Page 3023 - 3028

INTERNATIONAL JOURNAL OF LAW MANAGEMENT & HUMANITIES

[ISSN 2581-5369]

Volume 4 | Issue 2

2021

© 2021 International Journal of Law Management & Humanities

Follow this and additional works at: https://www. ijlmh. com/

Under the aegis of VidhiAagaz – Inking Your Brain (https://www. vidhiaagaz. com)

This Article is brought to you for "free" and "open access" by the International Journal of Law Management & Humanities at VidhiAagaz. It has been accepted for inclusion in International Journal of Law Management & Humanities after due review.

In case of **any suggestion or complaint**, please contact **Gyan@vidhiaagaz.com.**

To submit your Manuscript for Publication at **International Journal of Law Management & Humanities**, kindly email your Manuscript at **submission@ijlmh.com.**

An Overview of Legal Regulation of Biosimilars

DR. NANDITA S. PATIL[1]

ABSTRACT

Innovations in pharmaceutical sector is subject to patent and test data protection. Biosimilars is one of the pharmaceutical innovations for which there is a huge potential in developing economies. The importance of biosimilars is because of the expiration of patents and other Intellectual Property exclusivity rights. With regard to biosimilar regulatory matters, Europe is ahead of the USA. The Indian Government launched its biosimilars guidelines in Boston at the BIO industry conference on June 19, 2012. These guidelines are now revised and now Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India, 2016 is applicable. For India biosimilars could be an affordable treatment option. Approval of 98 biosimilars in India is a positive development in the field of pharmaceutical innovation.

Keywords: *Biologics, Biosimilars, patent, pharmaceutical innovation, India.*

I. INTRODUCTION

Pharmaceutical innovation is mostly based on granting patents and test data protection to innovative products.[2] Pharmaceutical innovation includes pharmaceutical drugs, vaccines, biologics and the like. Biologics are typically large protein molecules derived from living material including human, animal or microorganism. They are complex in structure and often are not fully characterized. Examples of biologicals are Insulin and erythropoietin (EPO).[3]

From a global perspective, the USA lags behind other regulated markets, specifically the European Union (EU), in terms of biosimilar competition. EU recognizes 'Bolar' clause and allows the development of conventional generics and similar biologic products during the life of an innovator's product patent, thus removing the risk of patent infringement during product development.[4] Bolar clause is introduced to overrule the decision in *Roche v. Bolar* where the court held that a generic company could be sued for patent infringement for doing necessary

[1] Author is an Assistant Professor at Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, India.
[2] Joan Rovira, et. al.,*The impact of biosimilars' entry in the EU market* ,Andalusian School of Public Health 13 (2011) available at https://www.researchgate.net/profile/Jaime-Espin/publication/281504554_Theimpact_of_biosimilars%27_entry_in_the_EU_market/links/5e95f66a92851c2f529f8660/The-impact-of-biosimilars-entry-in-the-EU-market.pdf, (last visited Feb. 20, 2021)
[3] VOET MARTIN A., THE GENERIC CHALLENGE- UNDERSTANDING PATENTS, FDA .AND PHARMACEUTICAL LIFE-CYCLE MANAGEMENT, 123 (Brown Walker Press 2011)
[4] Joan, *supra* note 2, at 19.

© 2021. International Journal of Law Management & Humanities [ISSN 2581-5369]

testing to file an ANDA (An Abbreviated Drug Application)[5] before the patent expired.[6]

There is a huge market potential for biosimilar in developing economies. For drug makers biosimilars is the next big thing, it may take a few years before it start as a mainstream revenue segment given challenges like huge investments and regulatory hurdles in developing economies.[7] The importance of biosimilars is because of the expiration of patents and other Intellectual Property exclusivity rights.

II. US LAW FOR BIOSIMILAR

Previously the FDA (US Food and Drug Administration) signaled that the first likely biological products it would consider for generic approvals are the older drugs, recombinant human insulin and human growth hormone. Earlier these drugs were approved as NDAs (New Drug Applications), making them technically more subject to becoming generic drugs than other biotech drugs that were approved under a different legal scheme and were filed as Biological License Applications (BLAs). This is because BLAs were for biologically derived medicines and products and were under jurisdiction of a different branch of FDA than the branch responsible for drugs.[8]

The Biologics Price Competition and Innovation Act (The 'Biosimilars Act') was signed into law by President Obama on March 23, 2010 as Tile VII of the Patient Protection and Affordable Care Act. This new law amends the Public Health Service Act (PHS Act). To expedite regulatory approval of biosimilars, the Act for the first time creates an abbreviated approval pathway for biological products that are demonstrated to be "highly similar" (biosimilar) to or "interchangeable" with an FDA-approved biological product.[9] This new legislation establishes two different categories of biological products approvable under the abbreviated pathway: biological products that are "biosimilar" to an approved biological product that are "interchangeable" with an approved biological product. [10] Biosimilars are deemed to contain a new active ingredient while interchangeable are considered to contain the same active as the brand product. [11] FDA refer to these new statutory provisions of the Biologics Price

[5] An abbreviated new drug application (ANDA) contains data which is submitted to FDA for the review and potential approval of a generic drug product, See https://www.fda.gov/drugs/types-applications/abbreviated-new-drug-application-anda
[6] VOET , *supra* note 3, at 105
[7] No Biosimilars roll out for the next five years, Regulatory Hurdles, Huge Fund Requirements hold up plans, 1 Financial Chronicle, Delhi Edition, August 29, 2014
[8] VOET , *supra* note 3, at 122-123.
[9] *Id.* at 125.
[10] *Id.* at 125-126.
[11] *Id.* at 127.

© 2021. International Journal of Law Management & Humanities [ISSN 2581-5369]

Competition and Innovation Act of 2009 (BPCI Act).[12]

In order to obtain FDA approval, an applicant must demonstrate that the biological product is biosimilar to the reference product based on analytical studies, animal studies and clinical studies, that it uses the same mechanism of action, the same route of administration, dosage form and strength and is for the same indication and use. The biosimilars are required to meet the prevailing standards for safety, purity and potency for the facility where it is manufactured. The legislation also provides the FDA with the discretion to waive any of the foregoing requirements.[13] It establishes market exclusivity periods for the first biological product approved as interchangeable with the brand-name product. The range of the exclusivity period is 12 months to 42 months.[14]

Due to the challenges of developing biosimilars, the Biosimilars Act may encourage manufacturers to develop 'biobetters' instead of lower cost generic biologics. Biobetters are improved versions of existing biological drugs. A biobetter can make improvement upon the original in a number of ways including, for instance, reducing the side-effect profile of the drug. Since biobetters are innovative drugs that are regulated their approval is via the Biologics Licensing Application (BLA) route.[15]

Branded biological products approved as BLAs are entitled to 12 or 12.5 years of exclusivity from date of approval, consisting of 4 years of data exclusivity, 8 years of marketing exclusivity and 6 months of pediatric exclusivity. That means applications for approval of a biosimilar for such reference product will not be accepted by FDA until the end of 12 or 12.5 years from approval of the reference product.[16]

This new 12 year exclusivity for biological products is fairly longer and will likely to have a profound effect on the future commercial thinking of the pharma industry. A number of large pharma companies around the world have already reported that they are planning to focus future R&D investment on obtaining approval of new biological products.[17] Settlement agreements are permissible under the Biosimilar Act because litigation of the innovator's patents is not a prerequisite of obtaining exclusivity as it is with the Hatch Waxman Act.[18] Omnitrope of Sandoz approved in USA was considered as biosimilar before the creation of

[12] *Id.* at 125.
[13] *Id.* at 127.
[14] BROUGHER JOANNA T., INTELLECTUAL PROPERTY AND HEALTH TECHNOLOGIES-BALANCING INNOVATION AND THE PUBLIC'S HEALTH 166 (Springer 2014)
[15] BROUGHER *supra* note 14, at 172
[16] VOET , *supra* note 3, at 127.
[17] *Id.* at 128.
[18] BROUGHER *supra* note 14, at 170

biosimilar regulations. Teva's biosimilar Tevagrastim (Neutroval) is also approved in USA under the BLA route.[19] Till December 2020, 29 biosimilars got approval in USA by the Food and Drug Administration.[20]

III. EUROPEAN REGULATION FOR BIOSIMILAR

The EU has led the process of regulating the authorization of biosimilars and has become a benchmark for other countries.[21] Since 2005 a number of generic biotechnology drugs have been approved in Europe as "biosimilars".[22] With regard to biosimilar regulatory matters, Europe is ahead of the USA. The EU Directive 2003/63/EC and Directive 2004/27/EC along with the guidelines EMES/CHMP/437/04, EMEA/CHMP/BWP/49348/2005 and EMEA/CHMP /BWP/ 42382/2005 regulates biosimilar.[23] On 1st July 2019 Regulation (EU) 2019/933 of the European Parliament and of the Council of 20 May 2019 amending Regulation (EC) No 469/2009 concerning the supplementary protection certificate for medicinal products entered into force. It allows exemptions to extensions of patent rights through supplementary protection certificates (SPCs)[24]. The waiver would enable companies to manufacture biosimilars before the SPCs on the original biologics expire.[25]

In late 2010, the EMA formerly EMEA published guidelines for biosimilar antibodies.[26] In the antibody market offers an opportunity to generic companies to enter into it as the patents on key brand products expire .The EMA has received requests for scientific advice on six biosimilar antibodies and Teva is already conducting clinical studies comparing its generic antibody to Roche's antibody RITUXAN.[27] The EMA (European Medicines Agency) has already approved 59 biosimilars as of 12 February 2021, including generic versions of human growth hormone, erythropoietin (EPO) and G-CSF.

IV. BIOSIMILARS PROTECTION IN INDIA

For marketing the biosimilar products in EU, Canada and elsewhere, India is becoming a major

[19] Andrew Bourgoin, Beth Nuskey, An Outlook on US Biosimilr Competition-White Paper 3 Thomson Reuters, (April 2013)
[20] *See* https://www.fda.gov/drugs/biosimilars/biosimilar-product-information
[21] Joan, *supra* note 2, at 7.
[22] VOET , *supra* note 3, at 64.
[23] Joan, *supra* note 2, at18
[24] Supplementary protection certificates (SPCs) are an intellectual property right that serve as an extension to some specific patented pharmaceutical and plant protection products that have been authorised by regulatory authorities, See,https://ec.europa.eu/growth/industry/policy/intellectual-property/patents/supplementary-protection-certificates en
[25] Marek Świerczyński & Zbigniew Więckowsk, Biosimilars and the Patent Law, 12 (2)MEDICINE, LAW & SOCIETY 24-25, 21-38 (2019).
[26] VOET , *supra* note 3, at 129.
[27] *Ibid.*

player in manufacture of such products At present bio-similar products are being treated as new drugs on an ad-hoc basis since there are no regulations on bio-similars. Therefore, science based specific regulations is needed to be developed for approval of bio-similar products by Ministry of Health and Drug Controller General of India.[28]

The Indian Government launched its biosimilars guidelines in Boston at the BIO industry conference on June 19, 2012. The guidelines are aimed at providing a "clear" regulatory pathway for manufacturers of biologic similars and will be applied to new filings now. These guidelines prescribe the quality, preclinical studies and clinical trial requirements of similar biologics in India.[29] The guidelines issued by India on similar biologics are comparable in many respects to those issued by the USA and EU.[30]

These guidelines are now revised and now Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India, 2016 is applicable. It defines a Similar Biologic product as the one "which is similar in terms of quality, safety and efficacy to an approved Reference Biological product based on comparability."[31] These guidelines on similar biologics provides for regulatory requirement for the pre-marketing, pre- clinical, clinical and post-marketing, and further provides for the requirements related to manufacturing process and quality control. CDSCO regulates the approval of drugs in India.

Major Indian drug manufacturers such as Dr. Reddy, Sun Pharma and Ranbaxy are already major suppliers of generic drugs in India and around the world including the U.S. Now they are gearing up to break into biosimilars. Indian generic companies are currently focusing on four biotech markets: EPO, human insulin, interferon and G-CSF. Biocon's experience with both novel and similar biologic therapeutics offers portfolio diversity that may prove to be a competitive advantage in global markets.[32]

One of the first Indian companies to be associated with follow-on biologic development, Dr Reddy's Labs, has had versions of both monoclonal antibody and recombinant protein products in less regulated markets for over 5 years.[33]

Reliance Life Sciences currently has multiple follow-on biologic therapies launched, including

[28]Report of the Task Force, Ministry of Commerce & Industry, 119 December 12, 2008. Available at http://commerce.nic.in/publications/Report%20Tas%20Force%20Pharma%2012th%20Dec%2008.pdf?id=16
[29]http://www.biospectrumasia.com/biospectrum/regulatory/1969/india-announces-biosimilar-guidelines (last visited February 13, 2015)
[30] Rajiv Kumar and Jagjit Singh, Biosimilar drugs: Current status, 4 (2)Int J Appl Basic Med Res.63-66 (2014) available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137643/ (last visited Feb.13, 2015)
[31]*See*https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NTU0NA==, p. 36
[32] Andrew, *supra* note 19, at 13.
[33] *Ibid*.

versions of filgrastim, epoetin, and interferon products. Additionally, the Indian based company is aiming to compete in the infliximab market with a similar version of Remicade, currently in clinical trials. BIOCON BIOLOGICS is among the top 5 insulins players globally, it's rh-Insulin is approved in 40+ countries and Insulin Glargine is approved in 60+ countries. As with regulated markets, a major driver for competition for biologic products in India and other emerging markets is to reduce the high cost of biologic medicines. Continued competition for biologics is expected in India following the adoption of guidelines regarding the approval process for similar biologics.[34] India has approved 98 biosimilars till 2019.[35]

V. CONCLUSION

Patent law is an incentive for innovation but it must be balanced with the public interest in fostering public health. Biosimilars can play a significant role in addressing the issues of affordability and accessibility of medicines. EU is the initiator in providing regulatory framework for biosimilars followed by other countries. The USA lags behind the European Union (EU), in terms of biosimilar competition. India issued its earlier biosimilar guidelines in 2012 and revised it in 2016. These Biosimilar guidelines aims to promote biosimilar products and thereby will help to balance biologic innovation and access to affordable biosimilar medicines. There is a huge market potential for biosimilar in developing economies like India. Approval of 98 biosimilars in India is a positive development in the direction of providing affordable treatment option.

*****

[34] *Id.* at 13-14

[35] Special report India: The emerging hub for biologics and biosimilars, Knowledge Paper, 2 available at https://birac.nic.in/webcontent/Knowledge_Paper_Clarivate _ABLE_BIO_ 2019.pdf (last visited Feb. 19, 2021)

© 2021. International Journal of Law Management & Humanities [ISSN 2581-5369]