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**SESSION 5: PATENT LAW
5A. *Biologics & Biosimilars***

Moderator:

John Lee

Gilbert + Tobin, Sydney

Speakers:

Brian D. Coggio

Fish & Richardson, P.C., New York

Biosimilars: The “Patent Dance”

“I Won’t Dance/Don’t Ask Me”

Cordula Schumacher

Arnold Ruess, Düsseldorf

Biosimilar Patent Litigation – Same Same but Different?

Nicola Dagg

Kirkland & Ellis International LLP, London

The Patent Trials and Tribulations of Launching a New Biologic Medicine

Shimako Kato

Abe, Ikubo & Katayama, Tokyo

Reasonable Protection of Antibody Patents —

The Right Balance Between Patentees and Competitors

Panelists:

Ron Vogel

Fish & Richardson P.C., New York

Roberto Rodrigues

Licks Attorneys, Rio de Janeiro

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MR. LEE: Good morning everyone. My name's John Lee. I'm from Gilbert + Tobin in Sydney, Australia, and, like Annabelle, I'm pleased to be here in civilization.

I am very pleased to be moderating this session on biologics and biosimilars. What we are discussing today is the new frontier, I think, in life sciences IP litigation. As we will hear, many of the world's leading biopharma companies are focusing a lot of attention, resources, time, money, effort, research and development, in terms of developing new therapeutics, biologics, for a whole range of treatments, from immunology through to oncology.

The technology, as we'll hear about, is very complex. In comparison to the so-called traditional small-molecule drugs, there are additional layers of scientific and technical complexity in biologics which add a whole new layer to what is already a pretty complex matrix in terms of the IP and regulatory frameworks. By way of a simple illustration of that, we recently litigated a biologics patent in Australia and the specification was 530 pages.

Fortunately, today we've got some of the leading experts in the field to help us navigate this maze. We've got a truly international panel, which is really good. I'll ask each of our panelists to introduce themselves briefly, name and affiliation. Thank you.

MS. SCHUMACHER: I'll start. My name is Cordula Schumacher. I'm at Arnold Reuss in Düsseldorf, Germany.

MS. DAGG: Good morning, everybody. My name's Nicola Dagg and I'm at Kirkland & Ellis in London.

MR. COGGIO: Good morning. I'm Brian Coggio from Fish & Richardson, but more importantly I've been teaching patent litigation here at Fordham for almost twenty years.

MS. KATO: Good morning. My name is Shimako Kato from Tokyo. I work for Abe, Ikubo & Katayama.

MR. VOGEL: Good morning, everyone. My name is Ron Vogel. I'm with Fish & Richardson here in New York.

MR. RODRIGUES: My name is Roberto. I'm from Licks in Brazil.

MR. LEE: Thank you, and thanks in particular to Roberto who's a late substitute for one of his colleagues.

We've got four speakers and two panelists. Broadly, Cordula is going to start, and her speech is more about an introduction to the biologics/biosimilars maze, and in particular the experience in Germany. Brian is going to teach us how to dance — or not, if we so choose. Shimako is going to focus on the PCSK9 litigation which has been running in Japan. Nicola is going to touch on something which has been quite topical at the Conference, and that is the eligibility of final injunctions or otherwise in the biologics space.

I will hand over to Cordula to kick us off.

MS. SCHUMACHER: Thank you.

As announced, I will start with some basic background, not only because that's interesting as such but because it sets also the stage for the legal discussion later on. So it is important to keep in mind what biologics and biosimilars are and how the markets work in this field.

What are biologics? As opposed to the small molecules, they are not chemically synthesized but they are produced by living cells, which makes it much more complex. The biologics can be antibodies; they are much larger in size; and there is an inherent variability

even within the same product because they are produced by the living cells which slightly differ one from the other one.

It very much depends on the manufacturing process, so the product is determined by the process you use, by the cell cultures you use.

Biologics are used for life-threatening and chronic diseases, so they are a very important part of the pharmaceutical development and I think a lot of hope is put on them. We are seeing they have brought us great improvements already.

Biosimilars are similar but not identical, and that is due to the different cell cultures and the different manufacturing conditions. The biosimilar manufacturer has to develop those himself; he has to come up with his own cell cultures and his own manufacturing conditions, because the ones of the originator are proprietary and usually not known.

This leads to a slightly different product. But of course, it is being tested, so that pharmaceutically in principle it has the same effect but it is not the same.

Because of these differences there is no automatic substitution, not like with the generics where you are just replacing a branded product. Here, it is at the doctor's discretion whether to replace a biologic with a biosimilar.

As mentioned, their economic relevance is increasing because of the progress that is being made and we are seeing new players entering the market here.

What are the key market factors? When it comes to development of biosimilars — and I'm addressing especially the differences to the classic generic situation — the development of a biosimilar is much more complex and more time-consuming. Sources mention eight to ten years as opposed to maybe two years plus for a generic, which is not just the time itself but it's also then the lack of predictability.

You do not know what the market will look like in ten years. That obviously makes it much more complex. Maybe a new development comes in and the biosimilar is completely irrelevant by that time. The costs are a couple of hundreds of, as opposed to a generic which should be available for a single-digit figure of millions, and there is obviously a high risk of failure, which all in all creates a higher barrier for market entry. Equally, the manufacture is complex and costly.

Market approval is more difficult. To get a market approval of a biosimilar you have to comply with more clinical tests, albeit still less than for the original product.

Once you have the product you need more marketing efforts. Because there is no automatic substitution, you have to convince the doctors to actually change from the biologic to the biosimilar. But it might also be that doctors are then even changing from a small molecule to the biosimilar. It's a bit more complex market situation, and that usually leads to the effect that the market uptake is slower, and we do not see the massive price decrease and the massive price competition we see in the originator/generic situation. There is a smaller market impact.

What does that mean for infringement proceedings? I think we could see a higher incentive to launch at risk because:

- First of all, it is much more difficult to clear the patent situation in advance of the development decision because it takes so long, and patents might be granted in between while you are still developing.
- You have high investments, which could lead to sunk costs if you do not launch or launch too late.
- You have high potential gains because the price structure is higher than for the generics.
- You have lesser risk re damages. Because the price gap is smaller, the profits from a biosimilar might be closer to the potential damages of the biologic company, so it's

a lesser risk than if you have a generic company that is completely ruining the price-setting of the originator.

An infringement proceeding has more complexity. The manufacturing process is sometimes patented so it is more difficult to get access. It is more difficult to analyze the products. Sometimes it is not easy to show infringement, especially in preliminary injunction (PI) proceedings, while in generic cases infringement usually is a no-brainer. And the assessment of damages eventually might be more difficult because it is not a one-on-one replacement, generic vs. originator, but the market might have grown through the additional marketing efforts of the biosimilar.

In Germany we have to look at the balance of interests, although only usually in PI proceedings and only if validity and infringement are at question, while in generics cases there is always a clear answer: there is basically an automatic PI if infringement and validity is clear enough.

In biosimilar cases we are seeing the courts look much closer into validity and infringement because the balance of interests is not that clear. It is not a clear balance in favor of the originator, but the biosimilar also has substantial interests to put forward.

We saw that in a decision of the Court of Munich in 2017 on Rituximab the court explicitly said, "We cannot transfer the case law of the generics cases to the biosimilars. We have to look at the specifics here and with much more detail into infringement and validity."

The key takeaway is don't apply just the situations you have seen from the generics cases but you do need to look into the specifics there.

MR. LEE: Thanks very much, Cordula.

Are you able to comment a little more on the issue of lack of identity, which is obviously a significant part of the traditional small molecule regime where the generic is essentially identical to the originator compound, and the impact of that on an infringement-and-validity action?

MS. SCHUMACHER: Yes, absolutely. We had a case where the patent was relating to the specific composition of the biologic. Usually, you would show infringement in a generics case by just saying, "Well, it is the same molecule and therefore it is infringing" or "it has the same market authorization." Full stop.

Because it is biosimilar does not mean that it actually has the exact composition. In that case, it was about the number of acidic variants. The antibody is the active ingredient, but within the mixture of this active ingredient there is a certain number of acidic variants, and the number of acidic variants and the composition of the acidic variants of the original product is not necessarily the same when it comes to the biosimilar. So you have to look into the details.

In the end, the patentee has to show and provide an analysis of the actual composition of the biosimilar product. That might be difficult because you have to get hold of the product. Even if you get hold of market authorization documents, that might not be good enough. You actually have to look at the product. As in normal patent infringement proceedings, you actually have to analyze the product where it is infringing. You cannot just rely on the similarity.

MR. LEE: Thanks very much.

I might also ask Ron to comment on that particular issue and the different dynamics between an infringement-and-validity case in a small molecule context as opposed to a biologic.

MR. VOGEL: Before doing that, I want to ask Cordula a question. Given what you were talking about, the complexity of infringement and how these patents usually protect the manufacturing process, and given the limits in German discovery, how are courts pro-

ceeding with that in terms of requesting records? Is it like it is in the United States, where the parties are disputing the sufficiency of evidence?

MS. SCHUMACHER: Absolutely, that's a big issue because we do not have the disclosure and, in principle, the burden of evidence is fully on the patentee. In the case I just mentioned, the patentee tried to provide the evidence through a Section 1782 procedure¹ in the United States, getting documents from there, which is absolutely fine and admitted in Germany.

The problem here was that the number of acidic variants and the type of variants had to be determined not according to today's equipment and standards but those at the priority date. If you would apply today's equipment, you would find more and different types than twenty years back when the equipment wasn't there. But the equipment from twenty years back no longer existed, so basically there was no way to prove infringement because the chemical composition of the columns and how you measure it was no longer available.

The parties spent quite some effort trying to show infringement and trying to show how the actual composition would have been measured twenty years earlier, but in the end that would have been possible only through indirect evidence, and in that specific case the court said, "This is not enough; the indirect evidence so far provided is not good enough."

MR. LEE: Are there any questions from the floor for Cordula?

QUESTION [Angus Lang, Tenth Floor Chambers, Sydney]: Thank you for your presentation. In relation to the *Rituximab* decision in Munich, did the court grant an interlocutory injunction in that case?

MS. SCHUMACHER: No, it did not. It denied sufficient validity actually on the basis of lack of priority, the topic we discussed yesterday [Session 2B].

QUESTIONER [Mr. Lang]: I see. In Australia we had a rather excellent judge who did grant us an interlocutory injunction. Oh, there he is. [Laughter]

MS. SCHUMACHER: I was defending that case, so I think that was an excellent decision in Germany as well.

QUESTIONER [Mr. Lang]: That's a win/win.

MR. LEE: We might have one more quick question.

QUESTION [Jürgen Dressel, formerly of Novartis Pharma AG (Ret.), Basel]: Cordula, you showed the uptake of biosimilars in this area. When I look back at small molecules, in former times the uptake also was very slow. People were very worried about different salts and who knows what. Do you think with more confidence and more experience with biosimilars, firstly, the cost for bringing such a product to the market will decrease because maybe they will not have to do proof of therapeutic efficacy anymore, and that there will be more mechanisms by which the governments and the health-care systems can actually encourage biosimilar substitution?

MS. SCHUMACHER: Yes, I very much do think so. As far as I understand, there are many studies ongoing that increasingly show that actually biosimilars are more or less as efficient and as efficacious as the biologics. So the initial skepticism seems to be decreasing. It still might not be the case that within one treatment cycle you would change, that if you have a six-month treatment cycle of a cancer patient that you would change within that treatment cycle, which might make sense.

The first step will be the education of the doctors so that they will actually prescribe the biosimilar and lose their hesitance. It is quite interesting that we have a different landscape in Europe. As far as I'm aware, in Spain and in Portugal there is a great hesitancy to

¹ 28 U.S. Code § 1782.

actually prescribe biosimilars, while in the northern countries it is much more common to do so.

The second step, which is much more important, is then the regulatory framework. Similar to second medical use patents, as we discussed yesterday, the regulatory framework sets the stage. As soon as pharmacies are obliged to hand out the biosimilar, then we will have more or less the identical market situation.

MR. LEE: Thanks very much, Cordula.

MR. COGGIO: Thank you. It's a pleasure to be here. I want to thank Hugh for inviting me. My topic is the infamous "patent dance" that kicks off all biosimilar litigation in the United States.

My title is "Biosimilars — I Won't Dance/Don't Ask Me." What does dancing have to do with biosimilars? It's from the old Cole Porter song. It has a lot to do because the biosimilar can say to the sponsor (what I might call "the brand" from my Hatch-Waxman days), "I don't want to dance. I'm not handing over my Abbreviated Biologics License Application (aBLA) to you, and there is nothing you can do about it." We know that from recent court decisions.

So, in actuality, the biosimilar can say to the sponsor/brand, "I won't dance, don't ask me, and you can't force me to dance." That was questionable a while ago, but now we know that there is nothing the sponsor/brand can do to force the biosimilar to engage in the dance. This is so important I thought I'd review in a brief amount of time the pluses and minuses for the biosimilar to enter the dance, not enter the dance, or just ignore it totally.

This is a recent list of approvals in the United States.

Here is the "patent dance." You've heard about it. It looks crazy. It is. You see the very first step here, the (2)(A) step: "Biosimilar provides confidential information to the sponsor." You can put a big X through that because if the biosimilar doesn't turn over that information, all the rest of the dance never occurs. After the biosimilar turns over the information, then we have the sponsor/brand identifying which patents, which claims; then it goes back to the biosimilar to put up defenses; then it goes back to the brand; and so on and so forth. Actually, the patent dance could be split in two because, even though it is called the "patent dance," there are two different ways that the patent dance can end.

So, if you want to, the biosimilar can avoid all that. Should he? Should she? To dance or not to dance?

Benefits of dancing:

- If the biosimilar enters the dance, it controls the number of patents being litigated. Indeed, it can limit the number to one single patent.

- The biosimilar can ensure that certain patents are litigated in the "first wave" versus "second wave." I won't bore you with details on the waves, but it could be important for the biosimilar to get the most important patents on the table up-front.

- The biosimilar is going to know when the sponsor is going to file its complaint because once this dance starts every step is limited in time. Once the biosimilar turns over his aBLA, everything happens quickly.

- The dance is an early exchange of the contentions — the (3)(A), the (3)(B), the (3)(C) statements. That could be a plus because the sponsor/brand has to set out its positions early on, but — a double-edged sword — so does the biosimilar.

- The biosimilar will retain the ability to file a declaratory judgment action.

- Interestingly — there's a little bit of controversy — it is possible that the sponsor/brand has to list all the patents that it is going to assert or it will forever be barred from asserting them. Therefore, by entering the dance the biosimilar puts pressure on the sponsor to, as we might say, put up or shut up.

- Last, if the dance begins and the sponsor does not comply with all the rigid requirements, it loses the right to collect lost profits. If and when the biosimilar launches, it is limited to “reasonable royalty.”

The drawbacks of dancing:

- The biosimilar up-front has to turn over its aBLA² and all its process information. It may not want to do that. There is a very strict statutorily-imposed protective order, so that’s some protection. But many biosimilars balk at entering the dance for this very reason: they don’t want to turn over everything.

- It could take up to eight months. You saw on the chart how many steps there are. Maybe the biosimilar doesn’t want to wait and go through the dance; it doesn’t want to bother. But then that leaves it up to the sponsor to determine when the complaint will be filed.

- If the biosimilar enters the dance and it skips portions of the dance, it could run into trouble because then the sponsor does not have to file suit in a certain amount of time and the biosimilar will lose certain rights.

- Lastly — and this is mentioned in the Supreme Court decision in *Amgen v. Sandoz*³ — if the biosimilar does not choose to dance, that fact could be considered if the sponsor moves for a preliminary injunction down the line.

Pros/cons: to dance or not?

What happens if the biosimilar says, like the song, “I won’t dance, don’t ask me. Go away, sponsor. Go away, brand”? Then, in view of the first two entries, the sponsor/brand can assert all its patents — the formulation, the process, method of treatment.

The *Amgen v. Hospira*⁴ case is very interesting. You might ask, “Well, how can the sponsor/brand assert process patents? It has no idea what the biosimilar is doing.” Seemingly, that’s the position that Amgen took in *Amgen v. Hospira*: “How can we assert our process patents?”

In the United States we have Rule 11,⁵ which says that you have to have a good-faith belief that what you are accusing of infringement is in fact infringing. The district court and the Federal Circuit said, “Don’t worry about it.”

So when the biosimilar says, “I won’t dance, don’t ask me,” it is going to face all the patents that the sponsor wants to assert. Maybe that’s a reason for a biosimilar to choose to dance; if you cooperate with the sponsor back and forth, you possibly could limit the number of patents. The sponsor is going to avoid listing patents, so you don’t run into the (3)(A) problem.

Each case, of course, is *sui generis*. I have tried to highlight in this brief amount of time pluses and minuses for dancing, and also accentuate what will happen if the biosimilar says “I won’t dance, don’t ask me,” and there’s nothing the sponsor can do.

Many of you here are familiar with the Hatch-Waxman Act⁶. This slide is a comparison of the key provisions of the Hatch-Waxman Act versus similar or corresponding positions in the BPCIA, the Biosimilar Act.

Thank you for your time.

MR. LEE: Thanks very much, Brian. Personally I’m very happy that no one can force me to dance.

² abbreviated Biologics License Application

³ *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347 (Fed. Cir. 2015), *rev’d in part, vacated in part*, 137 S. Ct. 1664, 198 L. Ed. 2d 114 (2017).

⁴ *Amgen Inc. v. Hospira, Inc.*, 336 F. Supp. 3d 333 (D. Del. 2018).

⁵ Fed. R. Civ. P. 11.

⁶ The Drug Price Competition and Patent Term Restoration Act, 21 U.S.C. § 301.

It seems to me, that compared with the generic and the small molecule context, life for a biosimilar is more difficult. There is the twelve-year exclusivity; there are additional hurdles to getting approval; and now they have to know how to dance and whether they want to. Can you comment on that and how that might play out in the market compared to the small molecule environment?

MR. COGGIO: For the small molecules, we all know that under the Hatch-Waxman Act the key patents are going to be listed in the Orange Book — formulation patents, product patents, method-of-use patents — not process patents of course, but history shows us that process patents have not played a major role in Hatch-Waxman litigation.

We did a little survey and looked at all the biosimilar cases that had been filed, and found that, to the contrary, literally half the patents asserted are process patents. So it's a different world litigation-wise for biosimilars. That makes the biosimilar action, if you will, much more complicated.

And, indeed, history shows us in the Hatch-Waxman world usually there are two or three patents being asserted — maybe more, but not many. In the biosimilar world, looking at some of the complaints, according to a recent survey that my firm did, some complaints — this is after the dance is over and the patentee or the brand files an action — sometimes there are thirty different patents asserted.

I am, of course, ignoring *Humira v. AbbVie*⁷ and the “patent thicket.” I am talking about the situation where it is more normal to assert twenty-eight to thirty patents. But that's what the biosimilar is facing, and that could be one reason that — I don't want to say most; I don't have that much experience — many biosimilars want to enter the dance, with the hope that, even though it is a pain going back and forth, when the smoke clears, it is going to face two, three, or four patents as opposed to twenty-five patents, including half, twelve or thirteen, are process patents.

I don't know if that makes sense, but that's the difference between the biosimilar world and the Hatch-Waxman world.

MR. LEE: Thanks, Brian.

Ron, given the significance of process patents in the biologics world, it makes the discovery process much more important for the patentee because, obviously, they cannot see what the process used by the biosimilar is.

I understand there have been some issues in the United States in relation to discovery under the legislation. Can you comment on that?

MR. VOGEL: Sure, a few topical comments.

As Brian mentioned, manufacturing/process patents are often the lion's share or a significant portion of litigation.

All this dance, we have to remember, is before the official litigation begins. Given the uncertainty of the manufacturing process, sponsors or pioneers were originally hesitant about asserting things. As Brian mentioned, in *Amgen v. Hospira* basically the Federal Circuit said that you don't have to worry about the Rule 11 consequences; it is in your interest to assert as many patents as possible.

The language is a little unclear what the biosimilars have to present. They have to present their aBLA and “other related information.” Disputes have arisen there in terms of what is significant in that.

Again, courts have held that you can assert only a portion of a process. You can imagine a manufacturing process being many steps, and if you are asserting only patents

⁷ *AbbVie Inc. v. Boehringer Ingelheim Int'l GmbH*, No. 17-CV-01065-MSG-RL, 2019 WL 1428361 (D. Del. Mar. 29, 2019).

against a portion of it infringe — e.g., the purification process or something — you may be limited later in your discovery request.

Again, the guidance here is it's akin to "list it or lose it." Try to get as much out there because if you are limiting your patents in your assertions you may be later limited in discovery.

We are seeing discovery going both ways. It is not just the brand or pioneer asking for stuff. We are seeing that biosimilars have asked for and been granted discovery on settlement agreements or their manufacturing records that support the invalidity. There are various defenses.

So it is a two-way street.

MR. LEE: Thank you.

MR. COGGIO: Just one thing before we leave the topic. For any of you who are really interested, Ron and I just finished a chapter in a comprehensive book on biosimilars. We were asked to write the chapter on the patent aspects. We brought a few copies with us today of the chapter. If you are interested, just grab us and we'll see what we can do about giving you one.

MR. LEE: Ron will be signing those after the session. [Laughter]

Nicola?

MS. DAGG: Thank you.

For many in the room the conventional wisdom is that a patent right is almost an entitlement to be backed up by injunctive relief. But the first question I pose this morning is: Should we question that conventional wisdom for biologic medicines?

Of course, we already know about possible exceptions to injunctions:

- Life-saving medicines: For many it's a no-brainer and that there should not be an injunction. But the debate still brews. Cordula might have a different attitude for Germany — we'll see.

- Medicines for serious illnesses, especially when those medicines have therapeutic properties which are not available in other medicines — maybe an injunction shouldn't be imposed then.

- Likewise when the medicine has fewer side effects than other medicines that are available.

There are many people in the room with different legal cultures and heritages. This is a very abbreviated summary of common law and civil law differences with regard to preliminary injunctions and final injunctions.

Preliminary injunctions are relatively rare, of course, in biological medicine cases, given how complex these cases are and what a long lead time there is to having the medicines approved.

In relation to final injunctions, just pausing on one very important common-law country, the United States, we heard yesterday from David Kappos that the use of injunctions in the United States generally — he wasn't talking specifically about biologic medicines — has dropped off. And indeed, he observed a trend towards something that might be described as drifting towards a compulsory license-type scheme.

In the United Kingdom injunctions are still discretionary remedies. I think it's fair to say that they are almost always available, but I'll show you some examples of some of the flexibility in a moment.

Of course, in both the United Kingdom and in the rest of Europe we do have the IP Enforcement Directive⁸ which imposes a proportionality requirement where things must be looked at in the round.

⁸ Directive 2004/48/ of the European Parliament and of the Council of 29 April 2004 on

On that proportionality — or, indeed, flexibility, however you like to frame it — the infrastructure that is in place does already allow for some flexibility.

Article 44 of TRIPs⁹ tells us that the judicial authorities *shall have the authority* to order a party to desist from an infringement. But as I understand that wording — again I’m happy to debate this — that does not require a court to exercise its authority in a particular way.

As I mentioned, in the IP Enforcement Directive we have got the concept of a fair balance/principle of proportionality built in. The paragraphs in the Directive are scattered with words like “taking account of the specific characteristics of the case,” “the remedy must be *proportionate*,” and that you must ensure “the *balanced use* of the civil IPR enforcement system.”

And, of course, each case is very fact-sensitive. Mr. Justice Arnold in the United Kingdom in the *HTC v. Nokia*¹⁰ case — of course, not a biologic medicines case but a mobile phone case — went through the factors very carefully.

Again simplifying things in the interest of the short time available, the judge concluded that in that particular case it was a “yes” for an injunction to be awarded to the patentee Nokia against HTC; that the patentee had a “legitimate interest” in seeking a final injunction. The judge did say that in that particular case to not impose an injunction would be tantamount to a compulsory license.

When he analyzed whether it was proportionate or disproportionate (of course in the context of a mobile phone case), the judge said that “in this case the injunction will not deliver the defendant [HTC] over to the claimant [Nokia] bound hand and foot to be made subject to any extortionate demand.” But that was all in the factual matrix of the judge appreciating that there were some noninfringing alternatives available, or at least that they could become available, before the patent expired.

And of course, as Cordula just pointed out, on biologic medicines the thought of being able to do a design-around, coming up with a noninfringing alternative, is probably not very practical.

There is an exception in the United Kingdom, what we call the *Shelfer*¹¹ exception, so that an injunction might not be ordered where the damage is small and can easily be estimated. But again, it is hard to see how in a biologics case one could fall within that exception.

Just jumping to the box labeled “individual hardship,” it is a very tough judgment call whether these important medicines are life-saving or life-prolonging. I recently visited a colleague at Addenbrookes in Cambridge being treated for a form of cancer. When you tour an oncology ward in a hospital, no matter how firmly you feel about the value of patents and the strength of the patent system, it reinforces to all of us on a human level that imposing an injunction so that a medicine couldn’t be made available in circumstances where it would prolong the life of an individual might be a very, very harsh outcome.

More in a moment on my last line about financial remedies in lieu of injunctions.

I wanted to pause a little bit on flexibility or proportionality, however you would like to call it, in the second box from the bottom on the right-hand slide. In the *Edwards Life Sciences*¹² case, not a biologics case but a medical device case, it was agreed between

the enforcement of intellectual property rights, 2004 O.J. (L195) 16.

⁹ Agreement on Trade-Related Aspects of Intellectual Property Rights, art. 44, 33 I.L.M. 81 (1994).

¹⁰ *HTC Corp. v. Nokia Corp.* [2013] EWCA (Civ) 1759, [2014] RPC 31 (Eng.).

¹¹ *Shelfer v. City of London Elec. Lighting Co.*, [1895] Ch 287 (Eng.).

¹² *Edwards Lifesciences LLC v. Boston Sci. Scimed Inc.* [2018] EWHC 1256 (Eng.).

the parties when it came to the final order stage in the United Kingdom that the court should exercise its discretion in accordance with the IP Enforcement Directive. The injunction was stayed for twelve months and there was a carve-out to allow clinicians to use the infringing device when it would be the only suitable device.

I will ask for your indulgence for just one more minute to show flexibility on injunctions, at least in the United Kingdom — obviously, everybody on the panel must bring their own heritage.

This is the final order in *Regeneron v. Kymab*,¹³ a case in the United Kingdom based on biologic platform patents, Regeneron's patents for its Velocimmune transgenic mouse platform for generating therapeutic antibodies.

At the final order stage in the Court of Appeal after Regeneron had succeeded, you can see in the top right-hand corner the English injunction saying that Kymab should not infringe. That is the usual general U.K. form of injunction.

But you can see it has a couple of carve-outs. The first is in paragraph (a) that any acts done for the purpose of a medicinal product assessment are carved out. In other words, when those therapeutic antibodies are in clinical trials, even though they might be infringing antibodies, they are carved out from the injunction in this case.

Likewise, paragraph (b) tells you that things done in paragraph 10(b) below are also carved out. These activities that are limited to rendering the infringing transgenic mice noninfringing have been carved out of the injunction.

These are just snippets from the order; it's not complete. The injunction for the moment is stayed pending the outcome in the English Supreme Court.

Not a topic for today, but the final paragraph shows the flexibility. The English court said, "The patentee might want to come back to the Patents Court and ask for a springboard injunction for damage suffered after the patent expires."

I didn't get to damages in lieu of injunctions, and I apologize, but maybe we can deal with that in questions.

MR. LEE: Thanks very much, Nicola.

I would like to ask Roberto, who has been active in the biologic space in his home market of Brazil, to let us know what is happening there in terms of litigation and, in particular, whether there is any discussion of the injunction issues that Nicola covered.

MR. RODRIGUES: Sure. Thank you.

I don't know if I have good news or bad news after Nicola's speech, but out of so far eight cases against biosimilars in Brazil there were five injunctions, all of them preliminary injunctions. We have a really strong patent system for protecting patent owners, and the judges in those case were not very receptive to issues of public interest, like access to health.

Most of these cases were against pending marketing approvals. The judge said that, in view of the timeline, there was a chance that the biosimilar product would launch a product infringing the patent, so they are banned from importing and exporting and doing all the acts of infringement in Brazil.

MR. LEE: Thank you.

Are there any questions from the floor on the issue of injunctions or anything else that arises from Nicola's talk?

QUESTION [James Love, Knowledge Ecology]: This is on the issue of damages that relates to the patent dance. I have a technical question.

¹³ *Regeneron Pharm., Inc. v Kymab Ltd. and Novo Nordisk A/S* [2018] EWCA 1186 (Eng.).

The patent dance is premised on the idea that if you don't disclose your patents constructively, there is an inability to seek anything other than a reasonable royalty or no compensation at a later date. That is the statute in the patent dance legislation.

The trade agreement between Canada, Mexico, and the United States has a requirement that the United States would have to give the judge the ability to use any legitimate value for damages, including the suggested retail price of the product. That seems to us to be inconsistent with the language in the Affordable Care Act that caps compensation in the patent dance to a reasonable royalty.

I would ask Mr. Coggio or any other panelist if they have any thoughts on that issue.

MR. COGGIO: I think what you said about the patent dance was a little off. Whether or not the patentee, the brand/sponsor, is limited to a reasonable royalty and it waives or forfeits lost profits, it is really that during the dance the patentee does not live up to what he or she is supposed to do. So it is almost like a penalty for not following through on the dance once it starts.

Even if there is a dance, or even if there is no dance at all, and the patentee/sponsor asserts all its patents, it still has the right to lost profits, all things being equal. It is only if it doesn't comply with the dance or it doesn't file suit when the dance is over within thirty days, and there are some other factors that it loses its right to lost profits.

Maybe the way you stated it and the way I understood it are like ships passing in the night.

QUESTIONER [Mr. Love]: I agree that it is not a general restriction; it is a restriction that's triggered by things that happened in the course of the patent dance. But there is this restriction, and it is in fact one of the things that motivates behavior within the patent dance, the fact that you would face this cap on damages if you did not do certain things.

My question is really, is that consistent — and maybe you're not the right person to ask — with a trade agreement that doesn't allow such statutory restrictions on damages?

MR. COGGIO: I am not the right person to ask, you've got that right.

MR. LEE: I think Nicola has a quick final comment.

MS. DAGG: Actually a comment on the overall question of damages in lieu of an injunction — or, put another way, what is the right monetary substitute if an injunction is not imposed in a biologics case?

It strikes me that it is a really important part of the overall recipe to think about: *Okay, what's the quid pro quo for there not being an injunction? How can you properly value the economic right that the patentee is therefore deprived of?*

There is a risk that if you go with just a basic running royalty, that is again tantamount to the compulsory license. But how do you get to the real value, the profit that the infringer makes on the biologic medicine, or indeed the profits that are made downstream through the use of one of the biologic platforms or the new modes of delivery on vector viruses or whatever?

MR. LEE: Thank you.

MR. COGGIO: One point on injunctions. We are still working our way through that. Up until *eBay v. MercExchange*¹⁴ in the Supreme Court, which wasn't that long ago, in the United States if you won a patent case, you proved infringement and validity, an injunction was automatic except under very, very extenuating circumstances.

¹⁴ *eBay Inc. v. MercExchange, LLC*, 547 U.S. 388 (2006).

You have to go back to the early 1900s to the famous *Milwaukee Sludge*¹⁵ case that involved a patent that covered the sewer system of Milwaukee. The Seventh Circuit Court of Appeal said: “We are not going to allow you, patentee, to shut down the sewer system of the City of Milwaukee. Even though you won the case, the injunction is denied.”

That was pretty good law until *eBay*: unless you had some very, very unusual circumstance, an injunction was just routine. Now, with *eBay* on the books, we are working our way to nowadays having to show that not only do you have to prove infringement and not invalid patent, but you may also at trial have to prove that you are entitled to an injunction in view of the *eBay* factors.

MR. LEE: Thanks very much, Brian.

Our last speaker is Shimako.

MS. KATO: Good morning, everyone. It’s an honor to be here and to participate in this session. Today I will talk about the reasonable protection of antibody patents.

The antibody drug market is growing. As you see, out of the top ten drugs in 2018, six are antibody drugs. As a reflection of this situation, the number of disputes over antibody patents is increasing in Japan.

There are some characteristics of the disputes over antibody patents.

The first is the parties. In a patent infringement lawsuit both parties can be originators.

The second feature is the cost for the development of the alleged products. In general, the cost is very high, even for biosimilars.

Taking these features into account, I would say balanced protection is more needed for the antibody drugs.

Going to the issues of antibody patents, one of the biggest issues is claim drafting. If you claim an invention broadly and functionally, you can cover class of antibodies, but there is a risk of lack of written description requirements.

On the other hand, if you write a claim with the sequences in a limited way so that it is strong as to the written description, you may not cover antibodies that have slightly different sequences. That is a risk of the limited claim.

Another problem with an antibody patent is claim construction in cases where the claim is broadly described.

Let’s look at the recent Japanese decision in *Amgen v. Sanofi*.¹⁶ There are two decisions with regard to the same patent. One decision was rendered by the Tokyo District Court, which is an infringement court [2017 (Wa) 16468 (Jan. 27, 2019)]. The other decision was rendered by the IP High Court, which was an appeal of the invalidation trial by the JPO [2017 (Gyo-ke) 10225 and 10226 (Dec. 27, 2018)].

In this case the patent is directed to PCSK9 inhibitors to treat high cholesterol. As PCSK9 inhibitors, Amgen is selling Repatha™ (evolocumab) and Sanofi is selling Praluent™ (alirocumab). Alirocumab was not described in the specification of the patent at issue. You can see the patents at issue on this slide.

Invention 1 is directed to an isolated monoclonal antibody which is capable of neutralizing binding of PCSK9 to LDLR, wherein the antibody competes with 21B12 antibody, a specific antibody. But, as you see, in the Invention 1, such widely defined terms, “neutralizing” and “competes,” are used so as to cover a broader number of antibodies.

¹⁵ City of Milwaukee v. Activated Sludge, 69 F.2d 577 (7th Cir. 1934).

¹⁶ Amgen Inc. v. Sanofi, 872 F.3d 1367 (Fed. Cir. 2017), cert. denied, 139 S. Ct. 787, 202 L. Ed. 2d 568 (2019).

In this case Sanofi argued that the claim should be limitedly construed to antibodies obtained by substituting one or a few amino acids of the antibodies described in the specification.

But the Tokyo District Court said that the claim is not limitedly construed as Sanofi argues. The main reason is: Taking the description of the specification regarding how to screen and how to produce the competing antibodies with 21B12 and 31H4 into account, a person of ordinary skill in the art (POSA) would have understood that the antibodies which satisfy enablement are not limited to the antibodies obtained by substituting one or a few amino acids of the antibodies described in the specification.

Therefore, Sanofi's antibody falls under the scope of the claim. That is the decision by the Tokyo District Court.

As to the validity, Sanofi challenged lack of inventive step by submitting D1, which shows the results of a study [J. Clin. Invest., vol 116(11), pp. 2995-3005(2006)] that PCSK9 reduces the LDLR protein level in liver by binding with LDLR.

The D1 also describes anti-human polyclonal antibodies against PCSK9 obtained by injecting PCSK9 to a rabbit.

As to the validity, the IP High Court found that the invention is inventive because it is common technical knowledge that a difference in the process (e.g. process of obtaining immunized mouse) of producing antibodies leads to a difference in reaction against antigen of the antibodies. Therefore, optimizing the process for obtaining 21B12 antibody or 31H4 antibody needs an excessive burden of trial and error even for a POSA with the knowledge of D1. This is the reasoning for the core part of the antibodies.

In this case, the claim also covers "competing antibodies," but the court said that the same reasoning can be applied to such a wider scope of claims that the court finds that the patent is inventive. That is the decision by the IP High Court.

Let me briefly discuss the impact of the decision.

The infringement court broadly construed the functionally defined antibody claim and found infringement. This decision invites a rather big reaction by pharma industry. They are mostly negative, but some are positive.

What happens next? In this case Sanofi appealed against all decisions. It seems that the main issue would be whether the IP High Court will change the decision on infringement.

This is the final comment from me, my personal view on the decisions.

The IP High Court found that also the antibodies competing, 21B12 antibody or 31H4 antibody, would not have been conceived by a POSA because the processes to obtain those antibodies are different from the process of common technical knowledge.

If the screening and process to obtain claimed antibodies is the key factor to distinguish antibodies in the present patents, it still may be open to challenge the noninfringement of Sanofi's products because probably the screening process and the process to obtain Sanofi's antibodies is different from Amgen's.

Thank you much for your attention.

MR. LEE: Thank you very much, Shimako.

I think Shimako's presentation starkly highlights the complexity not only of the technology but of some of the patent issues we are dealing with.

Nicola has a question.

MS. DAGG: Shimako, is the Tokyo Court going to grant an injunction to stop Sanofi's PCSK9 high-cholesterol treatment being sold?

MS. KATO: In this case, the Tokyo district court granted the injunction, but Sanofi has appealed against the decision. Therefore, the injunction is not yet enforceable as of now.

MR. LEE: Thank you.

In the few minutes we've have left are there any further questions for Shimako or anyone else on the panel?

QUESTION [Bryan Zielinski, Pfizer Inc., New York]: I do have a question about the Japanese case. In the *Sanofi* case that is before the Japanese Supreme Court is validity at issue as well? I think it is, isn't it?

MS. KATO: Yes. It is an appeal of the IP High Court's case and the issue is validity. But in Japan the Supreme Court examines only matters of law, so probably it is not likely that the Supreme Court will change the decision of the IP High Court.

QUESTION [Jürgen Dressel, formerly with Novartis, Basel]: My question is for Brian and Ron. When I look at the BPCIA, it looks, at least coming from the outside, extremely complex, very difficult to predict. When I compare the generic uptake in Europe with that in the United States, it looks as if biosimilars are more successful in Europe. Do you think those are teething problems of the BPCIA and will be fixed over time, or do you think a fundamental change is necessary to the BPCIA?

MR. COGGIO: I think in the United States there are two problems. One is, I guess, because the biosimilars are not automatically substitutable, it requires marketing, and the price differentiation isn't as much as with the typical generic. I think that is slowing down somewhat the introduction and the market penetration of biosimilars.

However, you can layer onto that, if you will, the fact that the BPCIA is very complicated and it allows patentees to assert many, many patents. I've seen cases — I won't mention the company — where they are asserting in three separate cases twenty-five patents. I am not talking about AbbVie, which we know about.

I'm sure that the BPCIA and its complexity has played a role in slowing down the introduction of biosimilars in the United States versus Europe, where I think *Sandoz*¹⁷ years ago was the first one — you should know better than I — and in the United States, even to get a decision in the *Sandoz* case, they had to petition the court numerous times — and that was the first one — even to decide it.

So I think what you say is right. I don't know if a statutory fix will help the situation, and I don't know what the fix would be, but it couldn't hurt. I hope that answers your question in a longwinded way.

MS. SCHUMACHER: I have another comment on what Nicola presented.

I think we need to be very, very careful not to limit too much the availability of injunctions, regardless of the economic outline we discussed here, and maybe even particularly if we are talking about a life-saving drug. Maybe if patents of life-saving drug have less effect there won't be any more investment in producing and developing these life-saving drugs. And, especially in the situation of biologics and biosimilars, if we stop the biosimilar from coming on the market, there is always the biologic available to treat the life-threatening disease.

We always need to carefully evaluate the general economic context and set the right economic incentives on a global basis and not just look at the specifics of that case and the individual medicine there.

MS. DAGG: I would agree with Cordula on biosimilars in the sense that the alternative medicine, the branded medicine, is always going to be available.

But when it comes to a scenario where it is the only medicine that is suitable for the patient that is at risk of being enjoined, as I said before, just from a human perspective that is a very harsh outcome. That's why it seems to me that finding the right monetary substitute for the patentees so that the flexibility does exist to reward them monetarily

¹⁷ *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 198 L. Ed. 2d 114 (2017).

instead of an injunction — of course, that is rewarding them for the future when the injunction would otherwise have been binding — seems to be the best way to advertise the patent system and to make it work for human beings.

MR. LEE: Thank you very much for that final comment. Obviously, there is fertile ground for debate here and I am sure our panelists will be happy to answer further questions after the session.

Let's give the panel a final thank-you.