The Healthcare Bill, an IP Lawyer's Friend

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Biosimilars, or follow-on biologics, are the names given to officially approved versions of innovator biopharmaceutical products, licensed after patent expiration of the original, innovator, biologic. Biosimilars are to biologics as generic drugs are to brand-name drugs, but their complexity prevents the follow-on manufacturer from making an exact clone of the original, hence the name "biosimilar." Biologics generally have very high molecular complexity and may be very sensitive to minute differences in manufacturing processes. More-over the biosimilar manufacturer does not usually have access to the innovator's molecular clone and original cell bank, nor do they have access to the exact fermentation and purification processes. These nearly undetectable differences in the biosimilar are known to result in serious health implications compared to the innovator biologic. As a result, the simplified application process to license a simple generic drug is not afforded to biosimilar manufacturers, and before March 22, 2010, there was no pathway for a biosimilar to be licensed in the United States. In the EU a specially adapted approval procedure has been authorized for certain protein drugs, termed "similar biological medicinal products."[1] This procedure is based on a thorough demonstration of compatibility of the similar product to an exiting approved product.[2] When the EU regulations came about, the Food and Drug Administration declared that new legislation would be required to address the same concerns in the United States.[3] Such legislation was provided in the Patient Protection and Affordability Act, otherwise known as the Healthcare Bill, signed into law by the President on March 22, 2010.

Congress gave the FDA authority to give licenses to biosimilar manufacturers. Title VII of the Patient Protection and Affordable Care Act amends Section 351 of the Public Health Service Act[4] to provide an approval pathway for biosimilar biological products, and grants authority to the FDA to accept and grant applications for biosimilar licensure.[5] The would-be biosimilar manufacturer must provide, in its application, information demonstrating that its product is biologically similar to the innovator biologic, citing to analytical, animal, and clinical studies.[6] The applicant must also show that the biosimilar and the innovator biologic utilize the same mechanisms of action for the condition(s) for which they are prescribed,[7] that the condition(s) for which they are prescribed are the same,[8] that the route of administration is the same,[9] and that the facility in which the biosimilar is manufactured meets standards designed to ensure that the biosimilar remains safe, pure and potent.[10]

The critical difference between the biosimilar pathway paved in the U.S. compared to other countries is the ability to have the biosimilar designated as "interchangeable" with the innovator biologic. To be classified as interchangeable, the biosimilar applicant must demonstrate that the product "can be expected to produce the same clinical result as the reference product in any given patient,"[11] and allow patients to switch back and forth between the innovator biologic and the biosimilar without increasing the risk, to the patient, from that of using the innovator biologic alone.[12] Obtaining the

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[1] EMEA Guideline on Similar Biological Medicinal Products, (2005), http://www.ema.europa.eu/pdfs/human/biosimilar/043704en.pdf
[2] *Id.*
[3] *The Law of Biological Medicine: Hearing Before the S. Comm. on the Judiciary,* 108th Cong. (statement of Dr. Lester Crawford D.V.M., PhD, Acting Commissioner of Food and Drugs Department of Health and Human Services).
[4] 42 U.S.C. § 262
[5] Patient Protection and Affordable Care (PPAC) Act § 7002(a)
[6] *Id.* at § 7002(k)(2)(A)(i)(I)
[7] *Id.* at § 7002(k)(2)(A)(i)(II)
[8] *Id.* at § 7002(k)(2)(A)(i)(III)
[9] *Id.* at § 7002(k)(2)(A)(i)(IV)
[10] *Id.* at § 7002(k)(2)(A)(i)(V)
[11] *Id.* at § 7002(k)(4)(A)(ii)
[12] *Id.* at § 7002(k)(4)(B)

interchangeable classification will benefit the biosimilar manufacturer greatly if it leads to direct substitution of the innovator biologic for the biosimilar, allowing for very little advertising.

The hardest battle in creating the biosimilar pathway involved the exclusivity period for the innovator biologics. President Obama pushed for the same seven-year moratorium afforded to standard pharmaceuticals,[13] but eventually Congress awarded 12 years of exclusivity for innovator biologics.[14] In addition to the 12 years of market exclusivity, the biosimilar manufacturer cannot submit an application for a license of a biosimilar to the FDA for four years after the date on which the innovator biologic was first licensed.[15] This provides eight years for the biosimilar manufacturer to clear regulatory and IP hurdles for those innovator biologics approved since March 22, 2010. Those biosimilar manufacturers making biosimilars of innovator biologics approved before this date have to move quickly to ensure that their biosimilar is approved before the competition's (an innovator biologic licensed four years ago has eight remaining years of exclusivity and no filing moratorium). The incentive to conduct research and obtain interchangeability status comes from the Act's grant of a one-year exclusivity to the first interchangeable biosimilar for a particular innovator biologic.[16]

The Act is unusual because it does not give the FDA the usual six months or so to formulate goals and guidelines for applicants before the pathway comes into effect. The pathway was effective the minute the President signed the Act on March 22, 2010. The Act does, however, give great leeway to the FDA in how it will formulate its goals and guidelines and requires the FDA to report its goals and guidelines, with regard to biosimilars, to Congress by October 10, 2010.

The IP provisions of the Act are extremely demanding on both the innovator and the biosimilar manufacturer. They are designed to foster agreement between both parties to establish a limited set of patents which will be licensed or litigated, while leaving the door open for a possible second round of more extensive litigation. The patent term is 20 years from the date of filing, for patents filed on or after June 8, 1995, and for those patents issued prior to this date the patent term is the longer of 20 years from the date of filing, or 17 years from the date of issue.[17] This, being longer than the 12 years of exclusivity from the date of license afforded to the innovator, means that, on occasion, the biosimilar manufacturer may have to wait longer than the 12 years before being able to market their product. Naturally, this will lead to prolonged and highly contested patent litigation, which the Act, presumably, tries to avoid.

The Act requires the biosimilar applicant to provide all of the information, confidential or otherwise, contained in the biosimilar FDA application to the innovator upon whose biologic the biosimilar is referenced.[18] The information may not only contain publicly available information, such as that contained in issued patents or published patent applications, but also confidential business-critical information and trade secrets. To protect this confidential information the Act provides for a limited, rather complicated, set of individuals who are permitted to review the information. The structure is designed to preserve the confidentiality of the information, while allowing an analysis of the information in regards to patent infringement of the innovator's patents. Recipients of the information are as follows: (1) Outside-Counsel – one or more attorneys designated by the innovator, who are employees of an entity other than the innovator, and who do not engage, formally or informally, in patent prosecution relevant or related to the innovator biologic;[19] (2) In-House-Counsel

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[13] Daniel Cressy, *Biosimilars: Obama's seven year pitch*, Jun. 29, 2009, http://blogs.nature.com/news/thegreatbeyond/2009/06/biosimilars_obamas_seven_year.html (last visited May 18, 2010).
[14] PPAC § 7002(a)(7)(A)
[15] *Id.* at § 7002(a)(7)(B)
[16] *Id.* at § 7002(a)(6)(A)
[17] 35 U.S.C. § 154
[18] PPACA § 7002(a)(7)(A)
[19] *Id.* at § 7002(I)(1)(B)(ii)(I)

– one attorney that represents the innovator, who is an employee of the innovator, but does not engage, formerly or informally, in patent prosecution relevant or related to the innovator biologic;[20] and (3) The Patent Owner – a representative of the owner of a patent exclusively licensed to the innovator biologic manufacturer who has retained the right to assert the patent or participate in litigation concerning the patent.[21]

Of note, neither sub-set of individuals who are permitted to receive the confidential information from the biosimilar manufacturer is someone from the business side of the innovator. It is likely that General Counsel for the innovator will be formerly or informally involved with the patent prosecution of patents related to the innovator biologic. Therefore the innovator will have to rely on a member of their in-house counsel subordinate to their General Counsel, and their Outside-Counsel, to make very important, and potentially extremely costly, business decisions.

The sole purpose of the transfer of the confidential information is to determine whether a claim of patent infringement could reasonably be asserted against the biosimilar manufacturer if they make, import, or sell the biosimilar in the United States, after the 12 year exclusivity period expires.[22] The Act provides a specific set of rules to facilitate the determination, by both parties, on whether the biosimilar infringes any of the patent claims owned by, or licensed to, the innovator. Firstly, the biosimilar applicant has to give the innovator's group of people all of the application information within 20 days of filing an application with the FDA.[23] The innovator then has 60 days to provide the biosimilar applicant with (i) a list of all the patents for which the reference biologic manufacturer believes a claim of patent infringement could reasonably be asserted;[24] and (ii) the identity of all patents which the reference biologic manufacturer would license to the applicant.[25]

Within 60 days of receiving these lists from the innovator, the biosimilar manufacturer must provide for the innovator (i) a list of all the innovator's patents upon which the biosimilar manufacturer believes a claim of patent infringement could reasonably be asserted;[26] and (ii) with reference to each patent in the list of patents provided by the innovator, a detailed statement on a claim by claim basis of why the patent is invalid, unenforceable or not infringed,[27] or a statement stating the biosimilar manufacturer will not market their product until after the patent expires.[28]

The innovator then has the next 60 days to provide their detailed statement, to the biosimilar manufacturer, on a claim by claim basis, of the factual and legal bases for an opinion of why the patents are valid, enforceable, and infringed by the biosimilar.[29]

The next stage is for both parties to enter into good-faith negotiations to agree on which patents shall be the subject of an infringement action.[30] If the parties are unable to form an agreement, both shall provide each other with a list of patents that the other believes should be litigated.[31] Those patents which appear on each list make it to the court room.[32]

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[20] *Id.* at § 7002(l)(1)(B)(ii)(II)
[21] *Id.* at § 7002(l)(1)(B)(iii)
[22] *Id.* at § 7002(l)(1)(D)
[23] *Id.* at § 7002(l)(2)(A)
[24] *Id.* at § 7002(l)(3)(A)(i)
[25] *Id.* at § 7002(l)(3)(A)(ii)
[26] *Id.* at § 7002(l)(3)(B)(i)
[27] *Id.* at § 7002(l)(3)(B)(ii)(I)
[28] *Id.* at § 7002(l)(3)(B)(ii)(II)
[29] *Id.* at § 7002(l)(3)(C)
[30] *Id.* at § 7002(l)(4)(A)
[31] *Id.* at § 7002(l)(5)(B)(i)(I)-(II)
[32] *Id.*

The innovator is then required to bring a declaratory judgment action for validity, enforceability and infringement of their patents.[33] If the court decides that marketing the biosimilar would infringe on the innovator's patent claims, the FDA must hold on approving the biosimilar until the patent has expired.[34]

The innovator may wish to shield a patent from litigation and therefore omit it from the initial list of patents sent to the biologic manufacturer. The innovator may not wish to risk litigating the validity of a patent which underpins many of the innovator's products. However, the biosimilar manufacturer is permitted to list, in its initial opinion, any of the innovator's patents which it believes are relevant to the innovator biologic.[35] In addition, if the innovator omits a patent from their initial list of patents and the biosimilar manufacturer also omits the same patent from their list of patents, the innovator is forever barred from asserting the patent against the biosimilar manufacturer in subsequent litigation.[36] The exception are patents which are issued or published subsequent to the exchange of lists and opinions; these can be included in litigation, by the innovator, upon notification within 30 days of the patent's publication or issue.[37] These rules prevent the innovator from being able to shield patents from potentially invalidating litigation. The biosimilar manufacturer can list any patent of the innovator's it likes, forcing the innovator to litigate the patent.

The second window of litigation comes when the biosimilar manufacturer markets their product. The biosimilar manufacturer must notify the innovator 180 days before marketing the biosimilar.[38] If the innovator believes that the biosimilar manufacturer infringes on its patents then it may seek an injunction against the sale, import, or manufacture of the biosimilar in the US, until the patent expires.[39] Although the innovator cannot seek an injunction based on a patent not listed in either their initial list of patents or the biosimilar manufacturer's initial list of patents, it can litigate patents which were not previously litigated in the original declaratory judgment action. Although it is not clear why this second litigation opportunity is included, it does seem to create an incentive to test the validity of key patents as early as possible, while ensuring that the innovator has the opportunity to fully protect their intellectual property rights.

For law firms, with biotech IP specialists, the Act could mean a very lucrative opportunity. Not only is there the prospect of two rounds of lengthy, highly complex litigation, taking up to eight years to resolve, involving weeks worth of expert testimony; it also means many reams-worth of opinions, all to be written in relatively short periods of time. Both parties have to have full and detailed opinions written for every single patent relevant to the biologics, and these opinions must be written within 60 days. The opinions have to be both validity opinions and infringement opinions. The patents involved are highly complex and minutely intricate, adding to the difficulty in writing these opinions. To fulfill the requirements of the Healthcare Bill both the biosimilar manufacturer and the innovator will have to hire teams of outside-counsel, with the possibility of having 20 attorneys or more working solely on their opinions for two months. To reduce such burden, both will have to prepare in advance, as much as possible, for the prospect of requiring these opinions, hiring new outside counsel to pour over already issued patents and published applications, hypothesizing how the other party will form their opinions, and writing preliminary opinions on the validity and enforceability, or otherwise, of the patents. All this must be done while ensuring that the innovator's Outside Counsel, and the lone In-House Counsel, are kept wholly

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[33] *Id.* at § 7002(l)(6)(A)-(B)
[34] *Id.* at § 7002(c)(1)(D)
[35] *Supra* at 26.
[36] *Id.* at § 7002(l)(8)(A) The biosimilar manufacturer must provide notice to the reference biologic manufacturer 180 days before marketing of the biosimilar; *Id.* at § 7002(l)(8)(B) The reference biologic manufacturer may then seek an injunction against the biosimilar manufacturer as long as it is regarding a patent listed previously.
[37] *Id.* at § 7002(l)(7)
[38] *Supra.* at 33
[39] *Id.*

separate from prosecution of the biologic's patents. In addition, the Act sounds a signal bell to new innovators of biologics to ensure that they obtain the best possible IP protection in their patents.

It can take up to ten years from the time of inception of the invention of the new biologic to the time that the drug is first licensed by the FDA. The innovator then has 12 years of exclusivity in the market place. As a result, many of the patents which were obtained by the innovator at the start of the process will have expired before the biosimilar manufacturer is permitted to enter the market. Neither party will litigate these patents, nor write opinions on them. But for other, highly valuable patents, still be enforceable after the expiration of the 12 years of exclusivity, there will be fierce litigation.

Regardless of the course taken by any biologic manufacturer, their legal costs are set to soar. This will force an increase in the cost of research and development, and therefore an increase to the end cost of the product to the consumer, resulting in the very antithesis of the name "Patient Protection and Affordable Care Act."

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