

Session 2C

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**SESSION 2: PATENT LAW  
2C. Second Medical Use/Plausibility**

***Moderator:***

**John Richards**

*Ladas & Parry, New York*

***Speakers:***

**Robert Burrows**

*Bristows LLP, London*

***Plausibility in the United Kingdom***

**Klaus Grabinski**

*Federal Court of Justice, Karlsruhe*

***Infringement of Second Medical Use Patents in German Case Law***

**Lennie Hoffmann**

*Queen Mary University of London, London*

***Staking Out the Genome***

**Takeshi Maeda**

*Kobe University, Graduate School of Law, Kobe*

***Infringement of Medical Use Claims in Japan***

**John Pegram**

*Fish & Richardson, P.C., New York*

***Plausibility—An American View***

***Panelists:***

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**Kevin J. McGough**  
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MR. RICHARDS: Thank you, everybody, for staying this late.

We have put two topics together in this presentation, mainly because there was a Supreme Court decision in the United Kingdom last year, *Warner-Lambert v. Generics UK*,<sup>1</sup> which dealt with both of the issues that we are talking about. Both topics are related to what you need in order to get a patent, particularly in the life sciences field and probably particularly in the second medical use field, and then when you can enforce that patent. So they do have a nexus.

We are going to start off with Klaus Grabinski of the Federal Supreme Court in Germany, who will deal with the infringement aspect first, and then we'll go on to what is needed to get a valid claim in order to be able to enforce a patent in this area.

JUDGE GRABINSKI: John, thank you very much for your kind introduction.

Good afternoon. My topic is "Infringement of Second Medical Use Patents in German Case Law." There is an interesting development in the recent case law — not from my court, the Federal Court of Justice, but from the Higher Regional Court of Düsseldorf, and I am going to introduce you to that. But before that I would like to address the issue of patentability because this has consequences with regard to the infringement issue.

German law has always allowed patent claims directed to a specific use in general and a second medical use in particular.

There is also settled case law that second medical use patents do not fall under the exclusion from patentability of methods to treat the human body by therapy, pursuant to Section 2a(1) 2 of the German Patent Act<sup>2</sup> and Section 53 of the European Patent Convention.<sup>3</sup> Since 2007 the patentability of a second medical use patent is explicitly provided for in Section 3(4) of the German Patent Act and Section 54(5) of the EPC.

The reason for this is that second medical use patents are regarded as being susceptible of industrial application, and this industrial aspect is protected by the use patent.<sup>4</sup>

According to more recent case law, the subject matter of a second medical use patent is seen in the suitability of the known substance for the new medical use and, to that extent, as an inherent property of the substance.

This approach is different from the U.K. Supreme Court, which, as far as I understand the *Warner-Lambert v. Actavis*<sup>5</sup> decision, is regarded to be a method claim. The German approach is that, in principle, it is regarded to be a purpose-bound product claim and this relates to use claims, Swiss-type claims, EPC 2000 purpose-bound protection claims.

What does this mean for the infringement issue? It has always been recognized in Germany that manifest arrangement of the substance for the second medical use without

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<sup>1</sup> [2018] U.K.S.C. 56.

<sup>2</sup> Patentgesetz [PatG] [Patent Act], Dec. 16, 1980, Bundesgesetzblatt [BGBl] (Ger.).

<sup>3</sup> Convention on the Grant of European Patents, art. 53, Oct. 5, 1973, 13 I.L.M. 268.

<sup>4</sup> *Id.*

<sup>5</sup> [2018] U.K.S.C. 56.

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the consent of the rightsholder is an infringement of the patent. The reason for this is that the industrial part of the claimed use is covered by the exclusive right of the proprietor and therefore could be said to be an infringement.<sup>6</sup> This is quite similar to the approach mentioned in the *Warner-Lambert v. Actavis* case as the “outward presentation” test.

Examples of this kind of manifest arrangement for the second medical use are: formulation, confectioning, dosage, and repackaging of the medicament or the labeling or accompanying patient information leaflets. That is settled law confirmed by case law of the Federal Court of Justice.

Recent case law of the Düsseldorf Court of Appeal — there are now three decisions — extends the protection of a second medical use patent to forms of use beyond “manifest arrangements,” when the use can be related to the protected purpose of the substance. The requirements are:

- The generic medicament has to be *suitable* for the protected second medical use.
- The use of the generic medicament for the protected purpose (e.g., cross-label use) has to be of *some significance* in the markets. It should not be only 1 percent of the market; it has to be of some significance. However, the Düsseldorf court does not say what the borderline is.
- The implementer knows about it or, at least, blinds himself to the fact, and, by this way, takes advantage of circumstances that allow that the generic medicament is used for the protected purpose.

That is the test. What does it mean in practice?

I would like to introduce you to the fulvestrant case.<sup>7</sup> The patent protects the use of fulvestrant in the preparation of a medicament for the treatment of a patient with breast cancer. There is a further requirement: where the previous treatment of that patient with an aromatase inhibitor and tamoxifen has failed. So the treatment with two other substances must have failed before this patent is applicable.

In this case there was no manifest arrangement for that specific treatment and for that specific group of patients. However, it was alleged that the number of patients who used fulvestrant after a previously unsuccessful treatment with the two drugs over a period 2007–2014 was on average 4.1 percent of all patients and 0 percent in the last two years 2015–2017.

Applying this new case law to the facts of this case, the Düsseldorf Court of Appeal decided it is not good enough for infringement for two reasons, (1) the numbers are not significant and (2) because in the last two years there was no use with regard to this particular group of patients, that there was no risk of future patent infringement. Therefore, the court did not issue an injunction.

However, I think it will be interesting to see whether this approach of the Düsseldorf Court of Appeal will be confirmed by the Supreme Court — which at the moment is still an open question — but just assuming it will more or less be confirmed, what kind of injunctive relief can result from it?

I think one point is clear: Unrestricted injunctive relief is *not* available when such an order would not only cover the second medical use, assuming that is an infringement, but also the use of the substance for purposes not protected by the second medical use patent, in particular the first medical indication use, is of some significance.

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<sup>6</sup> *Id.*

<sup>7</sup> Oberlandesgericht Düsseldorf [OLGZ] [Düsseldorf Court of Appeal] Jan. 09, 2019, AstraZeneca AB vs. Hexal AG, I-2 U 29/18 (Ger.).

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So the question is: If unrestrictive injunctive relief is not available, how can an injunction then be tailored that is only hitting at the second medical use and not hitting at the first medical use that is no longer protected?

There are some approaches discussed — I underline they are only discussed at the moment.

One is that in some cases plaintiffs have requested that the defendants should only be allowed to market the medicament when it is mentioned in the patient information (e.g., in the accompanying leaflet) that the medicament may not be used for the second medical purpose.

However, there is a problem with EU law in that regard because it is a controversial legal issue whether from the point of view of medical regulatory law it is possible to print on the leaflet “it is not allowed to use this medicament for the second purpose.” There are two provisions in the respective EU Directive and in the EU Regulation depending on whether the national or the centralized authorization procedure is concerned.<sup>8</sup> It is at the moment definitely not clear whether these provisions allow in the case of cross-label use that on the leaflet it is said it is not allowed to use this substance for the second medical use. Possibly, if the right case comes up, this might be a question for a reference to the CJEU.<sup>9</sup>

Other injunctive relief that has been requested in the past by plaintiffs was that defendants should only be allowed to market the generic medicament after they have written to professional associations of doctors or pharmacists and other “multipliers” and asked them to inform their members that generic medicaments may not be prescribed for the patented second medical use and prescriptions of the original medicament require that the substitution of a generic medicament (the so-called *aut-idem* substitution) is not allowed. However, the problem with this is that, at the moment at least, I do not see a legal basis for requiring these associations to do so. Therefore, such an order would depend on the willingness of the professional associations, and it might be that they are not willing to do so.

Another injunctive relief that has been sought is plaintiffs have requested that defendants should only be allowed to market the generic medicament after they have written to databanks, which are very important for distributing and marketing medicaments, and the generic company requires them to inform users of the database via respective information in the databank that the generic medicaments may not be prescribed for the patented second medical use.

However, again, there is a problem here. It is unclear at the moment whether these databanks are obliged to follow such a request from the generic company or whether, again, such an order requires the willingness of the databanks.

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<sup>8</sup> See Art. 11 sentence 2 Dir. 2001/83/EC as amended by Dir. 2004/27/EC (national authorisation procedure): For authorisations under Article 10, those parts of the summary of product characteristics of the reference medicinal product referring to indications or dosage forms which were still covered by patent law at the time when a generic medicine was marketed need not be included. See Art. 3 (3b) Reg. 726/2004 (centralised authorisation procedure before the European Medicines Agency [EMA]): The summary of the product characteristics is in all relevant respects consistent with that of the medicinal product authorised by the Community except for those parts of the summary of product characteristics referring to indications or dosage forms which were still covered by patent law at the time when the generic medicine was marketed.

<sup>9</sup> Court of Justice of the European Union.

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So you see second medical use patent infringement is a work in progress. The courts are currently struggling with this. We do not have Supreme Court case law on this issue. It might require to some extent a reference to the CJEU. So keep tuned and see what is going to happen in Germany, and the same is also true probably for the United Kingdom.

Thank you.

MR. RICHARDS: Thank you, Klaus.

Mention has been made of the position in the United Kingdom. For those who are not up to speed, I should perhaps mention what happened in the *Warner-Lambert* case in the U.K. Supreme Court where their Lordships split three ways effectively after having found that the patent was invalid for the plausibility issues we are going to deal with next. So they didn't actually have to make a decision on infringement.

Lord Sumpton and Lord Reed basically took the view that the issue was a purely objective one: you look at the labeling and the objective indications of what came out of the infringer.

Lord Hodge and Lord Briggs took the view that you look at the intention of the person who is putting it on the market, see if they were putting it on the market in a way that would lead one to expect that its use was going to be infringing.

Lord Mance basically said he agreed with Lord Sumpton that it was an objective criterion, but he said under circumstances when it seems you could also look at the infringer's rise in profits, you could look at additional factors beyond that.

So we've basically got a three-way split, which is not too helpful. I don't know whether, Lord Hoffmann, you want to make any comment on that in addition to your presentation on plausibility.

Our next speaker is Lord Hoffmann, who in 1996 in *Biogen v. Medeva*<sup>10</sup> basically took up to the highest level, probably for the first time to my knowledge at least, the question of making sure the patent scope was commensurate with the invention made.

LORD HOFFMANN: Thank you.

I am going to talk about problems which have been created by two types of inventions: first, in the patents for bits of DNA; and, second, second medical use. What they have in common is that in both cases there are attempts to patent products — in one case new, in the other case old — on the basis that they *may* have some beneficial use. The reason why you can only say they may have some beneficial use is because both require clinical trials in order to show that they actually do have some medical use, and that as a practical matter cannot be undertaken until the patent has been granted.

The question that raises at the moment is: in a DNA patent, is the newly discovered molecule susceptible of industrial application? That's the way in which the problem arises there. In the case of second medical use, the question is whether the specification claiming such use is sufficient.

But they really come to the same question: how far upstream in the research that is being undertaken can you apply for a patent; how far do you have to have gone?

May I say both of the cases I am going to speak about in the Supreme Court have happened after I left.

The question first arose in the case of *Human Genome Sciences (HGS) v. Eli Lilly*<sup>11</sup> in 2011. There the discovery was a molecule called neutrokin-alpha. What was known about it is set out on the slide:

- It was a new member of the TNF ligand superfamily;

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<sup>10</sup> [1996] U.K.H.L. 18.

<sup>11</sup> [2011] U.K.S.C. 51.

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- There were features which all members of that family shared;
- There were other features which were not necessarily shared.
- It might play a role in the immune response and it might play a role in the control of tumors in malignant disease.

So there were hopes for it as something which would be medically useful.

The EPO<sup>12</sup> jurisprudence on that matter, which was analyzed at great length by the Court, was that “plausible” or “reasonably credible” or an “educated guess” — all sorts of forms of words are used — as to its future use was enough for the purposes of showing that it was susceptible of industrial application.

There was evidence before the Supreme Court from the Bioindustry Association, which obviously had great effect upon them. They said, “After discovery of a naturally occurring molecule ... a large amount of research and development is required before there can be any therapeutic benefit” but “funding for research and development is dependent on the funders being reasonably confident that a patent will be granted.” But they went on to say, “The purpose of the patent system is not to reserve an unexplored field of research for the applicant.”

Well, of course, that was a complete lie because that was exactly what they wanted: to reserve an unexplored field of research (namely, what you could use neutrokine-alpha for) for them. The question really should have been: was this justifiably the circumstances?

The question therefore is: what is the purpose of the patent system? You have to answer that question in order to be able to say whether it is justifiable or not to give it in the circumstances in which you could only show that there might be some use for it.

If the purpose of the patent system is simply to reward somebody who has produced a successful innovation, why not wait until the inventor has delivered the goods? Why offer a patent in advance, so to speak?

[Slide] I was interested to see an article that was written back in 1977 by Professor Edmund Kitch, who said that “the grant of a patent could also have the purpose encouraging further research on the patented subject-matter.” That, of course, is exactly what they wanted the patent for in the *HGS* case. Kitch said there was an analogy with a mineral claim: an area is staked out in which other people then couldn’t come and you were free to be able to carry on your research.

Incidentally, I thought *1977 is a long time ago*, and I looked up Professor Kitch to see if he was still with us. I was rather surprised to see that not only is he still with us, he’s actually five years younger than I am. [Laughter]

If one asked, “What would be the reasons for giving a patent; what would be the advantages?” he would say, “It avoids wasteful duplication of further research by other people. They know that area is closed off, so they stop”; and if it was to enable funding, that would be okay.

Well, this may perhaps be a competition issue; namely, that the people who need funding are the individuals who are doing lab research on genetics and, on the other hand, large companies that have lots of money do not need the patent in advance in the same way. That’s a possibility.

There are criticisms of Professor Kitch’s thesis because the analogy with a mining claim is not entirely accurate. Your upstream patent does not exclude further research by competitors, it may result in another patent being granted to a competitor, and therefore

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<sup>12</sup> European Patent Office.

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you've got a block between them and they've each got to get the license of the other if they want to be able to market the improved product.

Another reason perhaps is if a patent is granted early, it will expire early and in that way the public will get the benefits from it earlier than they might otherwise have done. But, on the other hand, it provides an incentive to the person who has the upstream patent to leave patenting improvements as late as possible because they need to extend it for as long as possible.

What is rather strange is that there was really no mention of any of these sorts of arguments in the *HGS* case. The whole discussion in the Supreme Court was really a sort of scholarly discussion of the effect of the jurisprudence of the EPO. There was no attempt to go into the pros and cons of having early patents in the way that some of the writers like Professor Kitch have done.

In the *Warner-Lambert* case, which John Richards mentioned earlier, the question there was how far again you have to go in order to satisfy the requirement of sufficiency. Again the EPO jurisprudence was gone into, and again the question was raised of what counts as being plausible so that it will have that secondary medical use.

What's fascinating is there was no mention, no reference, in that case to the earlier *Human Genome Sciences* case, which seems to me to be very much on point. There was no discussion, of course, of the policy issues that I've just been talking about.

So we've got these two elaborate discussions on what is meant by in one case "plausibility" and in the other case "sufficient for industrial application." They were treated as completely unrelated to each other and the arguments seem to be based simply upon analysis of what the EPO meant in a very obscure area.

MR. RICHARDS: Thank you.

I think we'll take questions and comments after everybody has spoken, unless anybody has any specific point they want to raise. Marty?

QUESTION [Prof. Martin Adelman, The George Washington University Law School, Washington, D.C.]: I do want to raise one point with Lennie. In fact, what he's describing is a defect in a first-to-file system, the requirement that you file so early. Any sensible system would say, "And boy, if you do that, you better then do the research which won't be prior art against you to prove up your speculation." And he didn't require it in the *Conor Medsystems v. Angiotech*<sup>13</sup> case, incidentally, which was equally speculative, although I'm never going to get him to admit it."

MR. RICHARDS: Okay. I think the Marty-Lennie discussion can take place later.

Next up is Robert Burrows from Bristows, who is also going to address the situation in the United Kingdom.

MR. BURROWS: I am also going to talk about the *Warner-Lambert* pregabalin case at the U.K. Supreme Court, which was already touched on a number of times today in this session, and really look at the decision and how the law might have changed.

Because the case has been going on for a number of years now and has been featured at Fordham for a number of years, I think it's worth taking a brief trip down memory lane.

Historically your panel has included Brian Cordery, who was due to speak here today, but, ironically, given the case is all about pain medicines, he is currently recuperating at home having had knee surgery, along with his son who's got a broken foot. But both are well. Obviously, Brian is very disappointed not to be here.

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<sup>13</sup> [2008] U.K.H.L. 49 (U.K.).

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Looking back at what was discussed in recent years, I understand a take-home message from the 2017 Fordham IP Conference was that, as Judge Rian Kalden said, “Wholly speculative patents should not be granted and it does not really matter which legal principle we use to prevent them from being granted/invalidated.”<sup>14</sup>

Also at the 2017 Fordham Conference we had Lord Justice Floyd in the Court of Appeal *Pregabalin* case saying that, “Plausibility is a low threshold test.”<sup>15</sup> So, provided there is some reasonably credible theory as to why the invention will work, that should be enough.

At last year’s conference, we focused heavily on the U.K. Supreme Court case itself, but what was missing was the actual decision, which didn’t come out until the very end of last year.

What was the decision? We still have plausibility. It is said to be a how hurdle, but it is one that the patentee here (and patentees often) do not seem to get over. Why might that be the case?

The decision was a split decision on plausibility and sufficiency. Two of the five Law Lords agreed with the lower courts that the treatment of peripheral neuropathic pain with pregabalin was plausible but not the treatment of central neuropathic pain. Whereas the majority ruling, with the lead judgment given by Lord Sumption, went further and said that neither the treatment of peripheral neuropathic pain nor central neuropathic pain with pregabalin was plausible. So they went further in terms of what was plausible in the sense that no type of neuropathic pain was plausible for pregabalin treatment. As a result, the claim for neuropathic pain was insufficient, as were subsidiary claims involving peripheral or central neuropathic pain.

Digging into the decision in a bit more detail as to why we got there, Lord Sumption went on about the “patent bargain” and the fact that we have this monopoly in return for disclosing your invention. He also talked about the importance of a technical contribution; the fact that the patentee not only makes but discloses a contribution to the art; and the fact that the disclosure in the patent must demonstrate in light of the common general knowledge at the priority date that the claimed therapeutic effect is plausible. So the patentee can rely upon the common general knowledge to interpret what is in the patent, but you must have something in the patent to interpret in the first place.

Where Lord Sumption and the Supreme Court started to diverge from the lower courts is in the sense of what this threshold might be. Unlike the Court of Appeal, Lord Sumption said that the plausibility test couldn’t be satisfied by “a prediction ... based on the slimmest of evidence” or one based on material which was “manifestly incomplete.” He also held that the *Salk Institute* case<sup>16</sup> (T 609/02), which is an Appeal Board case at the EPO, did lay down a general principle, which is perhaps surprising given that EPO case law can be persuasive but isn’t binding on the U.K. courts. So why one EPO Appeal Board decision should have a binding general principle for all cases in the United Kingdom is stretching what usually happens with such EPO decisions.

Lord Sumption said that the principle laid out in *Salk* is that the specification must disclose some reason for supposing that the applied assertion of efficacy in the claim is true. I think it is therefore worth reminding ourselves of one of the key passages in *Salk*

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<sup>14</sup> See *Sunrise Seminar I: Second Medical Use & UK Plausibility*, EMILY C. & JOHN E. HANSEN INTELL. PROP. INST. FORDHAM L. SCH. (2017).

<sup>15</sup> *Id.*

<sup>16</sup> Decision T-0609/02, *Salk Institute for Biological Studies v. Karo Bio*, ECLI:EP:BA:2004:T060902.20041027 (Oct. 27, 2004).



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*Institute*, which is that “the patent provides some information in the form of, for example, experimental tests, to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease.”<sup>17</sup>

This reason this requirement for some mechanistic nexus between the information and/or data in the patent regarding pregabalin and the treatment of neuropathic pain is where the patentee fell down, Lord Sumption said, was that mechanistic nexus didn’t exist between the information in the patent and the treatment of any type of neuropathic pain.

So the patentee lost on plausibility, even though it is supposed to be a relatively undemanding test, because its data was not enough to support the claimed therapeutic uses.

Picking up on a few broader conclusions from the case, I think it is important to note that Lord Sumption said that plausibility must be demonstrated across the whole scope of the claim as of the priority date; whilst you can rely upon later post-filed data to support your claim to plausibility, the sole basis for the plausibility of all or part of the claim cannot be based on post-filed data. Lord Sumption also held that the principle laid down in *Salk Institute* is not limited to those cases where the claimed therapeutic effect is inherently implausible.

I put in this slide on the minority view of Lords Hodge and Mance just so you have that, if you are interested in where they went based on assessing the same EPO case law as Lord Sumption.

In the time remaining it’s worth just looking at some of the U.K. case law since the Supreme Court decision.

The leading case so far is *Eli Lilly v. Genentech*,<sup>18</sup> which was decided by Mr. Justice Arnold, who is in the room, and so I hope I get this right. This was a slightly different case in the sense it concerned a first medical use claim rather than a second medical use claim. The claim was directed to certain IL-17A/F antibodies for the treatment of psoriasis. All the parties accepted that even though it was a first medical use claim, the guidance provided by Lord Sumption still applied but the different context should be borne in mind when applying that guidance.

The key question that Richard Arnold held needed to be asked was whether the skilled person would consider it was plausible that this type of antibody to IL-17A/F had a discernible therapeutic effect on psoriasis. It wasn’t enough for the skilled person to conclude that this IL-17A/F antibody was a potential target for psoriasis which was worthy of further research to find out whether such an antibody was likely to be efficacious.

Again, on the information/data in the patent, which included the absence of any data showing that IL-17A/F had any role in psoriasis let alone an antibody to it, this was a relatively straightforward reason not to allow sufficiency on the basis of lack of plausibility.

To wrap up, I should say that plausibility is alive and well in the United Kingdom. There is a requirement now for showing an actual technical contribution which is supported by some data or other information in the patent.

I would say that plausibility does apply to all claim types, but it is particularly relevant to medical use claims or any other type of claim where it is not immediately apparent once you have the product (or process) in hand that it is going to work. So it is going to be especially relevant for claims to broad classes of compounds and/or broad lists of therapeutic uses.

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<sup>17</sup> *Id.* at 12.

<sup>18</sup> [2019] E.W.H.C. 387 (U.K.).

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The plausibility bar has been raised slightly and we have a test which is “relatively undemanding,” but whether you satisfy it for a medical use claim will require this mechanistic nexus between your information/data in the patent and the therapy you are trying to claim.

Thank you.

MR. RICHARDS: Thank you.

Again, unless there are any specific question that anybody has, we will move on.

Our next speaker is Takeshi Maeda from Kobe University Law School in Japan on the situation in Japan on second medical use.

MR. MAEDA: Thank you.

I will talk about infringement of medical use claims in Japan.

First of all, I will briefly explain how medical use is protected in Japan. Medical use is defined in the *JPO Examination Handbook Annex B Chapter 3*:<sup>19</sup>

“Medical use” means:

- (i) an application to a specific disease; or
- (ii) an application to a specific disease in which *dosage or administration*, such as a dosing time, a dosing procedure, a dosing amount or an administration site is specified.

In Japan an invention is patented by either a product claim or a process claim. Some of you may think it is more natural to draft a process claim for an invention of medical use. But in current Japanese practice medical use is not patentable as a process claim. It is because methods of surgery, therapy, or diagnosis of humans are considered not patentable since they lack “industrial applicability.” So in Japan medical uses should be protected as product claims.

What is the difference between being protected by product claims and by process claims? The Japanese Patent Act<sup>20</sup> defines acts of carrying out inventions which are deemed to be infringed. For example, process claims are infringed if the process is used, and producing or transferring the product provided for the process may constitute indirect infringement. On the other hand, product claims are infringed if the product is produced, used, or transferred. If medical uses, such as certain methods to administer certain drugs, were protected by process claims, people who used the methods would be a direct infringer.

Producing the drug might be indirect infringement, but it is not direct infringement. If protected by product claims, producing or transferring the drug might be direct infringement.

As to ordinary product claims, producing or transferring the product for any purpose constitutes infringement. In the case of an invention of a chemical substance, if the specification discloses just one use of the substance, producing and transferring the substance for other uses can be infringement. But in the case of medical use claims, producing and transferring goods becomes infringement only if it is for the claimed use.

So the next question is: when are they deemed to be for the claimed use?

In this regard the so-called “Label” doctrine is predominant in Japan. The “Label” doctrine is the notion that a medical use claim is infringed when the product has a “label” which shows the claim use.

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<sup>19</sup> Japan Patent Office, EXAMINATION HANDBOOK FOR PATENT AND UTILITY MODEL IN JAPAN (2019) [https://www.jpo.go.jp/e/system/laws/rule/guideline/patent/handbook\\_shinsa/document/index/app\\_b3\\_e.pdf](https://www.jpo.go.jp/e/system/laws/rule/guideline/patent/handbook_shinsa/document/index/app_b3_e.pdf).

<sup>20</sup> Tokkyo-hō [Patent Act], Act No. 121 of 1959 (Japan).

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As you may know, pharmaceutical products are required to include the document called a “package insert.” This means that the description on the package insert determines infringement. For example, when the disease written in the package insert is different or when the dosage is different, it is not infringement because it is made or sold for the different use.

To be more specific, I will give you a brief overview of two cases.

The first one is the “Prophylactic agent for allergic asthma” case.<sup>21</sup> The point is whether the accused product is a prophylactic agent or not. Prophylactic agents are drugs given on a regular basis to prevent the patients who are diagnosed with asthma from getting attacks.

The court examined in this case the dosage and administration written in the package insert. As a result, the court found that the product is actually a prophylactic agent, so it infringes the patent. This decision is typical of the “Label” doctrine because the description in the package insert played an essential role to decide the infringement. But note there the court considered the description very carefully. It examined whether prophylactic effect is caused by the dosage and administration specified in the package insert.

The next case is “The Drugs for Ménière’s Disease case.”<sup>22</sup> In this case the claim defines the medical use as it is orally administered at 0.15 to 0.75 g/kg. On the other hand, the dosage in the package insert of the accused product is 1.05 to 1.04 g/kg. But the package insert also says that you can increase or decrease the dosage depending on the symptoms. If the patient decreases the dosage depending on this statement, it may fall within the scope of the claim.

In this case the court found that there was not infringement based on the description in the package insert. Actually, there is a possibility in general that the drug is used in the claimed dosage, but the court denied infringement because there was no sufficient evidence other than the package insert.

I think the notion which regards the package insert as important is supported by Japanese pharmaceutical regulations in which off-label use is avoided systematically, and it is related to the Japanese universal healthcare system.

Medical expenses including cost of drugs are subsidized from the national insurance in Japan. Approved drugs are priced by the government and listed in the Drug Price List of the national insurance. Drugs which are not on the list cannot be covered by the insurance and further use of the drugs is also not covered by insurance. I think this is why the “Label” doctrine is working in Japan.

This is a summary of my presentation. That is all I have to say. Thank you.

MR. RICHARDS: Thank you.

John Pegram from Fish & Richardson will now speak to plausibility of written description.

MR. PEGRAM: I was asked by John Richards to mention that we don’t have second medical use claims in the United States, for those of you who are not familiar, because we have method of treatment claims.

England and America are two countries separated by the same language. We’ve heard that in various forms of expression. In my presentation I want you to consider: is it the language that’s different, is it the law, or something else?

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<sup>21</sup> Sandoz AG v. Kyowa KK et al. (Tokyo D. Ct., Apr 11, 2002) (Japan.).

<sup>22</sup> Takeda v. Kowa KK (I.P. H. Ct., Jul. 28 2016) (Japan.).

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The “patent bargain” that was alluded to earlier is conceptually the same in Europe, the United Kingdom, and the United States. We describe it in the United Kingdom, for example in the *Warner-Lambert* case, as the inventor obtains a monopoly in return for disclosing. In the United States our *Festo*<sup>23</sup> case said that exclusive patent rights are given in exchange for disclosing.

It turns out that credibility, which in some of the European decisions was equated with plausibility, arises in the United States in connection with our utility requirement. Basically, you have to have a credible basis to support utility, but there need be only one credible assertion of specific utility; you don’t have to cover the whole breadth of the patent for that purpose.

We have in our Section 112<sup>24</sup> a requirement of both written description and enablement. For a long time at least some judges and some patent attorneys thought that the written description requirement only related to priority, but in the *Ariad*<sup>25</sup> case the Federal Circuit said “No, these are two separate requirements.” However, in reading the decisions both before and after *Ariad* the requirements are confused with each other.

The written description requirement is discussed in the *Amgen*<sup>26</sup> case where the Federal Circuit described it as relating to showing through the disclosure that the patentee “had possession” of the claimed subject matter and that demonstrating possession requires the “precise definition” of the invention.

How does one show that you have “possession” through a precise definition? In talking about the genus in particular, you must show that one has conceived and described sufficient representative species encompassing the breadth of the species.

Another phrase in the *Amgen* case required that one of skill in the art can “visualize or recognize” the members of the genus.

The case law in *Amgen*, which is quite helpful I’ve found, describes some of the ways that you can provide a “precise definition” of the genus and says that the definition should be “sufficient to distinguish the genus from other materials which may be present in functional terminology when the art has established a correlation between the structure and the function.”<sup>27</sup>

We will now move to enablement. In Europe and in the United States there is a close analogy between the concepts of enablement. The European Patent Convention Article 83<sup>28</sup> talks about “to be carried out” and Section 112(a)<sup>29</sup> refers to “enabling,” but they appear to be quite similar conceptually.

However, as the *Rasmusson* case has said, mere plausibility does not suffice: “If mere plausibility were the test for enablement under Section 112, applicants could obtain patent rights to ‘inventions’ consisting of little more than respectable guesses as to the likelihood of their success.” “When one of the guesses later proved true, the ‘inventor’ would be rewarded the spoils instead of the party who demonstrated that the method actually worked.”<sup>30</sup> This is, I believe, suggesting that “plausibility” *per se* does not have

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<sup>23</sup> *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co. Ltd.*, 535 U.S. 722, 737 (2002).

<sup>24</sup> 35 U.S.C. §112 (2012).

<sup>25</sup> *Ariad Pharm., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010).

<sup>26</sup> *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1373 (Fed. Cir. 2017).

<sup>27</sup> *Id.* at 1378.

<sup>28</sup> *Supra* note 3.

<sup>29</sup> 35 U.S.C. 112(a).

<sup>30</sup> *Rasmussen v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1325 (Fed. Cir. 2005).

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the same meaning, to the Federal Circuit at least in this case, as it has in the U.K. and European cases. Instead, in the United States our enablement requirement is that, “the specification of a patent must teach those skilled in the art how to make and use the *full scope* of the claimed invention without undue experimentation.”<sup>31</sup>

There are a number of factors in an older Federal Circuit case, *In re Wands*,<sup>32</sup> an application appeal, of the various factors that are to be considered in regard to undue experimentation. This I suggest is a lot more detailed than a mere plausibility test.

In the European cases we have seen that plausibility has also been raised under the inventive step standard. In the United States the obviousness determination does not require identification of an inventive step or a problem/solution analysis. So plausibility in the disclosure supporting the claim is not a requirement for unobviousness in the United States.

I would also add that there are probably five practitioners in the United States who understand what the inventive step analysis is — one of whom is John Richards, but then he is also qualified in Europe and in the United Kingdom, so maybe he is an exception. We could spend a whole afternoon on that subject. But we are not going to.

In the interest of time, I will skip my provocative thought. I thank you very much for staying. My substitute provocative thought is that I am the last person who you have to listen to other than the panel comments before the cocktail hour.

Thank you very much.

MR. RICHARDS: And the audience.

Thank you, John.

Laura, have you got anything you want to add to anything that has been said so far?

MS. WHITING: Yes, absolutely.

What occurs to me, and what we were discussing amongst the panelists earlier, is that there is a real difficulty in Europe for patentees in determining how much data should go into your patent filing. That is a particular problem because there appears to be some diversity in the courts in Europe as to how they approach plausibility.

The Supreme Court in the United Kingdom had a great deal to say about the various EPO cases, but of course the Technical Board of Appeal in the EPO doesn't itself operate a system of precedent, and so each of those cases in many ways turns on its individual facts and depends upon its context.

There are EPO cases, *Ipsen*<sup>33</sup> and *Allergan*,<sup>34</sup> which say you do not have to have any experimental evidence on file at all. But then *Salk* says you need to have some mechanistic theory. So how is the applicant to square the circle and work out how much data they should include?

That is particularly difficult, I think, when you are seeking to draw the line between how much data you need to have in there for plausibility versus how far along you are in your research, and when the decision as to how much data is really enough is not being made at the date that you file your patent, or even during examination, but substantially later, when you are litigating the patent either in opposition at the EPO or even further down the line, as Pfizer was in the *Pregabalin* case in the national courts, in litigation.

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<sup>31</sup> Amgen, 872 F.3d at 1375.

<sup>32</sup> 858 F.2d 721 (Fed. Cir. 1988).

<sup>33</sup> Decision T-578/06, *In Re Ipsen Pharma.*, ECLI:EP:BA:2011:T057806.20110629 (Jun. 29, 2011).

<sup>34</sup> Decision T-2368/12, *Allergan, Inc. v. Ipsen Pharma.*, ECLI:EP:BA:2018:T236812.20180605 (Jun. 5, 2018).

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MR. PEGRAM: May I ask, Laura, would you recommend that you follow these European standards or would you say for an important invention you should be following the U.S. standard?

MR. RICHARDS: I would just add that I would say “or the Japanese standard.”

MR. PEGRAM: True.

MS. WHITING: Clearly, the EPO and the United States have different standards, so if you want a European patent, you are going to have to pay attention to the EPO law as it stands.

MR. PEGRAM: I would suggest to you that the U.S. standard is harder to satisfy and that if you were to satisfy the U.S. standard, it would probably be plausible. What do you think?

MS. WHITING: I’m not a U.S. lawyer so I’m not sure whether I can adequately compare the two. I don’t know whether John is able to do so, since he is the single dual-qualified member of the panel.

MR. McGOUGH: I am a U.S. lawyer, so I should chime in. A case that actually bookends one mentioned by John, the *Rasmussen* case, is a *per curiam* affirmance by the Federal Circuit in October 2018 of a decision out of the Eastern District of Texas, an unusual venue for a pharma case.<sup>35</sup> The Federal Circuit held there was at least a triable issue of fact as to whether a patent owned by Erfindergemeinschaft, which disclosed merely in theory based purely on literature, the use of phosphodiesterase (PDE) V inhibitors to treat the benign prostatic hyperplasia (BPH) solely based on a literature disclosure, did in fact satisfy written description.

So I’m not quite sure it’s fair to say that our standards are more rigorous. In fact, I think it is equally interesting to bookend that with the *Rasmussen* case.

I will just pose a hypothetical that you can all think about as you gaze out over the New York skyline from the rooftop party. An increasing issue in the pharma industry that I think dovetails with all of this is clinical trial transparency and the need to have a certain level of detail when a clinical trial is published.

Here’s the hypothetical: what do you if your biopharma client comes to you and says, “We have a co-therapy, two known actives, new purpose, and [just to make it a little bit harder] one of them is an antibody against a well-characterized antigen, but we don’t know that it is going to work as a co-therapeutic in the indication of interest”?

So what do you do in that instance with, as you say, plausibility hanging over your head once you move outside the United States, or indeed in the United States, to satisfy cases like *Erfindergemeinschaft* or *Rasmussen* that you mentioned?

MR. RICHARDS: I actually wrote the patent in the *Rasmussen* case so I’m a bit biased on that decision. But there was a subsequent decision very shortly after on ADHD, which had a different panel of the Federal Circuit, where the facts were very similar, and it was held to be okay.

In Japan, I think I’m correct in saying, you need more than you need in either the United States or Europe; therefore, that is probably going to be the driving factor anyway. Am I right that in Japan you are going to definitely need to have some data?

MR. MAEDA: Yes, to satisfy the disclosure requirement. Japan has two disclosure requirements. One is an enablement requirement, which is equivalent to the U.S. one and the European one. The other is a support requirement. The Japanese Court case says that

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<sup>35</sup> *Erfindergemeinschaft Uropep GBR v. Eli Lilly and Company*, 739 Fed.Appx. 643 (Fed. Cir. 2018).

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to satisfy the support requirement it is necessary to describe the pharmacological data in the specification.

But recently this practice has been criticized. In one case the court said that it is not necessary to describe the data to satisfy the support requirement. So I think the situation is a little bit similar to the United Kingdom on that point. Of course, formerly the standards were very different between Japan and the United Kingdom, but in substance I think it is a little bit similar now.

MR. RICHARDS: Thank you.

Anybody in the audience?

QUESTION [Justin Watts, WilmerHale, London]: Any really important patent that we develop and file today is going to get tested in the Court of Appeal or the Technical Board of Appeal about ten years from now. So I wonder if you could tell me what the law on plausibility will be in ten years' time. [Laughter]

MR. RICHARDS: I take the moderator's privilege to say that's out of order.

MS. WHITING: Justin, I think that's a really good point. That is borne out by a lot of the cases that we have seen coming from the EPO Boards of Appeal: patents are being judged, ten years after they were granted, against a different standard for plausibility (or whatever other test) than applied at the date they were filed. That is a genuine problem and I don't see how we solve that.

MR. RICHARDS: Robin, I think you're next.

QUESTION [Prof. Robin Jacob, Faculty of Laws, University College London, London]: I am going to advance the proposition that the law has gone mad.

An inventor is entitled to have very long, wild, and woolly hair. He comes along and says, "Here is my invention; this is what you ought to do; and, if you do this, this is what will happen" — and in fact he is right. Why do you have to believe he might be right? Because you know he tells them what is going to work.

I think plausibility has gotten out of hand. At the most we should be saying, "You can't have it if it is implausible." Looking back in my career, even that is a problem. For example, I had a mechanical case, a civil engineering case. People didn't believe it, but he told you and it was true. Every highway, every motorway, every freeway in the world has got this invention on its side. You don't believe it works, but he told you how to work it and it does work.

I think we ought to be thinking very carefully about requiring clinical trials and experimental evidence.

*Pregabalin* was a disgrace. Think about it. They said it would work for both kinds of pain and it did work for both kinds of pain. So why should they lose their patent? You could say, "Oh well, it's a bit misleading and what not, and they haven't got a proper clue, and it's speculative." It doesn't matter if it's wrong; nobody would have used it anyway.

The point is we should get rid of plausibility and go to something rather different, which is "you don't believe it" as a good test.

MR. BURROWS: I think an argument raised by *Warner-Lambert* was actually that you should only have the *Salk Institute* principle applying in cases where the claimed effect was "inherently implausible," but it was not accepted by the Supreme Court.

QUESTIONER [Prof. Jacob]: Like all supreme courts, especially more now than I think it was in the past, understanding of patent law is getting thinner and thinner.

MR. RICHARDS: There is another question in the back.

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QUESTION [Cordula Schumacher, Arnold Ruess, Düsseldorf]: I think, at least in Germany, the problem of the second medical use claims really arose due to a change of the law.<sup>36</sup> So the one to blame here I think is the legislators.

Previously, there was only a change or a substitution of the original product by a generic product if there was an identical overlap between the indications in the SPC. But then there was a change of the law and it is now sufficient that there is just an overlap of one indication. If the originator product is admitted for two indications including the patented one and the generic product just for one indication, the pharmacists are legally obliged nevertheless to hand out the generic product for the patented indication.

Klaus has described all the questions that come into play even if there is an infringement found. What do we do then? What should the injunctions look like? And are the pharmacists and the other third parties obliged to act according to instructions by the generic company not to use the product for the patented invention?

So I think the real solution would be that the legislature changes that law again, or at least takes care of the patent situation. I realize that I am probably not addressing the right audience here, but I think that has to be considered when discussing these claims.

MR. RICHARDS: Klaus?

JUDGE GRABINSKI: When we talk about plausibility there are two sides of it. One side is about insufficiency and the other side is about obviousness. By and large, I think the standard has to be the same on both sides. Therefore, if you would consider something obvious to try on the obviousness side, then the same standard should apply for insufficiency in order to carry it out. I think it should always be kept in mind that there is some harmony between the two standards, and I personally would tend to say we should not put the threshold too high on both sides.

MR. RICHARDS: When I was in training, I was told “Never put the theory of your invention into your description because the examiner will just say ‘it’s obvious.’” That was the theory I had behind me when I wrote the patent which is in the *Rasmussen* case. I put into the specification all of the facts that the inventor had utilized in order to come up with her understanding as to why the invention was going to work — and obviously it did work — but I didn’t put in her rationale linking those facts. I must say I still feel aggrieved about that decision.

QUESTION [Joachim Feldges, Allen & Overy, Munich]: Robin Jacob, I am biased definitely, but I have some sympathy for your thought that there is some bad taste if something really works, and works very well, and ten or fifteen years later someone comes and says, “Well, I know something; the test you have written or specified in the patent is not the right test and so it’s implausible.” It is something which hurts somewhere because it works actually, so it was a right invention. But okay, I’m biased.

I want to add that in Germany the *Warner-Lambert* case was solved in a combination of contributory infringement actually by the Hamburg Court, where they said the generic companies contribute to infringement by the pharmacist, what you can do with a product claim construction; and in addition, there was tender law accompanying these decisions obliging the statutory health insurers to do two different tenders for the patented and nonpatented indications.

Obviously, you cannot solve these problems with patent law only. You need to take regulatory law into consideration as regards injunctions, as regards the right measures, and it must be a combination of that. That is not ideal, I agree, but we can at least do

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<sup>36</sup> *Supra* notes 2 and 3.



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something. In the past you could fix these patents to the wall, they had no value; and that prevented innovation because nobody invested in innovation if you would have no protection. That is the true concern behind it.

MR. RICHARDS: Any other comments or thoughts?

QUESTION [Judge Rian Kalden, Court of Appeal The Hague]: I just wanted to comment on the plausibility test. I believe it is helpful to carefully read the EPO case law on this. There are certain cases where it was said that there does not necessarily have to be something in the patent in relation to plausibility if there is no reason to doubt that the invention actually works. That is more or less along the line suggested by Robin. There is case law to that effect at the EPO. So maybe the Supreme Court of the United Kingdom just may have been unnecessarily strict about that.

QUESTION [Angus Lang, Tenth Floor Chambers, Sydney]: I have a question for Justice Grabinski in relation to the question of filing an injunction tailored to the second medical use infringement scenario. The question is, does the Düsseldorf court in any of its three cases attempt to grant an injunction or would it have refused the injunction in that case?

JUDGE GRABINSKI: They refused in all three cases, and I think in all the cases at least one reason was because they could not prove a sufficient amount of second medical use on the market.

MR. RICHARDS: Anything else from anybody?

QUESTION [Prof. Jacob]: I have one question for Klaus. The *Düsseldorf* case is one thing. The Supreme Court in England analyzed German law. Was it consistent with the *Düsseldorf* case or did the English court, which says it is basing itself on what it learned from German law, get it wrong? [Laughter]

JUDGE GRABINSKI: I think in the tendency at least they got it right, but I'm not sure about all details. They explicitly mentioned at least one or two decisions from the Düsseldorf High Court in their decision.

QUESTIONER [Prof. Jacob]: They seem to think you have to have a second medical use for infringement. However, the Düsseldorf court seemed to suggest if you know very well what is going to happen is significant — well, enough — then you might be infringing.

JUDGE GRABINSKI: Yes, there is a difference.

MR. RICHARDS: It goes back to the objective vs. subjective intent, an old knowledge issue. It all really comes back to the question of what does the word “for” mean in any patent claim, which I think they have been grappling with for the last 200 years almost.

Anything further from anybody?

MS. WHITING: Just to add to Robin's point: there is a big difference between the Düsseldorf court's approach in treating the Swiss-form claim as a product claim, albeit purpose-limited, and the U.K. Supreme Court's approach, which was to treat a Swiss-form claim as a purpose-limited process claim. That had a big impact on the infringement analysis and we can see that running all the way through the Supreme Court's decision.

JUDGE GRABINSKI: Absolutely. In that regard this is not only the Düsseldorf court but this is case law from the Federal Court of Justice, saying that it is a purpose-limited product claim.

MR. RICHARDS: Okay. The drinks are outside. Let's adjourn. Thank you.