HP: One of those most contentious issues in pharmaceutical IP law is the issue of biologics. Biologics are drugs developed from living organisms with the capacity to treat afflictions ranging from cancer to HIV. The legal issues have become fairly complex with instruction of biosimilars, which are drugs that have many similarities to biologics. To start off with, Geoff, what are biologics?

GM: Biologics are basically drugs that are derived through the metabolic activity of living organisms. Things like blood products, cells and tissues, gene therapies, vaccines, things of that nature; the big difference between a biologic, or one of the most notable differences between a biologic and a small molecule drug which is what we typically see a lot of patent litigation around in Canada, is that the small molecule drug—and the reason it's called a small molecule drug is it may have 15 to 30 atoms. Aspirins, for example, have as many as 21 atoms. Compared to a biologic, that has over 3000 or even over 20000.

They're much more complex molecules, much larger, much more complex, and show a lot more variability. What that means is that because they are derived from living organisms is any small change from the manufacturing process or various other—any small changes throughout the process at all can have a very significant impact on the molecule that is generated.

HP: Can you give an example of that?

GM: One example I've heard about it is where a company was manufacturing its biologic in Denver, Colorado, and they decided to move their facility to the east coast of the U.S, and the change in altitude resulted in variability within manufacturing processes such that they had to get new regulatory approval.

HP: Let's move to biosimilars—I know they're also called SEBs. Can you tell us more about that?

GM: Yeah, so a biosimilar is basically a biologic drug that is made to be similar or comparable to an originator biologic drug. In Canada, in March 2010, Canada provided guidance for companies that wanted to manufacture biosimilars in Canada, and they call them Subsequent Entry Biologics. The SEB is actually an acronym for subsequent entry biologics. It's effectively the same thing—it is a biosimilar. When seeking approval for a subsequent entry biologic or a biosimilar, rather than having to submit an extremely detailed NDS ,a new drug submission to health Canada, biosimilar manufacturer or SCB companies can file… it's called a New Drug Submission, but it's not quite as detailed as the original submission would've been.

HP: What is contributing to the popularity of biosimilars right now?

GM: In my view, one thing that is contributing to the rise in popularity of biosimilars is that a lot of the small molecule drugs that have been very popular, some would call them blockbuster drugs, like Lipitor might be a good example, are now off patent. Which means the key patent covering that molecule has expired and therefore generic drug manufacturers in Canada and abroad have been able to capitalize on that patent expiry and come up with generic versions of their own, which in turn, once those hit the market, have taken away market share from the brand companies. So those brand companies, many of them are looking for other drugs to pursue and biologics are out there, and SEBs (subsequent entry biologics) or biosimilars are an interesting area to focus on.

HP: And how does the cost compare between biologics and biosimilars?

GM: Well, typically a biosimilar is significantly less costly to the consumer than its biological comparator, so as an example, in Canada, one of the SCBs to be improved is Inflectra which was compared to Remicade, which is a Janssen product. In Canada, the biosimilar version was 34.2% less costly than the originator biologic product. That's a significant cost saving for the average consumer.

HP: What kind of afflictions are these drugs meant to treat?

GM: That particular drug is a monoclonal antibody used for rheumatoid arthritis, ankylosing spondylitis, and psoriasis and things of that nature. You see biosimilars useful for treating various kinds of indications, everything from Crohn's disease, to colorectal cancer, so there are a variety out there.

HP: I know one of the important distinguishing factors between biologics and biosimilars is the approval process. What are the difference sand why is this important?

GM: Right, so over the past 15, 20 years, the PMNOC regulations, which are the Patented Medicine Notice of Compliance Regulations have governed the approval process for small molecule drugs—you know, Lipitor is a good example, Nexium, things of that nature. Basically what happens in those cases is a brand or an originator files a new drug submission, an NDS, basically with a room full of boxes to support the safety and efficacy of that drug.

With a small molecule drug, a generic company can come along and file what's called an abbreviated new drug submission. An abbreviated drug submission is just that—it's as series of boxes much less substantive in size, but also in cost, whereby they just compare the bioequivalency, and they just have to establish that their product is bioequivalent to the brand's small molecule drug product.

With biosimilars or SEBs, it's not nearly that simple because the SEB is not bioequivalent to the originator biologic, it's merely similar. That distinction lies in the complexity of the molecules because of the size and the complexity trying to get one, arrive at a biosimilar product that's identical is very difficult, if not impossible.

HP: And so from an IP perspective, what is something that IP lawyers should be keeping in mind in light of this approval purpose. Are their IP considerations for the approval?

GM: When you're revising your clients, you're either as biosimilar sponsors or hoping to be biosimilar sponsors that they pay very close attention to what patents are listed on the patent register, as well as make sure they get their submission in a timely fashion if they anticipate there might be a pending patent application relating to the product of the innovator.

HP: How do you see this area of law shaping up the next few years?

GM: There has been a lot of discussion about that. Certainly when you look around the world and see all the both originator traditionally brand companies and the traditionally generic companies, they're all going after biosimilars. So you would expect the amount of litigation to grow, the amount of patent finals to continue to grow, so it's not developing quite as quickly as I think some may have suspected, but nonetheless, I think the patent impeachment action coming up, the PMNOC proceeding, I would expect to see more SCBs or biosimilars approved in Canada in the next few years, I would hope, and even more after that. It's an exciting time, it's a very interesting area, and for patent litigators, it's a lot of fun because it's complex. The issues are interesting and not clear cut by any means and you have to rely heavily on the expert evidence because the science at play is very complex and often new.

HP: And what are some other issues that IP lawyers should be aware of in light of this debate between biologics and biosimilars?

GM: One thing that came out of the Abbve v. Janssen was the injunction that was ultimately granted. The court seemed open to a more customized injunction that took into consideration the patients who ultimately used the medicinal ingredient or biologics in question. What you find with biologics is that which is again somewhat different from small molecule drugs, one person might react to a biologic different than they might react to a biosimilar. If a person is already using a biologic product, it might not be in their best interest to switch to a biosimilar product, or even between biosimilars and so, if a person has already started using, well in the case of Stelara for example, the Advi v. Janssen case, certain

patients were already using Stelera as a product. It may have been contrary to their health to take them off that product or they might have suffered adverse reactions if they went back to one of the other products that were already on the market for the same indication.

The court seems to be those types of issues—or aware of those types of issues and open to creative injunctions, and they seem to be willing to grant them.

HP: Given the complexity of this subject matter, what is something that IP lawyers should be mindful of if they are involved in a litigation matter of this sort.

GM: One interesting thing we saw in the Abbvie v Janssen case and actually has also been proposed in these PMNOC cases we've seen related to biosimilars is a technical primer. When you're preparing your case for a hearing, preparing a technical primer that can be submitted in advance to the hearing itself to get the judge hearing the case well up to speed on the science of it all because these are extremely complex technical issues you don't want to have to waste valuable hearing days trying to educate the judge on.

HP: Okay. Geoff, thanks so much for your time on this.

GM: My pleasure.