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Procopio Perspectives Podcast

Is Your Life Sciences Patent Enabled? The U.S. Supreme Court Is Considering That Question

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SPEAKERS:

- Jeff Morton, PhD, Procopio IP Partner and Life Sciences group leader
- Robert "Bob" Sloss, Procopio IP Litigation Partner
- Jeremy Edwards, Procopio IP Litigation Partner

Announcer (00:07): Welcome to Procopio Perspectives, a podcast featuring award-winning corporate and litigation attorneys providing useful legal insights on the latest issues of the day. Today's podcast features three Procopio IP partners discussing a forthcoming US Supreme Court ruling. The court will decide whether Amgen's patent, which claims antibodies by functional antigen binding, is invalid for not meeting the enablement requirements of Section 112(a). You'll hear from our San Diego based life sciences practice leader, Jeff Morton, who has a PhD in immunology, Bob Sloss, an IP litigator in our Silicon Valley office, and Jeremy Edwards, an IP litigator in our Washington DC office. This podcast was adopted from a webinar. We'll start with Jeff.

Jeff Morton (00:51): So this case is interesting for a number of reasons, and as we'll go into today, there's an interest from those of us that do a lot of preparation and prosecution of patent applications in front of the USPTO as well as for the litigators who ultimately argue for the validity or infringement of these types of patents. So just a little bit of background, given that there is a wide variety of attendees at today's webinar. These are just some very key legal statutory concepts in patent preparation and prosecution. And so, during the patent process there's four fundamental statutory requirements that need to be met in order to get a allowed and ultimately a granted patent. First of all, the patent claims need to claim eligible subject matter. Not everything is patentable. Secondly, the patent claims need to be novel. They need to be new over anything else that's come before it.

(01:45): Thirdly, and this is one where the prosecutors spend a lot of our lives, the claims need to be non-obvious or inventive over everything that's come before. And then the fourth point, which is where we're going to be focused today, is Section 35 USC 112, which focuses on the requirement that the patent specification contains a written description of the invention that's sufficient to enable any person to make and use the invention. This is an area that, as Bob will indicate, doesn't get litigated a lot and so it's of significant interest both to the litigators and then, ultimately, for those of us who are developing new IP protection for clients.

Announcer (02:24): Now we'll hear from Bob.

Bob Sloss (02:26): It's kind of the flip side. In litigation, what we try to do is take the things that Jeff mentioned that he needs to get in order to get a patent, we try to undo those. So, as most of you know, a patent is presumed to be valid once it's issued but that's not where the fight ends. In court, we have

the opportunity to try to invalidate the patent and these are the grounds we usually seek to do it; either that it's ineligible subject matter, that it's not novel or it's anticipated by prior art, that it's obvious in light of prior art combinations. As Jeff said, this is something he as a prosecutor spends a lot of time on. We as litigators spend a lot of time on it as well, trying to find and validating prior art and arguing to the court that the prior art does, in fact, validate the patent. And then finally, the one we're going to be talking about today is whether the patent sufficiently enables or contains a written description of the invention. As I said, there's a presumption that the patent is valid and it's up to the defendant to prove it's not by clear and convincing evidence.

Jeff Morton (03:27): Okay, so we'll delve into a little bit in terms of the background on this case. We're dealing with the world of heart disease and high LDL cholesterol, which can cause heart disease, which does cause heart disease. Amgen invented what are called monoclonal antibodies that lower LDL cholesterol levels and, essentially, Amgen's antibodies bind to a specific region of an enzyme called PCSK-9. That binding results in decreased degradation of the LDL receptor, which means that there's more LDL receptor to uptake LDL from the bloodstream. So that is what we're dealing with and this is ... Amgen's product is marketed as Repatha, and these are multi-billion dollar a year drugs that we're dealing with. In terms of what antibodies are, antibodies are components of the immune system and they target what's called an antigen, which is usually a protein, and it's a Y shaped biological molecule.

(04:26): One of the benefits of monoclonal antibody production is you can generate an unlimited supply of absolutely identical antibodies that can be used to treat whatever the antibody binds. Now historically, antibodies have been claimed in patents historically at two ends of the spectrum. In one end, it's by their primary sequence. Antibodies are proteins and they're made of amino acids and so you can identify, at a very granular level, the exact amino acid at the exact position. The challenge with that as we'll go into is that ends up usually being a fairly narrow claim because someone could come in and remove one amino acid and substitute it for another. So at the other end of the spectrum and the broad end of the spectrum, antibodies can be claimed based on what they interact with or what they bind with so the antibody is binding to an antigen, and that's exactly how the Amgen patents were prepared and drafted and prosecuted.

(05:25): So here are the two Amgen patents that are subject to this litigation. The first one is the 165 Patent, and the second is a 741 and they're actually quite similar. I'll just focus on the first one. It's an isolated monoclonal antibody that when it's bound to the enzyme that we're talking about it binds at least one of the following residues, and there's 15 amino acid residues in the enzyme that have been identified. And then, there is a limitation that there is a blocking of PCSK-9 to LDL receptor. It's quite a similar story with the second patent except it's focused on two residues. So the issue here is that when you actually extrapolate what is potentially claimed in these claims, there are a myriad of antibodies that could potentially carry out this function. And you certainly hear people throw out the idea that there's hundreds of thousands to millions of variant antibodies that could fall within this claim. So this is from a factual perspective how we're set up for the subsequent legal argument, that we have claims here that have the potential to have a significant amount of breadth because they are de facto genus claims in the biotech sector.

Bob Sloss (06:47): Okay, so let's get into the litigation itself but a bit of a backstory to this. As you see, the defendant in this case is Sanofi, another large pharmaceutical company. They actually independently developed their own antibodies that basically did the same kind of binding to this PCSK-9 and, because of the way they proceeded internally, actually made it to market first with a product called, I think it's pronounced Praluent. As I said, it was developed independently. A as you know, in patent law though independent development does not insulate you from liability. If there's a patent

out there, regardless of how you developed your product, if it infringes, it infringes. That being the case, Amgen sued Sanofi in 2014 so this case has been around for a long time. Sanofi stipulated to infringement. It basically concluded that, yes, its antibody does what's claimed in these patents so rather than trying to fight infringement, it challenged the validity of the patent with its main focus being on enablement.

(07:51): The case went to trial several years ago and the jury found that the patents were, in fact, enabled and so they ruled against Sanofi and in favor of Amgen. Sanofi appealed the first time and the federal circuit vacated the judgment and remanded to the district court again to again take up the issue of enablement. The second jury also found that the patents were sufficiently enabled but the court granted JMOL, which means a motion for judgment on the basis of law, saying that the jury was in error in finding that the patents had been enabled and had entered judgment of non-infringement based on invalidity in favor of Sanofi. Now, this is a very, very unusual thing for a court to do, to overrule the jury essentially, but the court found that there just wasn't enough evidence to find that the patents were enabled because the court concluded that they required undue experimentation to be able to fully realize everything that Amgen was claiming the patent covered.

(08:52): And so, the court, as I said, took the verdict away from the jury and entered judgment in favor of Sanofi. Amgen then appealed to the federal circuit. The federal circuit unanimously affirmed the district court's finding of no enablement and some of the language that the court used was that these genus claims face uniquely high burns in fulfilling the enablement requirement. That's because there are so many different possibilities that it would require substantial time and effort, too much time and effort for a person of skill in the art to identify and make all or nearly all variations of the invention that might exist within the genus. As Jeff said, there could be as many as a million plus different iterations of this that would lead to different antibodies. It's just a statistical calculation but when you take all the variables that go into it there are possibly as many as a million different combinations that would work. And so, the district court said, based on that, there's no way that the patent could be fully enabled the way Amgen was claiming it could be and, therefore, the patent was invalid.

Announcer (09:57): Now Jeremy joins the conversation.

Jeremy Edwards (10:00): What we see is that the claims are very broad, and you mentioned why that might be. When the court or the jury is engaging in an analysis of whether there's enablement, they look to the patent itself and the specification. And I'm curious, and maybe Jeff's looked at this closer, if you could tell us, in general, what did the specification of these patents look like? Was it bare bones, was it voluminous? How much guidance did it provide?

Jeff Morton (10:27): Yeah, it's a very good question and, in my view, this is a very well-prepared patent. I don't think this is a case of bad facts make bad law. This is a very significant patent document prepared by a very good firm. It's, I think, around 350 pages. There are 41 examples, page after page, outlining precisely how they prepared well over two dozen antibodies that all have a sort of similar function as it relates to the binding of this enzyme. Now admittedly, they did not go and generate a million different antibodies or a thousand antibodies, they did well over two dozen and I think, to a certain extent, you can certainly make the argument that they've outlined the steps necessary to produce and test those antibodies. And there's an interesting line in Amgen's petition for cert that says essentially, and I'll just read off the petition itself, it says that if a claim truly exceeds what the patent enables, the challenger will be able to provide concrete identification of at least one embodiment that cannot be made or used without undue experimentation.

(11:37): The argument is, here Sanofi identified no embodiment or no antibody within the claims that could not be generated using the patent's disclosures so that's certainly one line of argument that what we're dealing with here is a pretty robust patent filing. Again, understanding that part of the patent process and the experimental process in the life sciences is that you can't wait until everything is done because there's, at some point, going to be disclosures made. And so, I would look at this as a very high bar patent in terms of how they develop things. Now, as we'll get to later in the presentation, there are I'm sure things that, if you had the benefit of perfect hindsight, you'd go back and perhaps change. And I think that's one of the things that is changing in life sciences practice is having further fallbacks in terms of how you are preparing the application and how you're claiming these types of antibody inventions. But this is definitely not a case where I would say it's a bare bones patent that only discloses one antibody and leaves it to the general skill of the person skilled in the art to figure out the rest. That's my view.

Jeremy Edwards (12:45): Thank you Jeff. Bob, I think you were about to take us to the Supreme Court's grant so ...

Bob Sloss (12:50): Yeah, and I think some of the things that Jeff just talked about you'll see is kind of what's really at issue here in the Supreme Court. So the Supreme Court did grant Amgen's petition for Certiorari and I've laid out here pretty much exactly what the issue is that the Supreme Court is going to rule on, and whether enablement is governed by the statutory requirement that the specification teach those skilled in the art to make and use the claim invention. Or, and this is kind of what Sanofi's argument is, whether it must instead enable those skilled in the art to reach the full scope of the claimed embodiments, and this gets into what is the full scope? It doesn't have to be all one million possibilities or I think it was 26 different antibodies that are identified in the specification. Was that enough? And so, that's what the Supreme Court ultimately is going to be ruling on and this is just a very, very quick summary of the argument.

(13:44): I should say that the issues that were actually in this court and before the Supreme Court now are very complicated, very well argued by the parties and this is just really a very short summary of what's there, but it's all very nuanced and very difficult questions. So Amgen is essentially taking the position that the federal circuit ruling that the patents weren't fully enabled imposed a standard that really doesn't exist in the statute, that all the statute says is a person that's skilled in the art has to be able to enable what's invented, not to reach what the court of appeals call the full scope of the claimed embodiments. That's just not part of the statute according to Amgen.

(14:27): On the other hand, Sanofi is taking the position that what Amgen gets, if it doesn't provide more in the way of enablement, is ability to monopolize basically everything that the patent can functionally do. That's just too broad and that what it will do, it will deprive the marketplace of an alternative product here that could save lives and be of great help to people, but that the patent is preventing that from happening if it's allowed to proceed as Amgen wants it to proceed. So what we have here is really a ... As Jeff said, the patents are well drafted so this is not an issue of one lawyer being able to take advantage of another's mistake or anything like that. This is really a pretty deep philosophical issue. For particularly this type of life science patent, what should the scope be? And that's ultimately what the Supreme Court is hopefully going to decide.

Jeff Morton (15:20): Looking ahead both from the prosecution commercialization perspective as well as Bob will make some comments on litigation about why is this case important. And again, we don't know how the court is going to rule. First of all, in the biotech area, the chemical area, the pharmaceutical area, people are really paying attention to this case. Not a lot of patent cases come

before the Supreme Court and even fewer oftentimes relate to life sciences so this is kind of exciting for all of us. And, at a fundamental level, one of the reasons that we're interested in this is this concept of a genus claim, obtaining a claim where the commonality is a certain functionality of what's being claimed, albeit with different structures. So, in this case, we're dealing with antibodies that have a functional commonality even though the amino acid primary sequence could be distinguished.

(16:12): That's a fundamental part historically of life science patent work is dealing with this because biomolecules are large molecules and if you are limited to primary sequences, it's very easy to design around this. And so, certainly for those of us that work in the startup life sciences space, there is a real commercial importance to this. Startup clients need to obtain good patent protection to facilitate good investment and if you have very narrow patents with no prospect of getting broader coverage it's going to be harder to get further investment into your company and to ultimately develop a useful therapeutic. So again, where we're down to is this fundamental tension that I think Bob really spoke much better about than I am, which is this concept of is a broad patent an unreasonable monopoly versus a situation of a narrow patent that is easy to design around? Historically, one of the ways that you address these types of issues was working towards more and more working examples, more experimental data.

(17:20): But when you go and look at what Amgen did here, they did a really, I think a very, very good job of this. This is different from a lot of other cases where you might see a situation where someone has one molecule or one or two lead products and they're trying to get an expansive monopoly. We're dealing with a different situation here, in my respectful view. This is my final point, that this case as well as other cases, and I'd say a trend at the US PTO, has I think started to impact how life science applications are being prepared. And again, these are high level concepts. They're certainly open to debate, whether here or elsewhere. I've summarized these in three points. The first is there is a move towards more data, more examples. Some of the people I've trained with really pushed this on me when I was training and I think they're absolutely right, that the more data you have, the more examples you have, the better.

(18:15): A second point, which I think is a little bit more challenging, is that one of the things you see when you start reading about this case is this concept that there wasn't enough perhaps instruction to the person skilled in the art for how they could carry out the experiments necessary to realize the full scope of this patent. And again, that's up for argument as well, but I think there might be a movement towards patent drafting where there is a bit more instruction in terms of what people skilled in the art could do to look at other variants. I think there's a natural hesitancy to do that because the more you do that, I think, you might set yourself up for obviousness arguments against your own art later on. I think a lot of us were trained in a way to avoid poisoning the well for your own later IP and, in some instances, that might be coming back to haunt patent filings that don't provide as much instruction as they otherwise might.

(19:12): With respect to antibody claiming, there is definitely a tendency moving towards focusing on claiming the antibodies themselves instead of focusing on what the antibody binds. What's called the newly characterized antigen test in the United States, unlike many other places in the world, is kind of dead. And so, there is much more of a tendency now to focus on the sequences and the motifs in the antibody and focus less on the antigen, at least as a backup position. And then thirdly, as I said at the beginning of this presentation, historically there's been sort of polar ends of how you claim antibodies. At one end, you would have narrow primary sequence ways of doing that, and then at the other end what we're dealing with in the Amgen case, which is an antibody bound to a particular antigen.

(20:02): I think there is a middle ground and one of the middle grounds is that the ends of the Y portion of the antibodies are these variable regions that have these protein loops called CDR loops, which stand for complementarity determining regions. It's these protein loops that really are the key to the binding with the antigen and what you see in many instances is that there's highly conserved amino acid sequences within those CDR loops. So what a number of biotech companies and their council now do is try to find consensus sequences in those CDR loops so that you can have some level of certainty of what the protein needs to look like in those regions while still permitting a certain allowance of variability in the other amino acids that are actually not as important in the binding of the antigen and, thus, the efficacy of the antibody. I think that is something that is more prevalent now than looking at patent claims from 10 years ago where really they did a lot more of what Amgen was doing here. And so, with that said, I'll move over to Bob for his synopsis on litigation.

Bob Sloss (21:13): Actually, my comments are a little briefer because really we won't know until we get a decision, of course, but I think this is a big deal. As Jeff said, we don't get a lot of Supreme Court patent cases so anytime there's a patent case that the Supreme Court's going to decide those of us who are patent geeks get pretty excited about it. So that's really the main thing is what's the Supreme Court going to do on this. For this type of case, obviously if you're defending a company that's being sued for infringement of an antibody patent, this could give you a whole new line of defense. If you're representing the patent owner, you might have to rethink how you're going to approach the case. So it could throw open pending cases and cases that are perhaps being considered for filing as to what the approach should be for this type of patent.

(21:59): As I think Jeff said early on in the presentation, enablement isn't something that comes up a lot, and I think that's even more the case in non-life science type patents. And so, it's possible that the decision in this case will not have a major impact on other types of patent litigation. Having said that though, the issue of functional claiming, which is closely related to what we're dealing with in this case, is something that's getting a bit more scrutiny, both I believe at the patent office and in the courts. And so, the idea of claiming, say for a semiconductor, what it does versus how it's built, that could be affected somewhat by the Amgen decision depending on how broadly the decision is worded. Having said that though, it's unusual for the Supreme Court in this type of case to really go beyond deciding the particular issue it has to decide so I wouldn't expect there to be much of an impact in other types of cases, but we'll see. That's kind of the fun of it now is we get to kind of speculate about what might happen.

Jeremy Edwards (23:03): So the arguments on this case are a couple of weeks from now on the 27th, so stay tuned and I suppose the decision will come out some months thereafter. Thanks everyone again.

Jeff Morton (23:13): Yes, thank you very much.

Announcer (23:16): We hope you enjoyed this Procopio Perspectives Podcast. Please subscribe if you haven't already and visit procopio.com to learn more about Procopio. Thank you for listening.