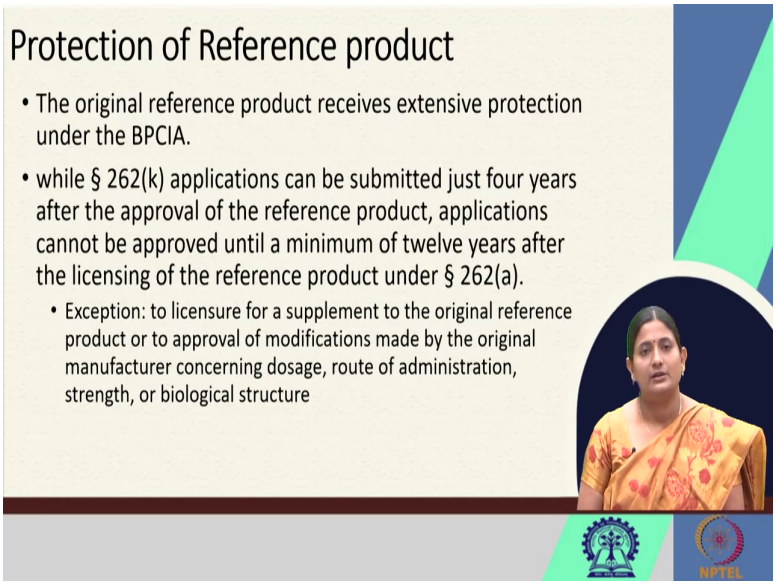
Unlike the generic segment or chemical drug, it is very easy and the regulatory requirements are also very easy to achieve. So, their numbers are greater and the drugs molecule are also available in cheaper prices. But that is not the case with the biopharmaceutical. And in many cases, it has to be case by case basis how it has been how it should be regulated.

For example, I was mentioning about the insulin. So, if we see the initial insulin preparation, so it was isolated from the pancreas of the animal cells maybe dog or pigs. But after that because severe side reaction happened because the insulin molecule where not pure, many contaminations were there or any others associated molecules were found along with the insulins.

Means the purity of the product was not sufficient then the recombinant DNA procedure helped in producing the human insulin by incorporating the human insulin gene into a viral vector or maybe which is a kind of a bacterial phase which can replicate by itself. And it gave to the human insulin which is more quiet similar to like human body and the purity can be ascertained in a better way, through the downstream processing.

So, these because insulin just smaller molecule, again it comes under the purview of the CDER instead of CBER. So, that is a different issue, but the main point is that for the biopharmaceutical the requirements are always higher than the normal generic drugs. So, that is why it has is separate approval pathway.

(Refer Slide Time: 22:35)



Coming next, again there are different regulatory requirements or regulatory provisions associated with the drug molecule. As I said, this drug development biopharmaceutical development is a long process. It may take 10 to 12 years or more than that, and the final product or the number of products, which are trialled which undergo the clinical trial and the final drug molecule which is effective against certain indications are very less.

So, that is why there should be certain incentive to the manufacturers, so that first of all the long-term production period or the high cost may be like they can get the benefit after when the drug is approved for marketing. So, for that reason there are different provisions in the drug regulation, particularly in the developed nations which helps the manufacturer or which provides a kind of incentive to the manufacturers to go for production of this kind of molecule.

So, under this BPCIA or Biological Price Competition and Innovation Act, so there are number of extent protection given unto the biopharmaceuticals. For example, under this 262, when the biosimilar applications are submitted, so 4 years of exclusive period is granted to the reference product.

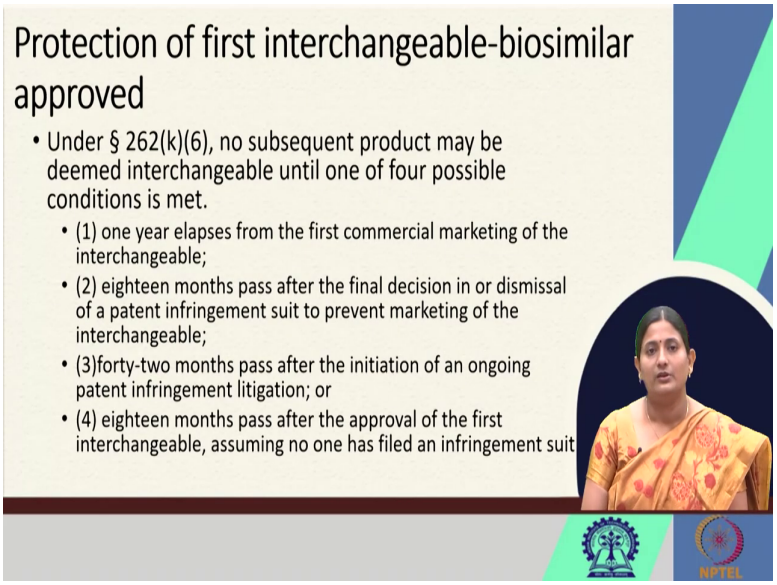
Means till the time if the first drug is approved, till next 4 years no biosimilar can be, no biosimilar application can be submitted. And the applications cannot be approved until a

minimum period of 12 years after the licensing of the reference product, means 12 year marketing exclusivity remains with the reference check product. So, till 12 years no biosimilar product can enter into the market.

So, again there are certain exception, but suppose there is again a kind of a supplement to the original reference drug which is again for new indications or new route of administration or the doses is a changed. Same reference product, but with new indication and dosage or structure, then that can be approved, but no biosimilar product can be approved for marketing till the next 12 years.

And first 4 years even the applications for the biosimilar cannot be submitted. Because you know these long gestation period or long R and D period should be compensated in some way. So, those compensations are given through, which we called data exclusivity or the marketing exclusivity which we will again deal with the next chapter.

(Refer Slide Time: 25:32)



And the first interchangeable biosimilar, they also get certain protection under this BPCIA Act means the first biosimilar which is highly similar to the reference product. So, under this section 262 k subsection 6, no subsequent product may be deemed interchangeable until one of the 4 possible conditions are met. So, if any of the following conditions which I am going

to explain is met, then only the interchangeable can be introduced or else it cannot be introduced.

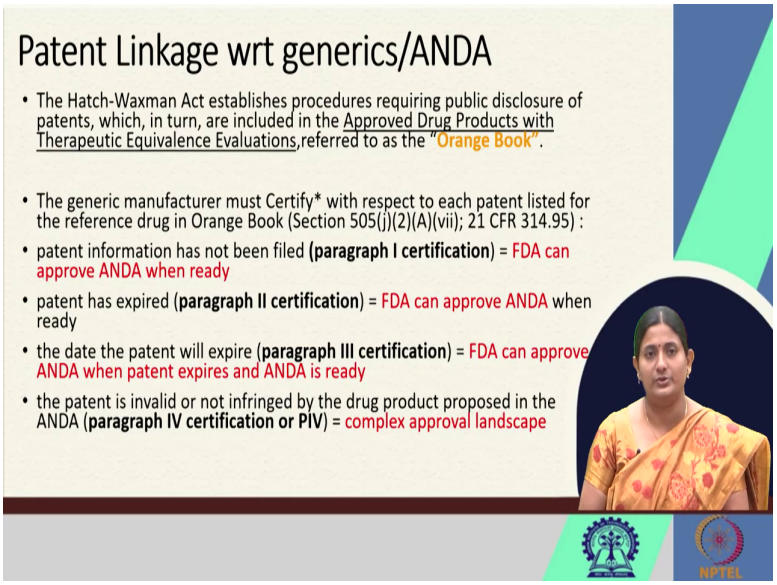
First, if one year elapses from the first commercial marketing of the interchangeable. So, means within the first year generally no second interchangeable product would be allowed. 18 months pass after the final decision in or dismissal of a patent infringement suit to prevent the marketing of the interchangeable.

So, generally the interchangeable may be introduced if the producer can prove that the patent concerned with the first biopharmaceutical is elapsed or is not valid. So, in this case minimum of 18 month must have passed, after the final decision that helps that this with besides the patent infringement suit regarding the intangibles.

Or 42 months passed after the initiation of an ongoing patent infringement litigation. If there no conclusion has been reached and 42 months has been passed then only second interchangeable can be, then only the interchangeable can be introduced. 18 months pass after the approval for the first interchangeable, assuming no one has filed an infringement suit.

So, if 18 months as pass for the first interchangeable drug molecule and no infringement suit has been filed by the innovator company then maybe the second interchangeable can be introduced. So, these are additional protection for the first interchangeable also available under this Act.

(Refer Slide Time: 27:36)



So, now, if you again come back to the generic drug and combine or we compare with respect to the biological versus generics then we can see that under the Hatch-Waxman Act we have again certain provisions through which abbreviated new drug application can be filed.

So, there are different conditions known as the para 1 filing, para 2 filing, para 3 filing or para 4 filing. So, here the information with respect, the information for the application with respect to the drug molecule and the patent information for the original drug product has to be linked in some way, which is generally known as the patent linkage where the drug regulator tries to interrelate interlink the patenting information along with the regulatory thing.

So, basically the purpose of this is that, patent is a kind of monopoly right which gives extensive protection to the manufacturer in terms of selling, licensing or manufacturing of the product. So, in no way that the approval of certain drug molecule would hamper the rights of a patent holder to take care of those main measures this kind of prohibition has been introduced.

So, for the normal chemical drugs generally all the patent related information for the active pharmaceutical compounds means which drug molecule have active compound and which is the patent by this active molecule has been protected. All these are established or in a

publicly available document which is known as the Orange Book. Means basically it lists all the patent information related to a drug product.

And accordingly, 4 different kinds of abbreviated applications like can be filed. First, like before that actually when a generic manufacturers like these company which wants to imitate a product or which is already available in the market make price to make the same product, they have some information with regard to the patent.

So, in that case, we have para one certification which means if there is no patent information for that drug molecule. So, the generic manufacturer can directly file for the abbreviated drug molecule. And the food drug authority can accept the application whenever the application is completely ready which is known as the para 1 certification.

Then, second is the para 2 certification where once the patent for the innovator drug has been expired the FDA can approve the abbreviated new drug application when the application is ready. Means, that there will not be any infringement.

Third, para 3 certification. Under the para 3 certification the generic manufacturer has to provide the date on which the innovator drug patent would be expiring and after that date the FDA can approve the abbreviated application. So, that again there is no patent infringement.

And under the para 4 certification, the generic company has to establish that the given patent in the orange book for the active pharmaceutical ingredient is invalid or it is not being infringed by the drug product which the generic manufacturer is proposing. So, it is a complex process in which the innovator company may file an infringement suit and the generic company may prove that he is not infringing upon the process, notices has to be sent.

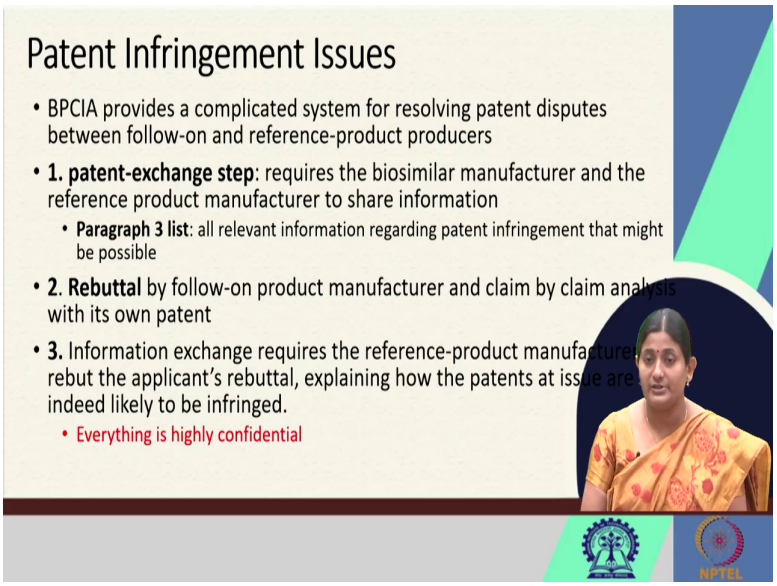
So, once this kind of application comes, the notice has to be sent to the innovator drug company more then again there is an elaborate process where they decide and give rebuttal, how it is infringing or not. And then finally, the innovator company may sue the generic company.

And so, there is a time period for all these things like for the certification when a new drug has been introduced and it is approved for marketing, the innovator company has to enter all the patent related information within the third within 30 days after the marketing approval.

Suppose, some companies do not give the patenting data for the drug molecule in the next 30 days. So, in that case the first 3 cases, the first 3 like paragraphs certification may be given like because there is no information the application may be accepted early and the marketing approval can be given early.

Only they can go for this when someone goes for the para 4 certification, then the again complex process and sewing, and then litigation starts. So, this is also a complex process. But we have definite information, we have the patenting information to which the generic company is going to give certain declaration how it is not infringing the corresponding patent and accordingly abbreviated new drug application will be approved.

(Refer Slide Time: 33:12)



But when we come to the biosimilars or biopharmaceuticals this process is little bit different from the normal generic process. And this is a little bit more complicated. So, here the first step is, if somebody wants to apply for a biopharmaceutical approvals a manufacturer, then they have to go through a patent exchange step. So, patent exchange step means here both the

biosimilar manufacturers and the original product or the reference product manufacturer they will share certain information regarding the patent.

So, they have to give all the relevant information. There might be number of patents associated with some single product. So, all the information has to be shared with each other, the reference product manufacturer as well as the generic product manufacturer. And now this is known as the paragraph 3 list where all the information are shared among the both the parties.

Then, there is a rebuttal by the generic drug manufacturer or the applicant for the biosimilar. And the rebuttal may be like, this they might be having certain patents through which it may not infringe the other patent or they may give the rebuttal based on the claims of the innovators drug like, we are not infringing your product or process whatever is covered under that patent.

And then, everything like this is basically based on a good faith where both of the party completely disclosed the information regarding different patents and go ahead. And all this process is highly complicated. Like we have something called orange book for the generic for the normal chemical entity, we do not have any information for the biological drug product.

And again, as I mentioned it is a complicated drug product, large molecules may be covered by many of the patent. So, this process of negotiation is highly confidential unlike the generic drug where everything is readily available in the orange book. So, that is one of the differences between the biosimilar and the biogeneric approval.

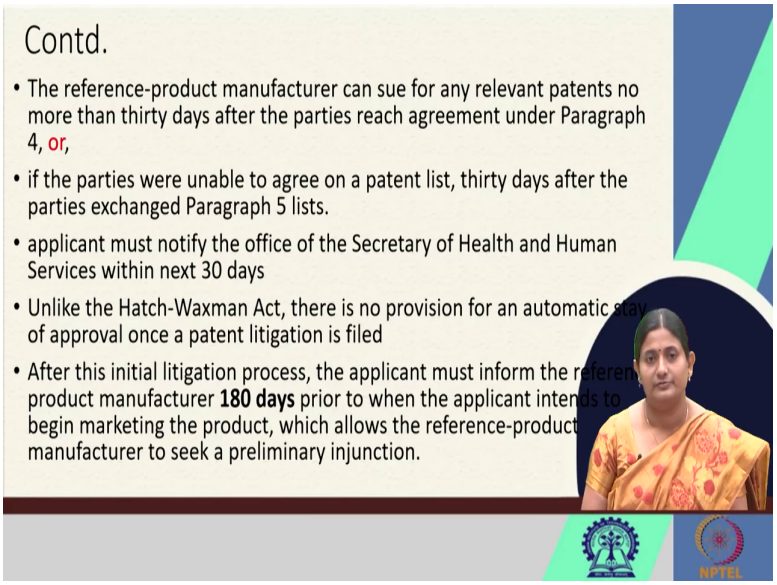
(Refer Slide Time: 35:30)

So, in the second step of this biosimilar approval, after the patent exchange happens patent information exchange happens between the two parties, the negotiation starts. Suppose, the negotiation of over the good faith is a not possible then we have something called patent resolution provision or the paragraph 5 provision.

So, here now what happens, the applicant notifies the reference product manufacturers on the different numbers of patents which he believes that it might be subject of an infringement and therefore, they will set a ceiling point or they will finalize the number of patents, but number of patents which the reference drug manufacturers might hold and then how they are infringing or not infringing.

And you know within 5 days of this submission both the parties provide this paragraph 5 list detailing all the specific patents which each of them believes to be infringed and that forms the basis of the infringement suit in the patent.

(Refer Slide Time: 36:42)



And so, the consequence of that is the reference product manufacturer can sue any relevant patents after that like once the list is ready. So, the reference product manufacturer has the right to sue over any relevant patent which has been mentioned under this paragraph or under this negotiation which has happened between the two parties.

And if the parties were unable to agree on a patent list, then if it is not readily available with the para 4 thing which they negotiate in good faith, then the paragraph 5 thing comes in place. And finally, once it is settled down then the applicant will notify the secretary of the health and human services within the next 30 days so. So, once it is notified to the health and second thing the there may be some provisions where the manufacturing processes can be stopped for some time for this and or the approval processes can be stopped for certain period of time. So, in the Hatch-Waxman Act there is no provision for the automatic stay or approval once the patent litigation has been filed. And here after the initial litigation starts, the application must inform the reference product manufacturer within 180 days prior to when the application intends to begin marketing the product.

So, the biosimilar manufacturing company has to notify the original product or reference product company, 180 days prior to the application like prior to when they want to begin the marketing. So, based upon which the reference product or reference drug manufacturer can

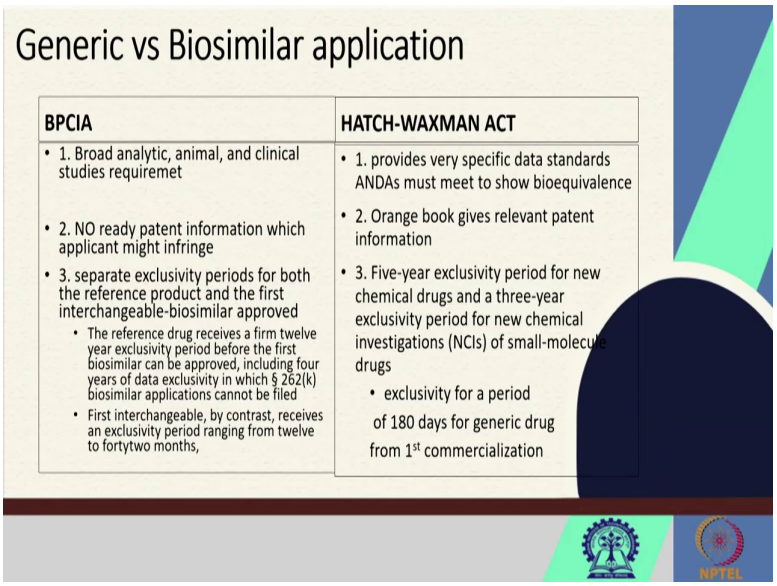
seek a preliminary injunction. So, this is very complicated process where lot of negotiation takes place and their prior information provision is there.

Before the biosimilar is allowed to enter the market the original drug producer has the right to go for a preliminary injunction where like it is a temporary period in which the product may not be marketed, injunction would be granted upon the to stop the marketing of the product.

Then Hatch-Waxman Act, the para 4 filing, and other things are very clear the steps are very clearly defined what perhaps to done, how and what is the procedure. But under this BPCIA Act, the steps are not that clearly defined and it and also the since the patent information are not public, and many a time the original drug manufacturer company they crosslink many patents.

So, for a single all the technologies associated with a drug product. So, it become very difficult to understand which patent it is infringing the similar product, device similar companies infringing and as accordingly the process may be very cumbersome.

(Refer Slide Time: 40:06)



So, overall if we see the difference between the biosimilar application under this BPCIA Act and generic application under Hatch-Waxman Act, though both are abbreviated drug

application pathways, but there are substantial differences between the two. So, I just try to enumerate the differences between the two processes.

So, just to give you a few major points. Under this Hatch-Waxman Act for the generic drug manufacturer we do not need extensive studies we required specific data standards and they have to show the bioequivalence. Whereas, for this biosimilars broad analytical, animal, and clinical study requirement again which are not specific. So, many a times for many of the molecule still there are no guidance document what has to be submitted. So, case by case basis they need the submissions.

Second, for the like for the generic drugs we have this orange book which gives the relevant patent information, for the biopharmaceuticals we do not have really ready patent information which the applicant might infringe. And the exclusivity period which is provided for the generic drug and exclusivity period which is provided for the biopharmaceuticals or biosimilars are different.

So, for example, in the generic drug, 5year exclusivity period for the new chemical drugs and 3 year exclusivity period for the new chemical investigation drug means those who will be going through the clinical trial application are given.

And exclusivity period for 180 days for the for the generic drugs are granted from the date of first commercialization. Whereas, in case of biopharmaceuticals the reference drug receives or 12 year exclusivity period before the first biosimilar can be approved among which 4 years are for data exclusivity means the data will not be reveal it to the any competitor.

And the first interchangeable again receives the exclusive period which may range for from 12 to 42 months. So, you may see and why so? Again, biologics are complex molecule needs more investment, needs more time, needs more critical data sophistication instruments. So, everything is very different for this biosimilar bio-pharmaceutical things.

So, that is why the biopharmaceutical regulatory approval is a very complex process and in India we have certain guidelines for the biosimilar. But if you compare with these developed nations like US or European Union also, we have not reached to that standard, but separate

provisions that we have certain bodies definitely we have seen we have RCGM, we have GEAC.

But the we do not have again the linkage between the patent information and regulatory information. Patent linkage is not there in India. We recognize some forms of data exclusivity like we consider a drug as a new drug for the first 4 years. So, 4 years that exclusivity also given. But again, there are many other dynamics associated with that because India is known to be a generic drug manufacturers where drugs are available in cheaper price.

So, depending on the countries, like nature of the country and the other things this has been taken. But to just give you an idea how this biopharmaceuticals are regulated, how these biopharmaceuticals are linked with the patenting thing this is what like I thought of giving the information to you.

Hope this will be helpful for you. So, in the next lecture I will give you certain explanation regarding the other exclusivity provision or other benefits for the biopharmaceuticals. So, stay tuned.

Thank you.