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AN ANALYSIS OF THE PATENT LINKAGE SYSTEM AND DEVELOPMENT OF THE BIOSIMILAR INDUSTRY IN TAIWAN

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INTRODUCTION

Traditional drugs typically consist of small molecules produced by chemical processes. In contrast, biologics—including many vaccines and purified proteins—are protein-based therapeutic drugs produced by biological processes.[1] Current biologics with global sales of five billion dollars or more include Humira® for the treatment of rheumatoid arthritis; Rituxan® for Non-Hodgkins lymphoma; Avastin® for breast, colorectal, and ovarian cancer; Harvoni® for hepatitis C and Seretide® for asthma.[2] With billions of dollars' worth of biologics (originator)[3] going off patent, Variant Market Research estimated that the global market for biosimilars[4] (non-originator biologic pharmaceutical products) will reach $46 billion by the year 2025.[5] Biosimilar companies in Taiwan—such as Tanvex, Mycenax, Eirgenix and Glyconex—are pushing for their own

1.Linfong Tzeng, *Follow-On Biologics, Data Exclusivity, and the FDA*, 25 BERKLEY TECH. L.J. 135, 136 (2010).

2. Kathlyn Stone, *The Top 10 Biologic Drugs in the United States*, BALANCE (Oct. 13, 2016), http://bit.do/Topl0BiologicDrugs.

3. In this article, the term "originator" refers to drug manufacturers who hold the patent rights to a particular drug approved by the food and drug authorities.

4. In the United States, the term "biosimilars" is also known as "Follow-on biologic" (FoBs) or "Follow-on protein". Sahil Kumar, Shalini Chawla & Siddhartha Dutta, *Biobetters: Betting on the Future*, 4 J. RATIONAL PARMACOTHER. RES., 13, 14 (2018). In Canada, it is known as "Subsequent Entry Biologics" and in the European Union, "Similar Biological Medicinal Product". *Id*.

5. *Brief Discussion on the Biosimilar Industry*, HUA NAN SHEN NEWS (March, 5, 2018)https://events.entrust.com.tw/news/20190305weekly-499 (translation by author).

versions of biosimilars in order to get a slice of this lucrative market.[6]

The Government of Taiwan has been supportive of the development of local biosimilar industry. In an effort to join the Trans-Pacific Partnership Agreement (now the Comprehensive and Progressive Agreement for Trans-Pacific Partnership (CPTPP)),[7] the government introduced a patent linkage system by amending the Pharmaceutical Affairs Act (PAA).[8] The system is modeled after the US's patent linkage system designed for small molecule drugs under the Hatch Waxman Act (HWA).[9] However, unlike the US's system,[10] the Taiwanese system covers both small molecule generic drugs and large molecule biosimilars.[11] Based on their experience with the pa-

6. *Grabbing A Slice of the $43.1billion Biosimilar Pie*, BUSINESS TODAY (July, 3 2019), https://www.businesstoday.com.tw/article/category/80392/post/201907030036/搶生物相似藥341億美元大餅　台廠妙打「特色戰」才能贏/ (translation by author).

7. Ya-Hsin Weng, *An Observation on the Legislative Amendment Process of the Pharmaceutical Affair's Act for Patent Linkage: The Lost National Health Welfare and Interests of the Local Drug Industry*, 23 TAIWAN BAR J. 14,14 (2019) (translation by author).

8. The official English text of the Pharmaceutical Affairs Act, also known as "Yao Shi Fa" ((藥事法) in Mandarin) can be found at http://law.moj.gov.tw/Eng/LawClass/LawAll.aspx?PCode=L0030001, while the Mandarin version can be found at http://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=L0030001. When referring to any provisions of the Pharmaceutical Affairs Act, this Article cites or quotes the official English text.

9. Ping-Hsun Chen, *Analysis of the Proposed TPP-Related Patent Linkage System in Taiwan*, 30 J.L. & HEALTH 55, 58,59 (2017).

10. The United Sates promulgated two systems of abbreviated new drug application for both small molecule drugs under the HWA and for biologics under Biologics Price Competition and Innovation Act (BPCIA) of 2009 (Public Law 111-148), 42 U.S.C. § 262. However, some commentators argue that there is no reasoned basis for treating generic biologics and traditional generics disparately. *See* Gregory N. Mandel, *The Generic Biologics Debate: Industry's Unintended Admission that Biotech Patents Fail Enablement*, 11 VA. J.L. & TECH. 1, 14 (2006).

11. *生物相似藥不可納入專利連結* [Biosimilar Should Not Be Included in The Patent Linkage System], TAIWAN PHARM. MFR. AND DEV. ASS'N 4 (Mar. 12 2019), http://www.cpmda.org.tw/file/Laws/1080416v10.pdf (translation by author) [hereinafter Biosimilar Should Not Be Included in The Patent Linkage System].

tent linkage system under the HWA,[12] biosimilar industry representatives in Taiwan contended that the adoption of patent linkage system will be detrimental to the development of local industry.[13] They argued that, as an emerging industry in Taiwan, most biosimilar companies are small and medium in size without significant funding for research, product lines, or production capacity.[14] By adopting a patent linkage system, foreign biologics companies would implement evergreening strategies[15] to delay the marketing of locally produced biosimilars,[16] conduct improper patent listing,[17] and abuse automatic stays.[18]

These concerns are not unfounded, as between 2016-2018, over 60% of of drug-related patents in Taiwan are applied by foreign companies.[19] As biologics are becoming increasingly im-

12. Anna B. Laakmann, *The Hatch-Waxman Act's Side Effects: Precautions for Biosimilars*, 47 LOY. L. A. L. REV. 917, 927-932 (2014) (discussing the implications of HWA such as evergreening and pay-for-delay).

13. Biosimilar Should Not Be Included in The Patent Linkage System, *supra* note 11, at 8-9.

14. *Winning with Biosimilar- Opportunities in Global Markets*, 12 DELOITTE (2016), https://www2.deloitte.com/content/dam/Deloitte/tw/Documents/life-sciences-health-care/tw-biosimilars-inglobal-markets.pdf.

15. C. Scott Hemphill & Bhaven N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. HEALTH ECON. 327, 327–28 (2012) (stating that such strategies include obtaining patents on a drug's specific ingredients, an intermediate product, or on new uses for the product).

16. Branded drug manufacturers have devised several ways to extend their exclusivity, for example by marketing authorized generics, to pay generic manufacturer to delay market entry or adding irrelevant and trivial amendments to prolong the exclusivity of the patent on active ingredient. *See generally* Janet Freilich, *The Paradox of Legal Equivalents and Scientific Equivalence: Reconciling Patent Law's Doctrine of Equivalents with the FDA's Bioequivalence Requirement*, 66 SMU L. REV. 59, 104 (2013).

17. Jacob S. Wharton, *"Orange Book" Listing of Patents under the Hatch Waxman Act*, ST. LOUIS UNIV. L. J. 1027, 1038 (2003) (discussing that improper listing of patents has been a source of criticism).

18. Kyung-Bok Son, Ruth Lopert, Deborah Gleeson & Tae-Jin Lee, *Moderating the Impact of Patent Linkage on Access to Medicines: Lessons from Variations in South Korea, Australia, Canada, and the United States*, 14 GLOBALIZATION HEALTH, 1, 2–3 (2018). (Automatic stays "enables the rights holder to obtain a de facto injunction against a potential infringer without any evaluation of the merits of its claim or the nature of the putative infringement.")

Biotechnology Industry in Taiwan White Paper 2019, 276-277 MINISTRY OF ECONOMIC AFFAIRS (July 2019), https://

portant in clinical medicine, high prices for biologics could increase the financial burden for Taiwan's National Health Insurance (NHI).[20] Studies show that, from 2014 to 2016, expenditure on biologics amounted to 13-14% of Taiwan's NHI targeting on cancer treatment and autoimmune diseases.[21] For example, Herceptin, a biologic for breast cancer, accounts for nearly 3 billion New Taiwan Dollars each year.[22] Without competition from biosimilars, there may be significant issues, such as financial burden on the government and limited patient access to medicine.[23] In addition, biosimilars are far more costly and time consuming to develop than small molecule generic drugs.[24] In the US, the Federal Trade Commission (FTC) has estimated that entry into the biosimilar market will take $100 to $200 million and between 8 to 10 years compared to the $1–5 million for a small molecule generic drug.[25] Hence, in order to develop biosimilar industry in Taiwan, the government should

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www.biopharm.org.tw/images/2019/Biotechnology-Industry-in-Taiwan-2019.pdf.

20. Weng, *supra* note 7 at 16, 19. National Health Insurance was launched on March 1, 1995 to safeguard the right to health care of all of the country's citizens. The National Health Insurance program is compulsory for all citizens starting from birth. It is founded on the concept of mutual assistance and depends on the insured paying their premiums according to regulations. By law, every Taiwanese citizen with official residency or foreign national living in Taiwan with an Alien Resident Certificate (ARC), regardless of age, gender, or employment status, must enroll in the program. Also, this insurance program lasts an entire lifetime. No one may arbitrarily withdraw, except for those who lose their insurance eligibility (such as people who give up their Taiwan citizenship, move abroad, let their Alien Resident Certificate expire, or a person who goes missing). NAT'L HEALTH INS. ADMIN., PROGRAM OVERVIEW (2016) (Taiwan), https://www.nhi.gov.tw/English/Content_List.aspx?n=7B24D0240347DAA8&topn=BCB2B0D2433F6491.

21. Biosimilar Should Not Be Included in The Patent Linkage System, *supra* note 11 at 3.

22. *Id*.

23. Yenyen Chen, *"[To Please the United States] Patent Linkage for Biosimilars Stifles Taiwanese Manufacturers and Impacts on the National Health Insurance Expenditure"* UPMEDIA (June 25, 2019, 6:20PM), www.upmedia.mg/news_info.php?SerialNo=65954 (translation by author).

24. Brendan McArdle, *Rumble in the BPCIA: Biologics vs. Biosimilars*, 17 HOUS. J. HEALTH L. & POL'Y 381,384 (2017).

25. FED. TRADE COMM'N, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION (2009).

ensure that it balances incentives for both biologic and biosimilar companies.

This article explores whether the adoption of a patent linkage system in Taiwan will deter the development of local biosimilar industry. Part I explores the unique characteristics of biosimilars. Part II reviews the patent linkage system in CPTPP and Taiwan's newly adopted patent linkage system. Part III and IV explore the potential issues for Taiwan's patent linkage system. Part V examines the patent linkage system in South Korea that is favored by Taiwan's biosimilar industry as a model to follow. Lastly, in Part VI, this paper identifies two areas in which the current patent linkage system could improve.

I. BIOSIMILARS

A. What Makes Biosimilars Unique?

Pharmaceutical drugs can be roughly divided into two categories: chemical compounds (small molecule drugs) and biologics (large molecule drugs).[26] Biologics are protein-based drugs typically made by utilizing cell lines with recombinant DNA technology to synthesize the biologic molecule.[27] Unlike small-molecule drugs, which are one-dimensional and chemically-defined molecular entities, biologics are much larger in size and have greater structural complexity, including primary, secondary, tertiary and sometimes quaternary structures.[28] According to the World Health Organization (WHO), a biotherapeutic product similar in quality, safety and efficacy to an already licensed reference biotherapeutic product is called a biosimilar.[29] In Taiwan, "a biosimilar is defined as a biotherapeutic derived using biotechnology, and is similar in quality, safety

26. McArdle, *supra* note 24, at 381.

27. Joyce Wing Yan Tam, *Biologics Revolution: The Intersection of Biotechnology, Patent Law and Pharmaceutical Regulation*, 98 GEO. L.J. 535, 535 (2010).

28. *See* Lynne A. Bui, Susan Hurst, Gregory L. Finch, Beverly Ingram, Ira A. Jacobs, Carol F. Kirchhoff, Chee-Keng Ng & Anne M. Ryan, *Key Considerations in the Preclinical Development of Biosimilars*, 20 DRUG DISCOVERY TODAY 3, 4 (2015).

29. *WHO Expert Committee on Biological Standardization*, WORLD HEALTH ORGANIZATION [WHO], annex 2 (2013), https://www.who.int/biologicals/expert_committee/TRS_977_60th_report.pdf?ua=1.

and efficacy to an already licensed biotherapeutic in Taiwan."[30] Taiwan approved its first biosimilar in 2010, and administrative regulation guidelines on monoclonal antibody and biosimilars in general were introduced in 2012 and 2013, respectively.[31]

Biological drugs are molecules produced by living cells under complicated manufacturing steps..[32] The key characteristics of these molecules, known as critical quality attributes (CQAs), can vary either in the manufacturing process or on post-translational modifications that occur in the cellular.[33] Changes in CQAs can occur at different stages of the manufacturing process, and small modifications to the process can alter biosimilar attributes impact clinical effectiveness and safety.[34] Developing robust biosimilar manufacturing capabilities requires a pointed focus on matching the originator CQAs as closely as possible.[35] With the current level of scientific knowledge, it is not possible to determine whether two biologics are, in fact, identical.[36]

B. The Process of Reverse Engineering Biosimilars

Unlike small molecules generics, which usually include an identical active ingredient that is chemically identical to the originator's active ingredient and can be chemically synthesized in a predictable and replicable way,[37] replication is rather

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30. *生物相似性藥品查驗登記基準* [*Guideline on Similar Biological Medicinal Products*], TAIWAN FDA (June 12, 2015), https://www.fda.gov.tw/TC/newsContent.aspx?id=13721&chk=51be588f275b4cdab798e1a5ebeaaa59&param=pn%3D2%26cid%3D3%26cchk%3D46552e96810a42c383e1bd5e42344633%26key1%3D%25e5%2585%25ac%25e5%2591%258a (translation by author).

31. I-Chun Lai, *Introduction to Taiwan's Guideline on Similar Biological Medicinal Products- Clinical Point of View*,
53, J. CHINESE STAT. ASS'N 1, 2,6 (2015) (translation by author).(translation by author).

32. Arnold G. Vulto & Orlando A. Jaquez, *The Process Defines the Product: What Really Matters in Biosimilar Design and Production?,* 56 RHEUMATOLOGY IV14, IV14 (2017).

33. *Id*.

34. *Id*.

35. *Id*. at iv15.

36. *See* Erika Lietzan & Emily Alexander, *Biosimilars: What US Regulators Might Learn from Others*, REG. AFF. PHARMA 18, 19 (2011).

37. *See* Jeanne Yang, *A Pathway to Follow-On Biologics*, 3 HASTINGS SCI. & TECH. L.J. 217, 223 (2011). (While generic chemical drugs can be identical

complicated for biosimilars.[38] In order for a biosimilar manufacturer to be confident that it has duplicated an originator firm's biologic, it must have knowledge of the originator's manufacturing process and cell lines.[39] The selection of the host organism, the identification of the particular cell line, the culture and media conditions, and purification process—all of which can impact the characteristic attributes of the final products.[40] This requisite knowledge highlights how difficult it is to exactly mimic the molecular structure of the original biological product[41]—a challenge perhaps even more difficult than developing an originator.[42] European biosimilar product manufacturers, on average, expend between $100–$250 million and often seven to eight years on the reverse engineering processes necessary to bring these products to market.[43]

A biosimilar manufacturing process's development is complicated early on by a number of constraints encountered at the start of development.[44] First, the development must identify the originator fingerprint's qualitative attributes so as to set limits on the potential variability of the biosimilar.[45] Second, because the biosimilar manufacturer does not know the originator molecule's manufacturing process, it must develop a new process that ensures the biosimilar will match the originator fingerprint as closely as possible.[46] Third, the biosimilar candidate must be thoroughly characterized before it can be subject-

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to the original, brand name drug, it is virtually impossible to create identical follow-on biologics. Chemical drugs are easy to reproduce because their structures are precisely defined.)

38. *Id*. at 223.

39. Huub Schellekens, *Commentary, How Similar Do 'Biosimilars' Need to Be*?, 22 NAT. BIOTECHNOLOGY 1357, 1357 (2004).

40. Paul J. Declerck*, Biologicals and Biosimilars: A Review of the Science and its Implications*, 1 GENERICS AND BIOSIMILARS INITIATIVE J. 13, 13 (2012).

41. Fernando de Mora, *Biosimilar: What It Is Not*, 80 BRIT. J. CLIN. PHARMACOLOGY. 949, 952 (2015).

42. Vulto & Jaquez, *supra* note 32 at iv20.

43. Gary Walsh, *Biopharmaceutical Benchmarks 2014*, 32 NAT. BIOTECHNOLOGY 992, 995 (2014).

44. Vulto & Jaquez, *supra* note 32 at iv20.

45. *Id*.

46. *Id*. This requires "the cell culture and purification process conditions to be adjusted continuously, while screening hundreds of new cell lines during development until the fingerprint of the biosimilar is guided into the range of similarity, one qualitative attribute at a time." *Id*.

ed to confirmatory clinical trials.[47] The complexity of both biologic molecules, the necessity of producing them in living organisms, and the end-product structure's sensitivity to differences in the manufacturing process, crafting an exact biosimilar replica is nearly impossible.[48]

II. COMPREHENSIVE AND PROGRESSIVE AGREEMENT FOR TRANS-PACIFIC PARTNERSHIP AND TAIWAN'S PATENT LINKAGE

Patent linkage is a regulatory mechanism that links drug regulatory approval to patent status.[49] With patent linkage, drug regulatory authorities are required to deny marketing approval of a generic if there is a patent covering the reference product.[50] Thus, an expired or invalid patent is a prerequisite to marketing authorization.[51] Patent linkage systems provide a complex web of protection to the originator.[52] First, patent exclusivities prevent others from using, selling, or importing the patented product.[53] Second, patent linkage also provides data exclusivity that supplements patent protection by prohibiting generic manufacturers from relying on an originator's clinical data to demonstrate the safety and efficacy of generic drugs.[54]

Theoretically, by preventing competitors from free riding on the efforts of originators to establish safety and efficacy, data exclusivity provisions incentivize biopharmaceutical companies

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47. *Id.*

48. *See Biotech Drugs: Hearing Before S. Comm. on Health, Educ., Labor and Pensions*, 110th Cong. 2 (2007) (statement of Nicolas Rossignol, Admin'r of European Comm'n Pharmaceuticals Unit).

49. Ravikant Bhardwaj, K D Raju & M Padmavati, *The Impact of Patent Linkage on Marketing of Generic Drugs*, 18 J. INTELL. PROP. RTS. 316, 316 (2013).

50. *Id*, at 316– 18.

51. Eugenia Costanza Laurenza, *The Scope of Patent Linkage in the US-South Korea Free Trade Agreement and the Potential Effects on International Trade Agreements*, 6 EUR. J. RISK REG. 439, 439 (2015).

52. Erika Lietzan, *The Myths of Data Exclusivity*, 20 LEWIS & CLARK L. REV. 91, 96-100 (2016).

53. WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 316 (2003) (the strongest case for patents in their present form is said to be found in a subset of the drug industry).

54. *See generally* Jerome H. Reichman, *Undisclosed Clinical Trial Data under the TRIPS Agreement and Its Progeny: A Broader Perspective*, IPRSONLIINE (2004), http://www.iprsonline.org/unctadictsd/bellagio/docs/Reichman Bellagio4.pdf.

to invest in the development of novel biologic products.[55] They serve to prevent drug regulatory entities do notfrom inadvertently contributing to patent infringement by granting marketing rights to a competitor of the originator company.[56] Further, this prerequisite also serves to allow for the early resolution of patent disputes and prevent complex litigation for marketing an infringing product.[57]

A. Patent Linkage in The CPTPP

Taiwan's newly implemented patent linkage is a result of the partial effort to join the CPTPP.[58] Although patent linkage is not a requirement of the WTO Agreement on Trade Related Aspects of Intellectual Property Rights (the TRIPs Agreement),[59] under the CPTPP, patent linkage is mandatory.[60] Patent linkage is applied after the term of test data protection. Under Article 18.50(1) of the CPTPP, if a previously approved

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55. Kristina M. Lybecker, *Essay: When Patents Aren't Enough: Why Biologics Necessitate Data Exclusivity Protection*, 40 WM. MITCHELL L. REV. 1427, 1431 (2014).

56. Son, Lopert, Gleeson & Lee, *supra* note 18, at 1–2.

57. *Id*.

58. The TPP is a multilateral trade agreement between twelve countries which include Australia, Brunei Darussalam, Canada, Chile, Japan, Malaysia, Mexico, New Zealand, Peru, Singapore, the United States, and Vietnam. *Summary of the Trans-Pacific Partnership Agreement*, DEP'T FOREIGN AFF. TRADE (Austl.) https://www.dfat.gov.au/trade/agreements/not-yet-in-force/tpp/Pages/summary-of-the-tpp-agreement. After the US left the TPP in 2017, led by Japan and Australia, TPP continued under the name CPTPP in 2018 and the provisions of the TPP Agreement, done at Auckland on 4 February 2016 are incorporated into and made part of the CPTPP. See *Taiwan Seeks Japan Backing for CPTPP Membership*, VOICE OF AMERICA (Sept 7, 2019), https://www.voacantonese.com/a/taiwan-seeks-japan-backing-for-cptpp-membership-20190906/5073053.html.

59. *See* Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 299.

60. *See* Trans-Pacific Partnership Agreement, art. 18.51, signed Feb. 4, 2016 (not in force), https://ustr.gov/trade-agreements/free-trade-agreements/trans-pacific-partnership/tpp-full-text [hereinafter TPP Agreement] (last visited Oct. 19, 2020). The United States withdrew from TPP. Presidential Memorandum Regarding Withdrawal of the United States from the Trans-Pacific Partnership Negotiations and Agreement (Jan. 23, 2017), https://www.whitehouse.gov/presidential-actions/presidential-memorandum-regarding-withdrawal-united-states-trans-pacific-partnership-negotiations-agreement.

product is a new pharmaceutical product,[61] any later applicant may not rely on the safety and efficacy data of such previously approved product for at least 5 years after the date of its marketing approval. However, member states are presented two options: "hard" or "soft" patent linkage.[62]

Article 18.51 of the CPTPP mandates that no one can obtain regulatory marketing approval for a patented drug unless they either own the patent rights to the drug or have given the patent holder notice and opportunity to address any potential patent infringement.[63] However, Article 18.51 requires only that "a system" be put in place to provide notice to patent holders that others are seeking to market their products.[64] Article 18.51 does not specify what form the system should take, apparently leaving each CPTPP member to craft a system for themselves.[65] According to Article 18.53(1)(a) of the CPTPP, a system is required to provide notice to a patent holder or to allow for a patent holder to be notified prior to the marketing of such a pharmaceutical product, that such other person is seeking to market that product during the term of an applicable patent claiming the approved product[66] or its approved method of use.[67]

With regard to biologics, Article 18.51(2) of the CPTPP defines "biologic" so include, at least, products that are, or contain, a protein produced via biotechnology processes meant for human consumption to prevent, treat, or cure diseases or conditions.[68] The CPTPP leaves member nations with two options

61. *Id.* art. 18.52 (a new pharmaceutical product means a pharmaceutical product that does not contain a chemical entity that has been previously approved).

62. Max Rubinson, *Exploring the Trans-Pacific Partnership's Complexities through the Lens of Its Intellectual Property Rights Chapter*, 31 EMORY INT'L. REV. 449, 460 (2017). "Hard patent linkage requires coordination between a country's patent office and regulatory agency and automatically prohibits regulatory approval of a generic-the patent holder need not seek private enforcement of rights to bar approval. Under soft patent linkage, a patent holder must be notified of prior approval and have adequate time to seek remedies." *Id.*

63. See TPP Agreement, *supra* note 60.

64. TPP Agreement, *supra* note 60, art. 18.51(1)(a).

65. *Id.* art 18.51.

66. *Id.* art. 18.53(1)(a) (introducing a new pharmaceutical product with a chemical entity that has been previously approved in that Party).

67. See TPP Agreement, *supra* note 60.

68. *Id.*, art. 18.51(2).

regarding biologics. Countries can either provide: (1) eight years of market exclusivity from the date the biologic is approved in the country concerned,[69] or (2) five years of market exclusivity from the date the biologic is approved in the country concerned and other measures to deliver a comparable market outcome. [70]

B. Taiwan's Amended Pharmaceutical Affair Act

Taiwan's patent linkage system was introduced via a revision to the Pharmaceutical Affairs Act (PAA), which was approved in December 2017 and entered into force on August 20, 2019.[71] The PAA governs drugs, medical devices, pharmaceutical companies, pharmacies, and other relevant matters.[72] Chapter 4 of the PAA regulates the proceedings of registration and market approval of medicaments. Chapter 4-1 provides a patent linkage system for generic drug permit applications, which also apply vis-à-vis to biosimilars.[73] The patent linkage system forces a generic drug company to confront patent lawsuits brought by an originator company. To do so, the Taiwan Patent Act has also been amended to provide a cause of action for a pioneer company to sue a generic company if the latter files an Abbreviated New Drug Application (ANDA) application.[74]

According to Article 48-3 of the PAA, an eligible patent is a patent claiming: (1) a material; (2) a combination or formula; and (3) pharmaceutical use. A biologic's patent application claims typically fall into one of three categories: (1) composition

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69. *Id.* art. 18.51(1)(a).

70. *Id.* art. 18.51(1)(b)(i).

71. Roger Chang., *Four Important Aspects of Upcoming Implementation of Patent Linkage in Taiwan*, LEE & LI (Sept. 28, 2018), https://www.leeandli.com/EN/Newsletters/6114.htm.

72. Pharmaceutical Affairs Act, *supra* note 8, art. 1 ¶ 2.

73. [See "*The Explanation of the Draft Regulations for the Patent Linkage of Drugs* (西藥專利連結施行**辦法**草案逐條說明)", MINISTRY OF HEALTH AND WELFARE (Jan. 30, 2019), https://www.mohw.gov.tw/cp-4261-46293-1.html.(Originally Taiwan's patent linkage only applies to small molecule drugs, however, despite protests from biosimilar industries, biosimilar have also been included. In the Draft, the Ministry of Health and Welfare stated that since generic and biosimilar are considered as drugs in the PAA and both rely on the data of the originator, they should be treated alike in patent linkage system.)

74. Zhuanli Fa (專利法) [Patent Act] (Executive Yuan, Proposed Amendments to the Patent Act, Government Proposal No. 15694), art. 60-1 (translation by author).

claims, (2) method/process claims, and (3) source claims.[75] Due to the close relation between biologic products and their manufacturing methods and processes, claims over their composition and method or process are often intertwined.[76] However, the PAA does not allow the claiming of manufacturing process patents.[77] Article 48-3 of the PAA requires a drug permit holder of a new drug to submit patent information to the central health authority within forty-five days from the day after the holder received a drug permit. Patent listing must be made online through the Taiwan Food and Drug Administration's (TFDA) database.[78] If the permit holder fails to do so, Chapter 4-1 will not apply.[79] According to Article 48-4.1(1)-(4), for each drug patent, a New Drug Permit (NDP) holder has to submit three pieces of information:[80] (1) the patent number; (2) the last day of the term of protection; and (3) the current owner's name or title, nationality, residence, domicile or business place;[81] additionally, it provides if the patentee or the exclusive licensee under the third item does not have a domicile or a business office in the R.O.C., an agent thereof shall be appointed. The appointed agent's name, place of domicile or business office shall be submitted.

Article 48-9 of the PAA requires that when applying for a drug permit, an applicant for Abbreviated New Drug Application (ANDA) must declare to the central health authority all of the following situations: (1) whether patent information was documented for the new drug; (2) whether patents corresponding to the new drug have expired; (3) after the patents corresponding to such new drug expired, whether the drug permit

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75. Eric Lawrence Levi, *Using Data Exclusivity Grants to Incentivize Cumulative Innovation of Biologics' Manufacturing Processes*, 66 AM. U. L. REV. 911, 943 (2017) (footnote omitted).

76. *Id*. (footnote omitted).

77. *See* Pharmaceutic Affairs Act, *supra* note 7, art. 48-3.

78. *See* Roger Chang, *New Rules in Taiwan Pharma to Enact Patent Linkage*, ASIA BUS. L. J. (Mar. 19, 2018), https://www.vantageasia.com/new-rules-taiwan-pharma-enact-patent-linkage/ (this is similar to the requirement under Hatch Waxman, when FDA approves an NDA, the patent information submitted therewith is published in a publication titled "Approved Drug Products with Therapeutic Equivalence" known as the "Orange Book. *See e.g.* Yang*, supra* note 37 at 228.).

79. Chen, *supra* note 9 at 72.

80. *See* Pharmaceutical Affairs Act, *supra* note 8, art. 48-4 (2018).

81. *See id*.

was issued by the central health authority; and (4) whether the patents corresponding to such new drug should be revoked or proof that the generic drug for the drug permit application does not infringe the patent corresponding to such new drug.[82] The fourth requirement is akin to the "paragraph IV" certification under the HWA and provides that such patent is invalid or will not be infringed.[83] The TFDA will then review whether the required data and information are complete.[84]

In the case that a declaration of the fourth situation is made, Article 48-12 of the PAA requires an ANDA applicant to serve a written notification to the NDA holder and TFDA within twenty days of the ANDA applicant's receipt of the completeness notification[85]. According to Article 84-13 of the PAA, after the patentee or exclusive licensee receives an Article 48-12 notification, he must bring any infringement claims against the ANDA applicant within forty five days starting from the next day of the receipt of notification.[86] Article 48 -13 of the PAA also prevents the TFDA from issuing a drug permit to the ANDA applicant within of the NDP holder's receipt of the notification.[87]

III. POTENTIAL ISSUES FOR TAIWAN'S PATENT LINKAGE SYSTEM—PART I

Critics of patent linkage often see the system as a mechanism to further promoting patent evergreening.[88] As long as an originator can continue to obtain sequential patent rights to its drugs, it can continue blocking generic market entry for the drug through patent linkage.[89] The CPTPP will allow a compa-

82. *See id*. art. 48-9.

83. 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (2010); *accord* 21 C.F.R. § 314.94(a)(12)(i)(A)(4)(i) (2010).

84. Pharmaceutical Affairs Act, *supra* note 8, art. 48-12.

85. See TPP Agreement, *supra* note 60.

86. *See id*. art. 48-13.

87. The twelve month stay only prevents TFDA from issuing the license but it does not stop the reviewing process for biosimilar. (See Article 48-15 (1) of the PAA, "[During the period of stay of drug permit issuance stipulated in Paragraph 2 of Article 48-13, if the examination for the application for a generic drug permit has been completed, the Central Competent Health Authority shall inform the same to the applicant for said generic drug permit".

88. Freilich *supra* 16 at 104. ,

89. *See* Michael Grunwald, *Leaked: What's in Obama's Trade Deal*, POLITICO (July 1, 2015, 5:24 AM),

ny that is in the process of filing a patent claim to prohibit the regulatory approval of a competitor without seeking a private enforcement action and without having to address the validity of its proposed patent claim.[90] Generic manufacturers end up suffering the consequences as originators use tactics to delay regulatory review—a process that could take years.[91]

From the experience of HWA, at least three issues need to be further examined in Taiwan: (1) whether TFDA will, or needs to, monitor and check the validity and scope of the patents listed; (2) whether generic companies or other third parties can challenge the validity and scope of the patents listed before filing for marketing approval; and (3) whether the evergreening of the originators' patent occurred. One issue that is not mentioned in either the HWA or the PAA but that is important for biosimilars is whether the method for manufacturing patents can be listed.

A. Patent Listing and the Role of TFDA

Not all countries adopt the patent linkage systems.[92] For example, the European Commission's Pharmaceutical Sector Inquiry of 2008 stated that the when determining whether to approve market authorizations for generic medicines, the process does not consider the patent status of the originator medicine.[93] According to the HWA, when FDA approves an NDA, the patent information submitted therewith is published in the *Approved Drug Products with Therapeutic Equivalence*, also known as the Orange Book.[94] Without patent listing, ANDA applicants would need to spend more time and resources searching for relevant patents covering the product.

Patent listing is required by law in Taiwan—as stated in Article 48-8(1) of the PAA, "The Central Competent Health Authority shall establish a Registration System for Patent Link-

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https://www.politico.com/agenda/story/2015/06/tpp-deal-leaked-pharma-000126/.

90. *See* Susan K. Sell, *TRIPS Was Never Enough: Vertical Forum Shifting, FTAS, ACTA, and TPP*, 18 J. INTELL. PROP. L. 447, 453–54 (2011).

91. *See id.*

92. *See* Laurenza, *supra* note 51, at 440 (2015).

93. *Id.*

94. *See* Terry G. Mahn, *Patenting Drug Products: Anticipating Hatch Waxman Issues During the Claims Drafting Process,* 54 FOOD DRUG COSM. L.J. 245, 249–50 (1999).

age of Drugs to list and publish the patent information submitted by the holder of a new drug permit. The [registration requirement] shall also apply to the amendment and deletion of the patent information."[95] A database is available to ANDA applicants that allows them to obtain information about relevant patents, identify opportunities to challenge weak patents, and determine the ideal time to enter the market.[96] Similar to the USFDA[97] the TFDA's role is purely administrative and merely reviews whether the formal requirements are met—it does not intervene in patent related issues.[98] The TFDA reviews patent listing applications for compliance with formal requirement, but declines to determine whether patents actually properly describe the approved pharmaceutical compounds or their uses.

Although third parties, such as generic manufacturers, do not have the right to request that the TFDA correct or delete an improper listing, however, they do a the right to notify the Central Competent Health Authority regarding improper listings under Article 48-7(1) of the PAA .[99] Article 48-7(1) states that "[a]anyone may notify any of the following items to the Central Competent Health Authority with written explanations and evidence: (1) The invention listed in the patent information is irrelevant to the approved drug. (2) The invention listed in the in the patent information does not comply with Paragraph 2 of Article 48-3. (3) The patent information listed is incorrect. (4) No amendment or deletion has been made for any of the occurrences stipulated in Article 48-6."[100] According to Article 48-7(3) of the PAA, the holder of a new drug permit shall, within 45 days of its receipt of said notification, respond to the central competent health authority with written explanations, and may amend or delete the patent information as the case may be.[101] If the NDP holder fails to reply or only partially replies, it is insufficient as an explanation as required by the PAA.

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95. Pharmaceutical Affairs Act, *supra* note 8 art. 48-8.

96. Son, Lopert, Gleeson & Lee, *supra* note 18, at 7.

97. *See Prioritizing Public Health: The FDA's Role in the Generic Drug Marketplace: Hearing Before the Subcomm. on Agric., Rural Dev., Food and Drug Admin., and Related Agencies, Comm. on Appropriations,*
114th Cong. 10 (2016) (statement of Janet Woodcock, M.D.).

98. *See generally* Pharmaceutical Affairs Act, *supra* note 8, art. 48-3–48-22.

99. Pharmaceutical Affairs Act, *supra* note 8.

100. *Id.,* art. 48-6..

101. *Id.* art. 48-3.

B. Automatic Stay and Patent Evergreening

Article 48-13(1) of the PAA states that, if the patentee or the exclusive licensee intends to file a patent infringement complaint on the basis of the listed patent(s) after its receipt of the notification stipulated by Paragraph 1 of Article 48-12, "it shall file the complaint within 45 days of its receipt of said notification and notify the Central Competent Health Authority."[102] According to Article 48-13 (2), "the Central Competent Health Authority shall stay the issuance of the drug permit for twelve (12) months as of the next day to the new drug permit holder's receipt of the notification stipulated in Paragraph 1 of Article 48-12." [103] One of the major arguments against the automatic stay, however, is the practice of "evergreening.[104]" Biosimilar industry representatives contend that the automatic 12-month stay is without a just cause absent proper TFDA monitoring[105]

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102. *Id.* art. 48-13(1).

103. *Id.* art. 48-13(2). Automatic Stay and the Exceptions. However, if there is any of the following matters, the Central Competent Health Authority may issue the drug permit if [said application is] examined to be in compliance with the regulations under this Act: (1) The patentee or the exclusive licensee, after its receipt of the notification stipulated by Paragraphs 1 of Article 48-12, fails to file an infringement complaint within the 45-day period. (2) The patentee or the exclusive license files an infringement complaint based on the patents which are not those listed before the date of the application for the generic drug permit. (3) The patent infringement complaint filed by the patentee or the exclusive licensee pursuant to Paragraph 1 hereof is overruled by the court according to Paragraph 1 or 2 of Article 249 of the Coded of Civil Procedure. (4) The court has determined that all of the patents pending in the infringement lawsuit shall be revoked, or a non-infringement judgment is obtained by the applicant for the generic drug permit. (5) All the patents under the declaration stipulated in Item 4 of Article 48-9 made by the applicant for the generic drug permit are determined as invalid by the Competent Patent Authority in a cancellation action. (6) A settlement or a mediation has been reached by the parties. (7) All the patents under the declaration stipulated in Item 4 of Article 48-9 made by the applicant for the generic drug permit have become extinguished.

104. Kate S. Gaudry, *Evergreening: A Common Practice to Protect New Drugs*, 29 NAT. BIOTECHNOLOGY 876, 876-78 (2011) (Evergreening occurs when a pharmaceutical company that has lost both FDA exclusivity and patent protection on the active ingredient of its drug seeks to extend its monopoly by protecting the drug with a series of peripheral patents that allow for additional FDA exclusivity and further patent protection).

105. *See Purepac Pharm. Co. v. Thompson*, 238 F. Supp. 2d. 191, 196 (D.D.C. 2002) (TFDA does not have the power to substantially check the validity and scope of the patent listed, similar to the US FDA which claims that

or court intervention to determine the validity of the patents listed. Interestingly, Minister Chen Shih-chung of the Ministry of Health and Welfare argued that the automatic stay would not create obstacles for the biosimilar industry, as the approval process would not stop during the period of automatic stay, and the approval period is usually longer than 12 months.[106]

Evergreening is widely frowned upon, as pharmaceutical companies employ it to exploit loopholes so as to obtain a longer patent term than they would otherwise entitled.[107] As the US experience shows, originator companies often use listings to deter generic entry.[108] As pointed out by Kesselheim and Darrow, "secondary patents often cover ancillary aspects such as different coatings, salt forms, crystalline structures, or metabolites of the approved pharmaceutical active ingredient".[109] Based on the experience of the HWA, BPCIA has included an "anti-evergreening" provision, which consists of a list of improvements in a drug that do not qualify for an exclusivity period.[110] The provision is intended to reduce the practice of producers making small, strategic improvements to small molecule drugs in attempts to extend their market monopoly.[111] In Taiwan, although Article 48-14 of the PAA seems to eradicate the issue of evergreening, the central competent health authority may only stay the issuance of the drug permit in accordance

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they do not have the resources or the expertise to determine the validity or scope of patent claims)." *Id.*

106. *因應生物相似性藥品納入專利連結制度之配套措施」說明會* [*The Third Explanatory Meeting on "Measures Taken for Including Biosimilar into the Patent Linkage System*,]*"* 40 TAIWAN FDA (May 15, 2019), https://www.fda.gov.tw/tc/siteContent.aspx?sid=10810 (translation by author).

107. Freilich, *supra* note 16, at 105.

108. Hemphill & Sampat, *supra* note 15, at 327–28.

109. *See* Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch Waxman Turns 30. Do We Need a Re-Designed Approach for the Modern Era?*, 15 YALE J. HEALTH POL'Y L. ETHICS 293, 345–46 (2015).

110. *See* 42 U.S.C. § 262 (2010)-Regulation of Biological Products.

111. *Id.* at § 262(jk(7)(c) the anti-evergreening provision provides that the following improvements will not receive exclusivity: a supplement for the biological product that is the reference product, an application filed by the sponsor of the original reference product for a change "that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength," or "a modification in the structure of the biological product that does not result in a change in safety, purity, or potency."

with Article 48-13 once.[112] According to Article 48-20, however, the provisions under Articles 48-9–48-15 that are related to the application for a generic drug permit shall apply mutatis mutandis to the new drugs not having a new ingredient. That is, originator companies could still bar biosimilar market entry by filing for new formulations and/or new method of use; therefore, Taiwan's market is still susceptible to evergreening and multiple delays of market entry.[113]

IV. POTENTIAL ISSUES FOR TAIWAN'S PATENT LINKAGE SYSTEM—PART II

One issue left unanswered in the PAA is whether the manufacturing process patents can be listed. As discussed above, with biologics, the process defines the product.[114] Thus it is imperative one understands the biosimilar process and the means by which a robust manufacturing process produces highly similar biosimilar molecules with consistent product quality.[115] In the US, biosimilars are regulated under the BPCIA.[116] Not only does the BPCIA create a new patent linkage system for biosimilars, it also places a new emphasis on the manufacturing process.[117] The BPCIA does not have a centralized patent registration system like the HWA's Orange Book;[118] rather, it is required by the law that biosimilar manufacturers disclose their

112. Pharmaceutical Affairs Act, *supra* note 8, art. 48-14 (stating that "the applications for the generic drug permits filed by the same applicant for the same drug, the Central Competent Health Authority may only stay the issuance of the drug permit in accordance with Paragraph 2, Article 48-13 once").

113. *See, e.g.* Kesselheim & Darrow, *supra* note 109, at 320 (similar to the US, this provides originators considerable incentive to engage in patent evergreening-filling the Orange Book with as many secondary patents as possible, no matter how small the change to the regulated product).

114. *See generally* Vulto & Jaquez, *supra* note 32.

115. *Id.* at iv 15.

116. Jon Tanaka, "*Shall" We Dance? Interpreting the BPCIA's Patent Provisions*, 31 BERKLEY TECH. L.J. 659, 659 (2016).

117. *Id.* ("The patent dispute resolution process included an exchange of information-the biosimilar maker's application and manufacturing information for the reference product sponsor's list of potentially infringed patents-termed the 'patent dance.'")

118. Michael P. Dougherty, *The New Follow-On Biologics Law: A Section by Section Analysis of the Patent Litigation Provisions in the Biologics Competition and Innovation Act of 2009*, 65 FOOD & DRUG L.J. 231, 234 (2010).

manufacturing process to the originator,[119] despite the potential for compromising biosimilar manufacturers' secretive manufacturing process.[120] In addition, unlike the HWA, the BPCIA allows infringement actions against any entity "making" the allegedly infringing product, so method of production patents can be asserted against biosimilar sponsors.[121] According to Article 48-3 of the PAA, Taiwan's patent linkage system for biosimilars does not require the inclusion of method of manufacturing patents to be listed with TFDA.[122] Due to the biosimilars' nature, the issue of whether manufacturing method patents should be included seems to have been overlooked by both the government and the biosimilar industry.

A. Importance of Manufacture Process for Biosimilar

Nondisclosure of manufacturing methods makes sense for small molecule drugs since they are easily synthesized, purified, and characterized.[123] It is thus unusual for originators to choose a patent which claims to be a manufacturing method.[124] In fact, making changes in the production process is a very effective way for small molecule drugs to work around a patent.[125] But for biologics, the method of production is crucial in

119. 42 U.S.C. §262 (L)(2)(A)(2018).

120. Kate S. Gaudry, *Exclusivity Strategies and Opportunities in View of the Biologics Price Competition and Innovation Act*, 66 FOOD & DRUG L.J. 587, 610 (2011) ("Disclosing manufacturing information presents both risks and rewards to the applicants. In terms of risks, the applicant may fear that such information may be used to its disadvantage. For example, an RPS may identify that the applicant is using a more cost-effective method of manufacturing the drug and may revise its manufacturing process in an effort to achieve similar cost savings . . . Despite these confidentiality requirements, a reasonable fear is that a competitor may nevertheless secretly use the confidential information. It may be difficult to prove such use if the secret relates to a manufacturing process that produces an indistinguishable product.")

121. 42 U.S.C. §262(l)(3)(A)(i)(2018).

122. *See* Pharmaceutic Affairs Act, *supra* note 8, art. 48-3.

123. Brian Coggio & Peter Ludwig, *Process Patents Are Vital In Biotech-Why Not Extend Them?,* LAW 360 (Aug. 10, 2015), http://bit.do/Law360_ProcessPatents.

124. *Id*.

125. *See Sanofi-Aventis U.S. LLC v. Sandoz, Inc.*, 2009 WL 1741571, Lead Civil Action No. 07-2762 (JAP) (D.N.J. June 18, 2009), *vacated*, 345 F. App'x 594 (Fed. Cir. 2009).

determining their chemical and clinical characteristics. [126] Their importance is on par with claims to compound, per se.[127] Each biotechnology manufacturer, whether producing a new molecular entity or a follow-up product, must independently develop its own cell expression, fermentation, isolation, and purification systems for the active ingredient in its product.[128] Thus, the manufacturing process for each active ingredient is unique to each manufacturer."[129]

Originators argue that because the steps involved in making biologics are so complex, it is very difficult to ensure comparability of biologic and biosimilars.[130] Hence, if production processes are not fully understood by biosimilar producers and small differences arise in the production process, production with the same process but in different facilities can have adverse clinical consequences[131] or cause variability in immunological responses.[132] The manufacturing process can be so complex that in some cases it is impossible for the manufacturer to identify which changes in the production method might be re-

126. W. Nichlson Price, II & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 IOWA L. REV. 1023, 1033–35 (2016).

127. Coggio & Ludwig, *supra* note 123.

128. Letter from Steven K. Galson, M.D. Director of the Center for Drug Evaluation and Research to Kathleen M. Sanzo, Esq. of Morgan, Lewis & Bockius LLP, Stephan E. Lawton, Esq. of Biotechnology Industry Organization, and Stephen G. Juelsgaard, Esq. of Genentech (May 30, 2006), (originally assigned Docket Nos.2004P-0231/CP1 and SUP1, 2003P-0176/CP1 and EMC1, 2004P-0171/CP1, and 2004N-0355 and changed to Docket Nos. FDA-2004-P-0339, FDA-2003-P-0003, FDA-2004-P-0214, and FDA-2004-N-0059, respectively, as a result of FDA's transition to Regulations.gov) (2006 Citizen Petition Response).

129. *Hearing on Biologics and Biosimilars: Balancing Incentives for Innovation Before the H. Comm. on the Judiciary, Subcomm. on Courts and Competition Policy,* 111th Cong. 10 (2009).

130. *See* Press Release, Biotechnology Indus. Org., *New Proposed Biosimilars Pathway Filled with Potholes, Says BIO: Proposal Jeopardizes Future Medical Breakthroughs* 8 (Mar. 11, 2009), https://www.businesswire.com/news/home/20090311006202/en/Proposed-Biosimilars-Pathway-Filled-Potholes-BIO.

131. Paul J. Declerck, *Biothterapeutics in the Era of Biosimilars: What Really Matters is Patient Safety*, 30 DRUG SAFETY 1087, 1088 (2007).

132. Shein-Chung Chow, Jun Wang, Laszlo Endrenyib & Peter A. Lachenbruchc, *Scientific Considerations for Assessing Biosimilar Products*, 32 STAT. MED. 370, 371–72 (2012).

sponsible for the alteration in the end product's quality.[133] For example, efalizumab, an immunosuppressive monoclonal antibody originally developed by XOMA, was later transferred to Genentech, its partner, for large scale manufacturing.[134] However, although Genentech had access to all the documentation and experience XOMA had accrued during its development of the monoclonal antibody, it was unable to precisely replicate the manufacturing process.[135]

According to Schellekens , biosimilar manufacturers face significant obstacles due to a lack of access to production details, in-house controls, and materials from the various stages of production at the originator company.[136] Apart from the commercially available formulated material, biosimilar manufacturers are limited to relying on only published data and monographs of the pharmacopeia as sources for comparison.[137] Still, a biosimilar product with the same gene sequence, vector, host cell line, culture conditions, and purification methods is not guaranteed to have the necessary similarities and still have substantial differences in its biological and clinical characteristics.[138] Ironically, it is possible that a wholly different manufacturing process produces a protein product that is sufficiently comparable to the originator.[139]

In Taiwan, the method of manufacture is not a subject listed with the TFDA.[140] The advantage is that, unlike the BPCIA, originators cannot use production method patents to deter biosimilars from entering the market under the patent linkage system, although biosimilar companies could still face patent infringement suits outside the system. In order to avoid potential patent litigation, biosimilar companies have to investigate whether there are process-of-manufacture patents covering the biologic. However, unlisted manufacturing process patents

133. Trevor Woodage, *Blinded by (a Lack of) Science: Limitations in Determining Therapeutic Equivalence of Follow-on Biologics and Barriers to Their Approval and Commercialization*, 9 STANFORD TECH. L. REV. 1, 13 (2012).

134. *Id.* at 13.

135. *Id.*

136. Huub Schellekens, *How Similar do 'Biosimilars' Need to Be?,* 22 NAT. BIOTECHNOLOGY 1357, 1358 (2004).

137. *Id.*

138. *Id.*

139. *Id.* at 1358.

140. *See* Pharmaceutic Affairs Act, *supra* note 8art. 48-3.

could also increase the potential cost for biosimilar manufacturer to search for possible patents covering the biologic.

In the US, the patent number discolosure in the Orange Book under the HWA enables generic companies to lower their patent search cost and to prepare for potential litigation.[141] However, the Orange Book does not list patents that claim manufacturing methods.[142] This is often justified as the manufacturing process could be easily reverse engineered ed in generics; on the contrary, with the importance of manufacturing proceeses for biologics, biosimilar companies in Taiwan will be disadvantaged if biologic companies do not have to list their process patents with the TFDA.[143] Even patent examiners at the Taiwan Intellectual Property Office (TIPO) admit that they too have difficulty in allocating the unlisted patents surrounding a product.[144] For example, unusual in the world of small molecule drugs, biologic company AbbVie has around 200 manufacturing patents protecting the production of Humira®, a biologic with over $10 billion in yearly sales and used to treat arthritis.[145] Without the patent listing of the manufacturing process patent, the time and cost for allocating the relevant patent add another hurdle for biosimilar companies.

B. A Look at the BPCIA's Patent Listing Exchange Process

As mentioned earlier, the US has created a separate patent linkage system for biosimilars under the BPCIA. Although there is no central depository for approved biologics and related patents as in the Orange Book, one particular characteristic is that biosimilar applicants must go through a fairly private process with the reference product manufacturer before obtaining

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141. Hui-cian Huang, "*Patent Linkage"-Impediment or Stimulant to Pharmaceutical R&D and Competition? An Overview on the Development of the Interaction between Patents and Pharmaceutical Regulatory Approval Part 1,* 21 (2) SCI. & TECH. L. REV., 24,27 (2009) (translation by author).

142. *Id.* at 27.

143. Taiwan FDA, s*upra* note 106 at 23.

144. *Id*. at 46.

145. Christopher Weaver, Jeanne Whalen & Jonathan D. Rockoff, *Biotech Drugs Still Won't Copy*, WALL ST. J., (Feb. 27, 2013), http://online.wsj.com/news/articles/SB10001424127887323864304578318111144984632.

approval.[146] An applicant must provide confidential access to a copy of the submitted application and other information that describes the process or processes used to manufacture the biosimilar that is the subject of the application.[147] The requirement that the applicant disclose their potentially secret methods of manufacturing the biosimilar has no equivalent in the HWA.[148] Since biosimilar companies usually have to reverse engineer and produce their own method of manufacture, and, unless the biologic company has manufacturing process patents, the requirement that biosimilar companies have to disclose their own proprietary information to biologic companies is also questionable.[149]

Amgen v. Apotex[150] demonstrates how manufacturing process patents can also be used by originator companies to deter biosimilar applications under BPCIA. In that case, Amgen brought an action alleging that the biosimilar product at issue would infringe their patent-directed method of refolding recombinant proteins expressed in mammalian cells, such as bacteria and yeast.[151] Prior to this patent, the industry faced a problem in producing certain refolded proteins on an industrial scale, and Amgen's patent purported to solve this issue by using a carefully controlled reduction-oxidation reaction to refold proteins—even large complicated protein molecules—at a higher concentration than was possible in prior methods.[152] Amgen's patent claims "a method of refolding a protein in a

146. Michael S. Montgomery, *Generics and Biosimilars: Mapping the Biosimilars Regulatory Approval Pathway against the Hatch-Waxman Act and Projecting Future Effects on the Biologics Market and Patent Protection*, 75 U. PITT. L. REEV. 387, 396 (2014).

147. 42 U.S.C. § 262(l)(1)(B)(i) (2011) ("PROVISION OF CONFIDENTIAL INFORMATION.—When a subsection (k) applicant submits an application under subsection (k), such applicant shall provide to the persons described in clause (ii), subject to the terms of this paragraph, confidential access to the information required to be produced pursuant to paragraph (2) and any other information that the subsection (k) applicant determines, in its sole discretion, to be appropriate (referred to in this subsection as the 'confidential information.')").

148. Dung Ching Fu & Chih-hsiung Chen, *On Regulation of Biosimilar: A Model or a Lesson by the U.S. Biologics Price Competition and Innovation Act of 2009*, 11 NCCU INTELL. PROP. REV. 107, 134 (2014) (translation by author).

149. *Id.* at 113.

150. *Amgen Inc. v Apotex Inc.* 712 Fed. Appx. 985, 988. (Fed. Cir. 2017).

151. *Id.* at 986.

152. *Id.* at 987.

non-mammalian expression system and present in a volume at a concentration of 2.0g/L or greater."[153]–The definition of protein concentration and volume were the two main issues in this case.[154]

Claim 1 in its preamble, calls for protein present in "a volume at concentration of 2.0g/L or greater." Amgen argued that the claimed "volume" was the volume of protein before coming into contact with the herefolding buffer that forms the refold mixture, and when employing that specification, the "refold mixture," requires a protein concentration of at least approximately 1.0g/L.[155] Apotex argued that "volume" refers to the refold mixture which must have a protein concentration of 2.0g/L or more.[156] The court agreed with Amgen on both points.[157]

Amgen contended that Apotex's abbreviated Biologic License Application (aBLA) identified an "inclusion body concentration" of "0.94-1.4g/L"; that is, the refold mixture used in its process to refold filgrastim and pegfilgrastim fell within the scope of their definition of "volume" and therefore amounted to a literal infringement for the 1.0g/L requirement.[158] However, Apotex presented evidence that the maximum concentration of protein in its refold mixture would actually be 0.708g/L[159]. Apotex presented two batch records showing the actual data from the manufacturing process of its filgrastim product, which never exceeded 0.56g/L.[160] Thus, the court ruled in favor of Apotex on this issue.[161]

Amgen also argued that the "washed-inclusion-body concentration" was interchangeable with their "protein concentration[162]." Amgen's argument depends on its inclusion bodies with protein.[163] However, the specification repeatedly makes clear that the proteins are not the same as , but instead are "in" or "deposited"… into or "disposed in" the "aggregates"

153. *Id.*
154. *See id*.
155. *Id*. at 988.
156. *Id.*
157. *Id.*
158. *Id.*
159. *Id.*
160. *Id.*
161. *Id.*
162. *Id*. 990.
163. *Id.*

called "inclusion bodies."[164] Because the court could not find any inference that equates protein with aggregates of proteins that are inclusion bodies, the court thus rejected Amgen's proposed claim construction of "protein concentration" as interchangeable as "inclusion-body concentration."[165]

By disputing the meaning of seemingly straightforward terms such as protein and volume, *Amgen* illustrates the traditional notion that manufacturing process patents are hard to enforce and involve an increased cost of disclosure coupled with a decreased exclusion benefit in small molecules is no longer valid.[166] Clarity in claiming manufacture patents not only defines the scope of the patent but could be used by biosimilar manufacturers to challenge whether the patent has met the enablement requirement.[167] In other words, manufacturing processes would become the focus of patent infringement for biologics. Hence, for biological manufacturing processes, patent protection strategies may differ because manufacturing methods are unusually central for biologics.[168]

V. SOUTH KOREA'S PATENT LINKAGE SYSTEM: A MODEL FOR TAIWAN?

The aforementioned issues created much debate amongst interested parties in Taiwan—the biosimilar industry, in particular, strongly opposes the inclusion of biosimilar into patent linkage system.[169] As stated above, Taiwan's adoption of a patent linkage system was not a result of necessity but rather a byproduct of wishing to join the CPTPP.[170] South Korea, on the other hand, adopted a patent linkage system as a result of the

164. *Id.*

165. *Id.* at 991.

166. W. Nicholson II Price, *Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing*, 55 B.C. L. REV. 491, 523 (2014) (for a general discussion on process patent that are hard to enforce and easy to invent around).

167. Mandel, *supra* note 10 at 23.

168. Michael A. Sanzo, *The Promise and Problem of Biologics*, 34 SANTA CLARA HIGH TECH. L. J. 78 (2017).

169. Taiwan Pharmaceutical Manufacture and Development Association, *supra* note 11.

170. Weng, *supra* note 7 at 14 (To successfully join the TPP Agreement, Taiwan has begun the legislation of a patent linkage system by proposing an amendment for the Pharmaceutical Affairs Act.)

US-Korea Free Trade Agreement.[171] Since both the patent linkage system and biosimilar industry are nascent in Taiwan, biosimilar industry representatives often compare Taiwan's systems to South Korea's, as the two have similar pharmaceutical industry structures that predominately focus on generics and biosimilars, and patent linkage systems that include both generics and biosimilars.[172] Like Taiwan, South Korea also has to consider the protection of generic drug makers and to maintain the NHI fund.[173] However, unlike Taiwan, whose patent linkage system has several lingering issues, South Korea has adopted a pro-generic approach, thereby creating a system that is essential to facilitate a faster and easier market entry for generics, and make it more difficult than the HWA for patent owners to delay market entry of generics.[174] The following discussion illustrates South Korea's response to similar issues faced by Taiwan.

A. Patent Listing

South Korea created the "Green List," essentially an equivalent to the Orange Book, though with a narrower scope.[175] The Green List may be sought for patents that: (1) are not expired based on patent term, patent invalidity, relinquishment, etc.; (2) claim a pharmaceutical substance, dosage, composition, or medical use; (3) directly relate to a pharmaceutical product with marketing approval or amended marketing approval; and (4) have a patent filing date prior to the marketing approval

171. Young Sun Cho and Hyunsuk Jin, *Overview and Implications of the Drug Patent-Approval Linkage System in South Korean Regulation*, PRACTICAL LAW (Feb 1, 2014), https://content.next.westlaw.com/3-557-9230?transitionType=Default&contextData=(sc.Default)&__lrTS=20170626003923370&firstPage=true

172. *Assessing the Implementation Possibility of Patent Linkage on Biosimilar*, Hearing before the Social Welfare & Health Environment Comm. Legislative Yuan 4 (2019) (Statement of the Ministry of Health & Welfare. (translation by author) (on file with the author)

173. *See generally* Ki Young Kim, Hyunsuk Jin & Samuel SungMok Lee, *The Korean Drug Approval-Patent Linkage System: A Comparison with the US Hatch-Waxman Act,* YULCHON (Feb. 2015), https://www.lexology.com/library/detail.aspx?g=5619213a-4714-4307-8bfd-8e12955841e1.

174. *Id.*

175. Kimberlee Thompson Raley, *The South Korean Patent Linkage System: A Model for Reforming the United States Hatch-Waxman Act,* 33 EMORY INT'L L. REV. 459, 475 (2019).

date or amended marketing approval date.[176] Unlike Taiwan, according to Korean Pharmaceutical Affairs Act (KPAA) Article 50-2(2)6, the NDA holder should list patents on a claim-by-claim basis.[177] More importantly, the Green List is limited to patents filed prior to the marketing approval date, which restricts the Green List to patents used in pharmaceutical development.[178]

B. The Role of South Korea's FDA

Furthermore, unlike the TFDA, South Korea's Ministry of Food and Drug Safety (MFDS), exercises the power and authority to substantially examine the patent listing.[179] It is required that the drug patent be "directly related" to the drug product for which approval is made. [180] As such, additional documentation is often required by the MFDS to show patents are directly related to the drug product.[181] The "directly related to" requirement is interpreted to require precise match between the patent claim and the approved pharmaceutical product.[182] Sometimes the MFDS will go so far as to edit listed patent claims to narrow the claimed scope to better match the approved product.[183] Furthermore, unlike Taiwan's patent linkage system, the MFDS has the authority to delete or amend the patent listed if (1) the drug no longer meets the listing requirements or (2) the listing process involves any fraudulent or other wrongful conduct.[184] One interesting point is that during the process of deleting or amending the Green List, the MFDS

176. *See* MINISTRY OF FOOD AND DRUG SAFETY NATIONAL INSTITUTE OF FOOD AND DRUG SAFETY EVALUATION, GUIDE TO DRUG APPROVAL SYSTEM IN KOREA 35 (2017).

177. Pharmaceutical Affairs Act, Act No. 300, December 18, 1953, *amended by* Act No. 14328, Dec. 2, 2016, art. 50-2(2)(6) (S. Kor.), *translated in* Korea Legislation Research Institute online database, https://elaw.klri.re.kr/eng_service/lawView.do?hseq=40196&lang=ENG [hereinafter Korea Pharmaceutical Affairs Act].

178. Kim, Jin & Lee, *supra* note 173, at 2.

179. *See* Raley, *supra* note 175, at 468.

180. Kim, Jin & Lee, *supra* note 173, at 2.

181. *Id.*

182. Raley, *supra* note 175, at 476.

183. *Id.*

184. Korea Pharmaceutical Affairs Act, supra note 177, art. 50-3(4).

must "seek the opinions of interested persons" in advance, including generic applicants for marketing approval.[185]

C. Automatic Stay in South Korea

In Taiwan, if the originator filed a law suit against the ANDA, the TFDA will automatically grant a stay for 12 months.[186] Under South Korea's model, however, a listed patent owner seeking market entry delay must, prior to application for marketing prevention, (1) initiate an injunctive action or an action prohibiting patent infringement or (2) initiate an action or counterclaim for confirmation of patent scope of the listed patent against all generic applicants providing notice of Item (6) certification.[187] Upon filing of the action, the patent owner then may apply for delay of market entry within 45 days of receipt of the Certificate Notice.[188] Upon receiving the patent owner's application, the originator company then must petition the MFDS for a stay of generic drug sales, which lasts nine months.[189] However, a stay of generic sales may be denied or cancelled if: (1) a patent owner did not apply within forty-five days from receipt of notice; (2) a Green List patent is ineligible for listing due to an expired, invalid, or fraudulent listings; (3)

185. *Id*. art. 50-3(3)–(4).

186. Pharmaceutical Affairs Act, *supra* note 8, art. 48-13 (2).

187. Korea Pharmaceutical Affairs Act, *supra* note 177, art. 50-5(2).

188. *See id*. art. 50-5(1).

189. *See* Korean Pharmaceutical Affairs Act, *supra* note 177, art. 50-6(1). (However, the delay might not be granted if any of the following has occurred: "(1) the patent owner fails to apply for a delay of market entry within the 45-day application period; (2) the patent owner applies for a delay of market entry based on a patent that cannot be asserted due to expiration, waiver or any other reason; (3) the patent owner applies for delay of market entry without filing a patent infringement action or a patent scope confirmation action; (4) the patent listing was fraudulent or otherwise wrongfully obtained; (5) the patent owner selectively applies for delay of market entry against one or some of the applicants filing for marketing approval of the same drug13 when there are two or more applicants providing certification for the same drug, which prevents collusion with specific applicants among the many applicants; (6) there already exists the same drug (i.e., as the drug subject to application for delay of market entry) for which the MFDS has already granted marketing approval and can be sold in the market; (7) the KIPT or a court has rendered a decision that the listed patent is invalid or the drug subject to application for delay of market entry falls outside the scope of the listed patent (in case of the Item 4 Certification); or (8) the listed patent is subject to compulsory licensing." See in general, Kim, Jin & Lee, *supra* note 168, at 6–7.)

the generic drug would not infringe the listed patent; or (4) a patent owner violates the Korean Monopoly Regulation and Fair Trade Act. [190]

D. Challenge to Listed Patents

In South Korea, the Korean Intellectual Property Office (KIPO) handles select patent disputes via the Korean Intellectual Property Trial and Appeal Board also known as the Korean Intellectual Property Tribunal (KIPT)[191] The KIPT is equivalent to the Patent Trial and Appeal Board (PTAB)[192] at the United States Patent and Trademark Office (USPTO).[193] The generic pharmaceutical manufacturer may challenge a patent before the KIPT prior to filing for MFDS marketing approval by filing:[194] (1) a negative scope confirmation claim seeking a judgment that a generic drug does not infringe the patent; (2) a patent cancellation claim by anyone within six months of issued patent publication on a narrow basis; or (3) a patent invalidation claim any time after patent registration by an interested party on a broad basis. An action seeking confirmation that a generic drug does not infringe an originator patent is a unique proceeding before the KIPT and is unavailable in the US.[195] The advantage of KIPT is that it "require[s] procedural

190. *See* Korean Pharmaceutical Affairs Act, *supra* note 179, art. 50-6(3)(9)

191. *Intellectual Property Trial and Appeal Board*, KOREA INTELLECTUAL PROPERTY OFFICE, https://www.kipo.go.kr/upload/en/download/brochure_IPTAB.pdf.

192. At the USPTO, the Patent Trial and Appeal Board (PTAB) can institute proceedings to review patentability such as a Post Grant Review (PGR) which takes place within nine months of patent grant and an Inter Partes Review (IPR) which takes place after termination of a PGR or at nine months after patent grant. See generally *Post Grant Review*, U.S. PATENT TRADEMARK OFF., https://www.uspto.gov/patents/ptab/trials/post-grant-review; *Inter Partes Review*, U.S. PATENT TRADEMARK OFF., https://www.uspto.gov/patents/ptab/trials/inter-partes-review.

193. Raley, *supra* note 175 at 480.

194. Teukheo beob [Patent Act], Act No. 4207, Jan. 13, 1990, *amended by* Act No. 14112, Mar. 29, 2016, art. 132-2(1) (S. Kor.) provides that "The Korean Intellectual Property Trial and Appeal Board shall be established under the jurisdiction of the Commissioner of the Korean Intellectual Property Office to take charge of trials and retrials on patents, utility models, designs and trademarks and investigations and research thereon."

195. Kim, Jin & Lee, *supra* note 173, at 5.

simplicity and rapidness as a part of administration and trials . . . ."[196]

E. Summary

South Korea has adopted a pro-generic approach.[197] There are limitations on the patents listed, making it much easier for generic industry to challenge patents listed, and the MFDS is active in monitoring the Green List.[198] For these reasons, the biosimilar industry in Taiwan criticizes their government's system as non-biosimilar friendly when compared with the South Korean system.[199] However, the aim of patent linkage is to create a delicate balance between rewarding the originator while accelerating generic competition.[200] One-sided protection might cause unintended consequences, such as the delayed release of innovative new drugs.[201] In addition, the South Korean patent linkage system is still relatively new, and there is scarce information from which to conclude whether it will achieve the desired growth of its generic pharmaceutical industry.[202] Last but not the least, there is no mention of the possibility of process of manufacture patent listing on the Green List.[203]

VI. WAYS FORWARD

Taiwan's patent linkage system is relatively nascent in comparison to those of the US and South Korea. However, unlike South Korea which adopted a pro-generic model, Taiwan's system is more akin to the HWA but provides a bit more flexibility

196. JAPAN PATENT OFFICE TRIAL AND APPEAL DEP'T., COMPARATIVE STUDY ON THE PATENT TRIAL FOR INVALIDATION AMONG JPO, KIPO AND SIPO 75 (2017).

197. *See generally* Raley, *supra* note 175, at 467–68.

198. *Id.* at 475.

199. Taiwan Pharmaceutical Manufacture and Development Association, , *supra* note 11.

200. Shawn P. Gorman, Adrian Pishko, John Iwanicki, & Judith Stone-Hulslander, *The Biosimilars Act: The United States' Entry into Regulating Biosimilars and Its Implications,* 12 J. MARSHALL REV. INTELL. PROP. L. 322, 325 (2013).

201. Kim, Jin & Lee, *supra* note 173 at 15.

202. Raley, *supra* note 175, at 491.

203. According to Article 50-2 (4)(1) (a-d) of the Korean Pharmaceutical Affairs Act, patents that could be listed include: a. substance; b. dosage form; c. composition; and d. medical usage.

for the generic industry.[204] Some observers believe that due to the unique nature of biologics and their manufacturing, the biosimilar market may not yield the same level of savings seen with small-molecule generic drugs.[205] Biosimilars often require more clinical trials than traditional generic drugs, face greater difficulties in replicating manufacturing methods, and firms more money on marketing.[206] In Taiwan, since pharmaceutical drug prices are capped by the NHI, price drops might not be as volatile as in the US.[207] As a nascent system, it is too early to tell the impact of the system on the biosimilar industry in Taiwan, however, there are still areas in which Taiwan could consider to improve.

A. Adding Process of Manufacture Patents to Patent Listing

Patent protection is usually more difficult to secure for biologics than for small-molecule drugs.[208] The products of biologics patents are generally closely related to substances that already exist in the human body, and broad composition of matter claims are usually disallowed for proteins that already exist

204. For example, according to PAA Article 48-13, the period of automatic stay is 12 months for Taiwan in comparison with 30 months in the US according to FDCA, 21 U.S.C. §§ 355(c)(3)(C).

205. C. Scott Hemphill & Mark A. Lemley, *Earning Exclusivity. Generic Drug Incentives and the Hatch Waxman Act*, 77 ANTITRUST L.J. 947, 952 (2011) (an example is the case of Zocor® (simvastatin), a top selling drug for treatment of high cholesterol, where after FDA approval of a generic version of simvastatin in 2006, the price of a one-month supply dropped from over $150 for Zocor® to $7 for the generic simvastatin by early 2007). Although the introduction of generics significantly reduced drug prices, whether there would be significantly the cost saving after the introduction of BPCIA remains uncertain. Woodage*, supra* note 135 at 17.

206. JOHN R. THOMAS, CONG. RSCH. SERV., R41483, FOLLOW-ON BIOLOGICS: THE LAW AND INTELLECTUAL PROPERTY ISSUES, Summary (2012).

207. David R. Francis, *The Effect of Price Controls on Pharmaceutical Research*, NAT'L BUREAU ECON. RES., https://www.nber.org/digest/may05/w11114.html (Originators also command premium prices due to the absence of price controls in the US). Whereas in Taiwan, drug price is controlled under The Standard for NHI's Drug Coverage and Reimbursement. *See The Standard for NHI'S Drug Coverage and Reimbursement*, MINISTRY OF HEALTH AND WELFARE, (2010), https://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=L0060035 (translation by author).

208. BIOTECHNOLOGY INDUS. ORG., FOLLOW-ON BIOLOGICS REGIME WITHOUT STRONG DATA EXCLUSIVITY WILL STIFLE THE DEVELOPMENT OF NEW MEDICINES, 1–3.

in nature.[209] Because biologics cannot be described precisely by structure, the only composition-of-matter patents that should be allowed for them are product-by-process patents; i.e., they are essentially manufacturing process patents, as the patentee's coverage is limited to the particular method it has used.[210] Due to this limitation, biologics developers may need to rely on protections offered by manufacturing process patents.[211] However, since slight variations in the manufacturing process can change the quality, safety, or efficacy of the final product, trade secrecy is pervasive in biologics manufacturing.[212]

In addition to the problem of trade secrecy, scholars have identified another issue: Even if there are manufacturing process patents, any disclosure made by the originator at the time it files its patent application may not be the final version of process needed to manufacture biosimilar.[213] This is a consequence of biologics patent applications typically being filed prior to clinical trials; therefore the biologic product and its associated process that ultimately receive FDA approval will likely be altered during trials.[214] There are a number of proposals addressing this issue, such as one arguing for a grant of broad patent protection to the originator that is contingent on continued disclosure when the manufacturing process has been modified, and another advocating for the disclosure of precise manufacturing methods as a condition for receiving FDA approval.[215] This paper proposes that allowing manufacturing process patents to be listed on the TFDA's database is another viable solution to the disclosure issue, especially when originator has opted for patent protection instead of trade secret.

Taiwan's lingering issues for patent linkage could have been solved partly by including manufacturing process patents to patent listing. First, unlike South Korea, the PAA did not set a restriction on patents to be listed prior to the marketing ap-

209. *Id.* at 2–3.

210. Dmitry Karshtedt, *Limits on Hard-to-Reproduce Inventions: Process Elements and Biotechnology's Compliance with the Enablement Requirement*, 3 HASTINGS SCI. & TECH. L.J. 109, 139 (2011).

211. BIOTECHNOLOGY INDUS. ORG., *supra* note 208, at 3

212. Price & Rai, *supra* note 126, at 1028.

213. *Id.* at 1050.

214. *Id.*

215. *Id.* at 1051–53.

proval date.[216] Therefore, the process patent could be more up to date to enable biosimilar companies to produce biosimilar drug. Second, patent linkage could ensure that originator will disclose or supplement the patent disclosure with whatever information necessary by linking the disclosure as a condition for granting 12 months stay. Third, in order for the biosimilar industry to avoid falling into litigation over claims of identical or equivalent patents,[217] it is essential that the patent be listed, allowing biosimilar companies to study the patent and to invent around it.[218] Therefore, the biosimilar industry would be able to use manufacturing processes that are different enough not to infringe upon the originator's process patent, but comparable enough to produce a biologic that would pass the FDA's biosimilarity requirements.[219] Not only will this save the biosimilar industry research costs, it also allows them to examine whether the biologic manufacturer has actually facilitated the

216. According to Article 50-2(4)(3)of the Korean Pharmaceutical Affairs Act, The South Korean Green List is limited to patents filed prior to the marketing approval date, which restricts the Green List to patents used in pharmaceutical development. On the contrary, in Taiwan, according to Article 48-3 of the Pharmaceutical Affairs Act, holder of new drug permit should submit patent information to the Central Health Authority within 45 days after the next day to the receipt of the drug permit. Pharmaceutical Affairs Act, *supra* note 8, art. 48-3.

217. Janet Freilich, *Patent Infringement in the Context of Follow-on Biologics*, 16 STAN. TECH. L. REV. 9, 26 (2012). ("However, the first biologics are starting to come off patent, meaning that they will go forward protected only by the weaker drug product, method, or product patents seen in the section on small-molecule drugs. This will spawn opportunities for follow-on biologic work-arounds which will, like their generic predecessors, struggle with maintaining sufficient similarity to the reference drug to satisfy the FDA while maintaining sufficient differences from the reference drug to avoid infringing by equivalents.")

218. For example, the court in Bristol finished its opinion by explaining that the generic product "did not achieve substantially the same result" as the brand name product because the generic product "prevent[ed] sticking and picking in long tableting runs, whereas the [brand-name lubricant could have] result[ed] in sticking" making the generic formulation "superior" and thus precluding infringement. *See Bristol-Myers Squibb Co. v. Teva Pharmaceuticals USA, Inc.*, 288 F. Supp. 2d 562, 583 (S.D.N.Y. 2003).

219. Robert N. Sahr, *The Biologics Price Competition and Innovation Act-Innovation Must Come Before Price Competition*, B.C. INTELL. PROP. & TECH. F., 1, 46 (2009).

invention.[220] If not, biosimilar manufacturer could challenge the scope or validity of the patent listed.

B. Collaboration between TIPO and TFDA

Both the USFDA and the TFDA serve merely administrative functions in their respective patent linkage system, while the Korean MFDS has substantive authority to check listed patents.[221] Although theoretically sound, this might be difficult to implement in practice as food and drug regulatory agencies usually lack the expertise to examine the patents listed.[222] This is evident in Article 48-7(1) of the PAA, although any interested third parties could inform the competent central health authority regarding irreverent or incorrect patents listed,[223] TFDA could only notify the patent owner for correction or deletion if necessary.[224] Instead of delegating the responsibility to amend or delete patents listed to the TFDA, it might be more proper to create a mechanism that could strengthen further collaboration between TIPO and TFDA.

The KIPT serves as a good example in this regard by allowing biosimilar applicants to identify and to challenge questionable patents listed and ascertaining that the biosimilar does not infringe the scope of originator's patent prior seeking for generic approval.[225] Like South Korea, TIPO can be delegated this role

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220. Jeff Kuehnle, *Hilton Davis Chemical Co. v. Warner-Jenkinson Co.: Opening the Floodgates on Nonliteral Patent Infringement Through the Doctrine of Equivalents*, 48 BAYLOR L. REV. 589, 604 (1996) (stating that the purpose of a patent is "to ensure that the inventor receives a limited monopoly on the invention in consideration for disclosing it to the public").

221. Kim, Jin & Lee, *supra* note 173, at 2.

222. This is similar to the US FDA which claims that they do not have the resources or the expertise to determine the validity or scope of patent claims. *See Purepac Pharm Co. v. Thompson*, 238F. Supp. 2d. 191, 196 (D.D.C. 2002).

223. Article 48-7(1) of the PAA, "1. Anyone may notify any of the following items to the Central Competent Health Authority with written explanations and evidence attached: (1) The invention listed in the patent information is irrelevant the approved drug. (2) The invention listed in the patent information does not comply with Paragraph 2 of Article 48-3. (3) The patent information listed is incorrect. (4) No amendment or deletion has been made for any of the occurrences stipulated in Article 48-6."

224. *A* According to Article 48-7(2). "The Central Competent Health Authority shall, within 20 days after the next day to its receipt of the notification under Paragraph 1 hereof, forward said notification to the holder of the new drug permit."

225. Kim, Jin & Lee, *supra* note 173, at 5.

by providing an administrative patent dispute resolution system that allows the biosimilar industry to file patent scope confirmation actions,[226] patent cancellation actions, or patent invalidation actions.[227] By doing so, the biosimilar industry can enjoy a speedier settlement of potential patent infringement litigation[228] and prevent improper stay initiated by originator companies.[229]

Currently, these options are not available to the biosimilar companies in Taiwan.[230] According to the proposed amendment to Patent Act Article 60-1, biosimilar companies may file for a declaratory judgment stating it has not infringed the patent listed, but may only do so after the originator has failed to file a patent infringement complaint within 45 days under Article 48-13(1)[231] of the PAA. In other words, under the current system, biosimilar companies can only engage in patent infringement litigation while triggering the automatic stay for 12 months or wait for 45 days until they could file for a non-infringement declaratory judgement, both after they have sought for biosimilar approval. Either way, biosimilar companies can only act as a defender, and issues surrounding HWA,[232] such as the abuse of automatic stays could still happen in Taiwan.[233] By adopting a KIPT-like mechanism, TIPO

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226. *Id.*

227. *New Patent Cancellation System for South-Korea*, LC PATENTS (July 25, 2017),
https://www.lcpatents.eu/en/news/new_patent_cancellation_system_for_south-korea/21 (last visited Sept. 13, 2020).

228. In the US, this adds $10 million or more to an ANDA Paragraph IV challenge. Hemphill & Lemley, *supra* note 207, at 952.

229. KIPT trials are usually shorter than district court trials. *See* Cho & Jin, *supra* note 171 *at* 2.

230. *See e.g. Q&A on Patent Infringement and Remedies*, TAIWAN INTELLECTUAL PROPERTY OFFICE (Dec. 8 2015), https://topic.tipo.gov.tw/patents-tw/cp-783-872578-ee01c-101.html (translation by author).

231. *PAA' Patent Linkage Went into Force Last Month but Just Half Way through the Legislative Amendment Process?* WISPRO (Oct 23, 2019), https://www.wispro.com/tw/2019/10/23/patent-linkage-6/ (translation by author).

232. HWA has been highly susceptible to originator manipulations such as "antitrust violations, further delays in the release of generic drugs, and significant increases in prescription drug prices." Melissa Ganz, *The Medicare Prescription Drug, Improvement, & Modernization Act of 2003. Are We Playing the Lottery with Healthcare Reform*?, 3 DUKE L. & TECH. REV. ¶ 6 (2004).

233. Weng, *supra* note 7 at 21.

could monitor the patents listed and make suggestions to TFDA to amend or delete any improper listings.[234] This approach allows each regulatory agency to fulfill the task according to its own expertise without creating unnecessary hurdles. This approach would also not create additional burdens for biosimilar industry since it is in their own interest to monitor the patent listed.

CONCLUSION

The primary objective for a patent linkage system is to facilitate research and development, and to accelerate generic entry.[235] Due to the nature of Taiwan's biosimilar industry that often lacks to sufficient funding to finalize product development, it is particularly important for the government to establish a system that would maintain the balance that patent linkage system aims to achieve.[236] Although the US has created a separate system for biosimilars under the BPCIA, Taiwan has adopted a HWA–like system.[237] Alternatively, although South Korea has also modeled its system after the HWA, it has been significantly redesigned to be more generic-friendly.[238] The benefit of being a late comer to the patent linkage system is that Taiwan can use others' experiences as policy lever to design a system that could be more akin to the US—pro-originator—or South Korea—pro-generic). With the newly implemented system, this paper recommends that based on the specific nature of biologics, manufacturing process patents should be included on to the patent list. Furthermore, the TFDA could strengthen collaboration with the TIPO by creating a similar patent dispute mechanism to that of South Korea's KIPT, thereby allowing better utilization of Article 48-9(d) of the PAA. By adopting these two approaches, this paper argues that Taiwan's current model would be further refined, es-

234. Collaboration between food and regulatory and patent agencies is not a rare phenomenon. For example, in the US, according to 21 U.S.C. § 3 7 2(d) (2012), calls for the FDA to assist the PTO in ordinary examination of drug patent applications.

235. Tzeng, *supra* note 1 at 141-142.

236. Weng, *supra* note 7 at 26.

237. *See generally* Chen, *supra* note 9 (Discussing HWA as the original system for patent linkage upon which the ANDA system is based and established in Taiwan).

238. Kim, Jin & Lee, *supra* note 175, at 15.

pecially to avoid the issue of improper patent listing, or evergreening, and to prevent triggering improper automatic stays. By adopting these two approaches, the delicate balance between rewarding originators and promoting biosimilar industry development could become a more achievable goal.