With One Exception Current Trade Agreements Do Not Appear to Include Biologic Medicines in their Data Protection/Data Exclusivity Provisions – Implications for TPP Negotiation

Professor Brook K. Baker
Northeastern U. School of Law, Senior Policy Analyst Health GAP
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Background on data exclusivity in the TPP

Twelve Pacific-rim countries are currently negotiating a trade agreement, the Trans-Pacific Partnership Agreement (TPP),[1] that, according to US negotiators, is supposed to establish a fresh template for 21st century trade relations. The U.S. tabled two intellectual property chapter proposals to TPP negotiators in 2011.[2] Included in those proposals are provisions dealing with traditional data exclusivity for pharmaceutical products involving new chemical entities[3] and a placeholder for biologics.[4] The placeholder on biologics may soon be filled as there is mounting pressure on the US from its biopharmaceutical industry to propose twelve years of market/data exclusivity on biologic medicines[5] in conformity with existing US law on the topic.[6] This long period of exclusivity seems at odds with the Obama administration's FY-14 budget proposal that

[1] According to the United State Trade Representative website, "Through the TPP, the United States is seeking to advance a 21st-century trade and investment framework that will boost competitiveness, expand trade and investment with the robust economies of the Asia Pacific, and support the creation and retention of U.S. jobs, while promoting core U.S. principles on labor rights, environmental protection, and transparency." *See* http://www.ustr.gov/about-us/press-office/press-releases/2013/july/statement-18th-round-tpp. The parties to the negotiation are Australia, Brunei Darussalam, Canada, Chile, Malaysia, Mexico, New Zealand, Peru, Singapore, the United States, Vietnam, and, as of July 23, 2013, Japan. With Japan's entry, TPP countries include 40 percent of the global economy. Other countries, including Thailand, are said to be interested. The U.S. is reportedly urging South Korea to join the talks as well. Park Hyun & Seong Yeon-cheon, "To counter China, US is seeking to expand its presence in the Asia-Pacific region, and wants SK as a partner," THE HANDKYOREH (March 21, 2013) *available at* http://www.hani.co.kr/arti/english_edition/e_international/579052.html. The 18th round of negotiations were held in Malasia, March 4-13, 2013, with the 16th round scheduled in in Lima, Peru in May 15-24, 2013. For an outline of the broad parameters of the TPP, *see* http://www.ustr.gov/about-us/press-office/fact-sheets/2011/november/outlines-trans-pacific-partnership-agreement. For a detailed analysis by the Congressional Research Service, see Ian F. Feargusson et al., THE TRANS-PACIFIC PARTNERSHIP NEGOTIATIONS AND ISSUES FOR CONGRESS (March 19, 2013), *available at* http://www.fas.org/sgp/crs/row/R42694.pdf.

[2] Trans-Pacific Partnership, Intellectual Property Rights Chapter February Draft (TPP-I), *available at* http://keionline.org/sites/default/files/tpp-10feb2011-us-text-ipr-chapter.pdf; Trans-Pacific Partnership, Intellectual Property Rights Chapter September 2011 Draft (Selected Provisions) (TPP-II), *available at* http://www.citizenstrade.org/ctc/wp-content/uploads/2011/10/TransPacificIP1.pdf [hereinafter US TPP IP Chapter]. With respect to substantive IP issues affecting access to medicines, there are proposals to relax standards of patentability, to eliminate certain patent exclusions, to extend patent terms to compensate for regulatory delays, to limit required disclosures, to forbid pre-grant opposition procedures, and to require data exclusivity and patent-registration linkage, all TRIPS-plus measures. *See* Sean M. Flynn, Brook Baker, Margot Kaminski & Jimmy Koo, *The U.S. Proposal for an Intellectual Property Chapter in the Trans-Pacific Partnership Agreement*, 28 AM. U. INT'L L.R. 105, 149-183 (2013).

[3] TPP-II, *supra* note 2, at Article 9.2.

[4] *Id*. at Article 9.9.

[5] On July 18, 2013, the Biotechnology Industry Organization (BIO) submitted a letter and a "white paper" to the USTR urging at least 12 years of market/data exclusivity in the TPP. BIO, letter, *available at*: http://www.bio.org/sites/default/files/letterhead.pdf; BIO, TRANS-PACIFIC PARTNERSHIP AND INNOVATION IN THE BIOECONOMY: THE NEED FOR 12 YEARS OF DATA PROTECTION FOR BIOLOGICS (BIO WHITE PAPER), *available at*: http://www.bio.org/sites/default/files/TPP%20White%20Paper%20_2_.pdf.

[6] The Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), was a portion of the Patient Protection and Affordable Care Act that amended the Public Health Services Act to create a abbreviated approval pathway for registering biosimilar products in the United States and at the same time established a twelve-year period of market and data exclusivity for biologic products. *See*, 42 U.S.C. § 362(k) generally and § 362(7)(A) specifically with respect to the period of exclusivity.

would shorten biologic exclusivity in the U.S. to just seven years and bar evergreening of such extensions based on minor variations to an existing biologic.[7] More recently, however, there are reports that the U.S. has been moving towards formally promoting twelve years of exclusivity for biologics in the TPP, although a formal text to this effect has not yet been filed.[8] This paper clarifies that existing US trade agreements do not presently provide data exclusivity for biologics and argues further that it would be unwise for other Parties to accept such a requirement.

With only one possible exception, current US trade agreements do not provide data exclusivity for biologics, but rather only for pharmaceuticals containing "chemical entities"

In the course of backroom negotiations, questions have arisen whether data exclusivity provisions in existing trade agreements already cover biologics or not. To answer that question, it is important to examine the text of several representative trade agreements, most particularly those that apply to any of the current or prospective Parties to the negotiations. A careful review of the North American Free Trade Agreement (NAFTA),[9] which applies to the U.S., Mexico, and Canada, the United State-Peru Free Trade Agreement (US-Peru FTA),[10] the Dominican Republic-Central American Free Trade Agreement (DR-CAFTA),[11] and the Korea-United States Free Trade Agreement (KORUS)[12] all reveal that existing pharmaceutical-product data exclusivity provisions in these agreements apply to pharmaceutical involving "chemical entities" only, not to

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> The Budget also proposes to accelerate access to affordable generic biologics by modifying the length of exclusivity on brand name biologics. Beginning in 2014, this proposal would award brand biologic manufacturers seven years of exclusivity, rather than 12 years under current law, and prohibit additional periods of exclusivity for brand biologics due to minor changes in product formulations, a practice often referred to as "evergreening." The proposal will result in $3 billion in savings over 10 years to Federal health programs including Medicare and Medicaid.

Office of Budget and Management, FISCAL YEAR 2014: BUDGET OF THE UNITED STATES GOVERNMENT, 40, *available at*: http://www.whitehouse.gov/sites/default/files/omb/budget/fy2014/assets/budget.pdf. During a March 19, 2013, Senate Finance Committee hearing on the President's 2013 Trade Agenda, Ambassador Marantis commented that there is "a lot" of opposition from participating countries to a 12-year exclusivity period for biological products and that the Administration has not yet decided on whether to propose a 12-year exclusivity period. *Available at*: http://www.finance.senate.gov/hearings/hearing/?id=bf63ffa8-5056-a032-5283-bd347de7362c. Perhaps in response to that oral testimony, on March 22, 2013, Senators Baucus and Hatch wrote letters to the USTR urging that the US propose twelve years of exclusivity for biologics in the TPP. Letter, *available at*: http://infojustice.org/wp-content/uploads/2013/03/Baucus-and-Hatch-03222013.pdf.

[8] "U.S. Moves Toward Promoting 12-Year Protections for Biologics in TPP," Inside U.S. Trade (July 19, 2013).

[9] NAFTA, Article 1711.5-7, *available at*: http://www.sice.oas.org/trade/nafta/chap-172.asp#A1711. Note: Article 1711.6 grants data exclusivity for a "reasonable period of time" which "shall normally mean not less than five years … taking into account the nature of the data and the person's efforts and expenditures in producing them."

[10] US-Peru FTA, Article 16.10.2, *available at*: http://www.ustr.gov/webfm_send/1031. Note: Article 16.10.2(b) also grants data exclusivity for a "reasonable period of time" which "shall normally mean not less than five years … taking into account the nature of the data and the person's efforts and expenditures in producing them."

[11] DR-CAFTA, Article 15.10.1, *available at*: http://www.ustr.gov/sites/default/files/uploads/agreements/cafta/asset_upload_file934_3935.pdf. Note: Article 15.10.1 provide for "at least five years" of data exclusivity.

[12] KORUS, Article 18.9.1-2, *available at*: http://www.ustr.gov/sites/default/files/uploads/agreements/fta/korus/asset_upload_file273_12717.pdf. Note: Korus Article 18.9.1 provides for "at least five years" of data exclusivity for new pharmaceutical products that do not contain a chemical entity that has previously been approved in the territory of the Party for use in a pharmaceutical product. Article 18.9.2 contains provisions granting additional three year periods of data exclusivity where a pharmaceutical product containing a previously approved chemical-entity if accompanied by new clinical information essential to the approval by the regulatory authority.

biologics.[13] The only US trade agreement that is ambiguous in this regard is the United States-Singapore Free Trade Agreement (US-Singapore FTA), which covers all, not just new, "pharmaceutical products" and which references "new chemical entities only in a footnote clarifying a grandfathered exception to the five-year period of data exclusivity for pharmaceutical products that do not involve a new chemical entity.[14] In contrast, there is a precedent for explicitly providing for biologic data exclusivity in the European Union-Peru/Columbia Trade Agreement, but even here there is an escape clause at least for Peru.[15] The US's anticipated TPP proposal will be unique in seeking both explicit coverage of biologics and even longer data monopolies on biologic regulatory data than on chemical entity data.

The language of existing trade agreements, with the exception of the EU-Peru/Columbia TA and the US-Singapore FTA referenced above, explicitly limit data exclusivity to pharmaceutical products containing "chemical entities." The fact that the E.U. and U.S. are just beginning to address biologic exclusivity with separate language and provisions provides additional confirmation that the "pharmaceutical-product/chemical-entity" language in existing FTAs does not apply to biologics. More precisely, in each of the relevant US FTAs included in this analysis except for US-Singapore, the operative language limits initial terms of data exclusivity to pharmaceutical products that (1) "utilize new chemical entities,"[16] or (2) ones that do "not contain a chemical entity that has been previously approved in the territory of the Party for use in a pharmaceutical product."[17]

The only US FTA that is ambiguous in this regard is US Singapore. There, in Article 16.8, there is five years of data exclusivity with respect to any pharmaceutical product, new or not. However, to safeguard US law,[18] a footnote to Article 16.8 says:

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[13] *See*, Appendix 1, *infra*, with relevant provisions and definitions highlighted.

[14] US-Singapore FTA, Article 16.8, *available at*: http://www.ustr.gov/sites/default/files/uploads/agreements/fta/singapore/asset_upload_file708_4036.pdf.

[15] Article 231.

> 1. Each Party shall protect undisclosed test or other data related to safety and efficacy of pharmaceutical products[72] and agricultural chemical products, in accordance with Article 39 of the TRIPS Agreement and its domestic legislation.
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> 2. According to paragraph 1, and subject to paragraph 4, when a Party requires, as a condition for approving the marketing of pharmaceutical or of agricultural chemical products which contain new chemical entities, the submission of undisclosed test or other data related to safety and efficacy, that Party shall grant an exclusivity period normally of five years from the date of marketing approval in the territory of that Party for pharmaceutical products, and 10 years for agricultural chemical products, period during which a third party may not commercialise a product based on such data, unless he/she presents proof of the explicit consent of the holder of the protected information or his/her own test data.
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> 3. For the purpose of this Article, a 'new chemical entity'is the one which has not been previously approved in the territory of the Party for its use in a pharmaceutical or chemical agricultural product, pursuant to its domestic legislation. Accordingly, the Parties need not apply this Article with respect to pharmaceutical products that contain a chemical entity that has been previously approved in the territory of the Party.
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> [72] For Colombia and the EU Party, this protection will include data protection of biological and biotechnology products. For Peru, the protection of the undisclosed information of such products shall be granted against disclosure and the practices that are contrary to honest commercial practices, in accordance with Article 39.2 of the TRIPS Agreement, in absence of specific legislation regarding thereof.

Trade Agreement between the European Union and its Member States, of the one part, and Columbia and Peru, of the other part (Dec. 21, 1012), available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:354:0003:2607:EN:PDF.

[16] NATFA, Article 1711.5, *supra* note 9; US-Peru FTA, Article 16.10.2(a), *supra* note 10.

[17] DR-CAFTA, Article 15.10.1(c), *supra* note 11; KORUS, Article 18.9.1(c), *supra* note 12.

[18] US law provides five years of exclusivity on new chemical entity medicines but only three years of data exclusivity on pharmaceutical products not involving a new chemical entity but requiring submission of new clinical trial data in order to secure marketing approval. *See generally* 21 U.S.C. §§ 355, 360cc and 35 U.S.C. §§ 271, 282.

> Where a Party, on the date of its implementation of the TRIPS Agreement, had in place a system for protecting pharmaceutical or agricultural chemical products not involving new chemical entities from unfair commercial use that conferred a different form or period of protection shorter than that specified in paragraph 1 of Article 16.8, that Party may retain such system notwithstanding the obligations of that paragraph.[19]

Although the US-Singapore FTA does not, like other US FTAs, have the usual explicit limitation of data exclusivity to chemical-entity pharmaceutical products, footnote 16-14 does indirectly suggest that the US continued with this distinction even in this agreement. The permission for a period of shorter exclusivity for pharmaceuticals not involving a new chemical entity would not make much sense unless it was being contrasted with pharmaceutical products that did contain a new chemical entity, which would therefore be entitled, without exception, to five years of data exclusivity.

Treating biologics differently from traditional small-molecule, chemically synthesized products makes a lot of sense. Biologics are different from small molecule pharmaceutics in many fundamental ways, not just with respect to the size and complexity of organic compounds versus small-molecules but also with respect to regulatory concern over biological versus chemical manufacturing processes. Small molecule chemicals are easily duplicated to create identical generic clones, thus allowing abbreviated registration based typically only on evidence of bioequivalence and GMP. In contrast, biologic medicines are incapable of precise replication by other manufacturers and thus national drug regulatory authorities have had to come up with complex regulatory pathways to evaluate, compare, and register biosimilars.[20] Accordingly, in order to receive abbreviated marketing approval, biosimilars typically require additional, exacting clinical trial and therapeutic/side-effect data that is not required with respect to traditional small-molecule medicines.

BIO and the USTR want to have it both ways. BIO, and U.S. negotiators on its behalf, argue repeatedly that biologics are different (as detailed further below),[21] that they entail different

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[19] US-Singapore, *supra* note 14, Article 16.8, n. 16-14.

[20] The European Union was the first to develop a mechanism for market approval of so-called similar biological medicinal products. *See* Directive 2001/83/EC, as amended. *Available at*: http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83_cons/dir2001_83_cons_20081230_en.pdf. Despite passage of the Directive, the European Medicines Agency did not publish guidelines for abbreviated approval of biosimilars until 2005. The impact of the EU regulatory regime has been relatively modest so far with only 14 biosimilar medicines registered as of October 2010. Joan Rovira, Jaime Espin, Leticia Garcia & Antonio Olry de Labry, THE IMPACT OF BIOSIMILARS' ENTRY INTO THE EU MARKET, EmiNet (2001), *available at*: http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_market_012011_en.pdf. Since then, two additional biosimilars have been approved, but two have been withdrawn from the market. Generics and Biosimilars Initiative, Biosimilars approved in Europe (2013), *available at*: http://www.gabionline.net/Biosimilars/General/Biosimilars-approved-in-Europe. In contrast, the U.S. did not pass legislation on biosimilars until 2010. *See supra* note 6. The FDA has still not finalized regulatory guidance on an abbreviated approval pathway for biologics. Nonetheless, even prior to the implementation of the BPICA, two follow-ons biologics have been authorized via simplified procedures allowed for small molecule generics, namely Menotropins (January 1997) and Enoxaparin (July 2010), and a further eight biologics were registered through the 505(b)(2) pathway. In Canada, biosimilars are referred to as subsequent entry biologics. The Canadian Health Products and Food Branch issued guidance re biosimilar applicants in 2010. INFORMATION AND SUBMISSIONS REQUIREMENTS FOR SUBSEQUENT ENTRY BIOLOGICS AND RELATED DOCUMENTS, *available at*: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/brgtherap/applic-demande/guides/seb-pbu/seb-pbu-2010-eng.pdf. Mexico already makes some provisions for what it calls biocomparable biotech drug in 2009, available at http://www.gabionline.net/guidelines/ mexican-guideline-for-biocomparables, although there are currently additional proposals under review. PROYECTO de Norma Oficial Mexicana PROY- NOM-177-SSA1-2013, the PROYECTO de Norma Oficial Mexicana PROY-NOM-257-SSA1- 2013, and the Norma Oficial Mexicana de Emergencia NOM-EM-001-SSA1-2012. In terms of other TPP Parties, it appears that Malaysia issued final guidance on biosimilars in 2008, Singapore did so in 2009 with reliance on designated "reference agencies", and Australia adopted the European guidelines in 2008. PPD, Developing Biosimilars in Emerging Markets: Regulatory and Clinical Considerations (2013), *available at*: http://www.healthtrustpg.com/biosimilars/pdf/ppd.pdf.

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therapeutic risks, that they are not protected by patents to the same extent as small-molecule medicines, that the research, development, registration, and manufacture of biologics all entail greater uncertainties, and thus that the bio-tech industry need different provisions on data/market exclusivity than that provided with respect to chemistry-based pharmaceutical right holders.[22] But then, in lobbying TPP negotiators, BIO and the USTR argue that negotiating Parties shouldn't worry about the pending US proposal for extended periods of data exclusivity on biologics because other countries, including some of the existing parties, have already indirectly agreed to data exclusivity on biologics in previously trade agreements. The analysis in this paper concludes that such an argument is without merit. TPP negotiators from other countries, especially low- and middle-income Parties, remain free to conclude that data exclusivity is not required by TRIPS[23] and that an even more extended form of data exclusivity for biologics is counter to the interests of their health systems, their patients, and their economies.

Biologics are treated differently from chemically synthesized pharmaceutical products both in relevant U.S. statutory and regulatory language and in regulatory pathways

Under the Biologics Price Competition and Innovation Act of 2009, 42 U.S.C. § 262(i)(1), "The term 'biological product' means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings."[24] In the U.S., the pathway for abbreviated approvals of biosimilars is much more complicated[25] than for chemical entity pharmaceutical products where chemically

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- A biologic is manufactured in a living system such as a microorganism, or plant or animal cells. Most biologics are very large, complex molecules or mixtures of molecules. Many biologics are produced using recombinant DNA technology.
- A drug is typically manufactured through chemical synthesis, which means that it is made by combining specific chemical ingredients in an ordered process.
- Drugs generally have well-defined chemical structures, and a finished drug can usually be analyzed to determine all its various components. By contrast it is difficult, and sometimes impossible, to characterize a complex biologic by testing methods available in the laboratory, and some of the components of a finished biologic may be unknown.
- Therefore, for biologics, "the product is the process." Because the finished product cannot be fully characterized in the laboratory, manufacturers must ensure product consistency, quality, and purity by ensuring that the manufacturing process remains substantially the same over time. By contrast, a drug manufacturer can change the manufacturing process extensively and analyze the finished product to establish that it is the same as before the manufacturing change.

BIO, *How do drugs and biologics differ?*, *available at*: http://www.bio.org/articles/how-do-drugs-and-biologics-differ.

[22] *See*, BIO WHITE PAPER, *supra* note 5.

[23] *See*, Brook K. Baker, *Ending Drug Registration Apartheid: Taming Data Exclusivity and Patent/Registration Linkage*, 34 AM. J. LAW & MEDICINE 303, 315-317 (2008); Carlos Maria Correa, PROTECTION OF DATA SUBMITTED FOR THE REGISTRATION OF PHARMACEUTICALS: IMPLEMENTING THE STANDARDS OF THE TRIPS AGREEMENT, (2002).

[24] "FDA regulations and policies have established that biological products include blood-derived products, vaccines, in vivo diagnostic allergenic products, immunoglobulin products, products containing cells or microorganisms, and most protein products. Biological products subject to the *PHS Act* also meet the definition of *drugs* under the *Federal Food, Drug and Cosmetic Act (FDC Act)*. Note that hormones such as insulin, glucagon, and human growth hormone are regulated as drugs under the *FDC Act*, not biological products under the *PHS Act*." FDA, *Frequently Asked Questions About Therapeutic Biological Products*, *available at*: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ucm113522.htm.

[25] An abbreviated application for a biosimilar product must meet the following conditions:
42 U.S.C. §262(i)(2) Content
(A) In general
(i) Required information: An application submitted under this subsection shall include information demonstrating that—

synthesized active ingredients are typically homogenous collections of identical molecules, therefore allowing substitution of manufacturing processes and of suppliers of active ingredients.[26] This differential treatment in abbreviated regulatory pathways strongly suggested

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(I) the biological product is biosimilar to a reference product based upon data derived from—
(aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;
(bb) animal studies (including the assessment of toxicity); and
(cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency in 1 or more appropriate conditions of use for which the reference product is licensed and intended to be used and for which licensure is sought for the biological product;
(II) the biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism or mechanisms of action are known for the reference product;
(III) the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product;
(IV) the route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product; and
(V) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.
(ii) Determination by Secretary The Secretary may determine, in the Secretary's discretion, that an element described in clause (i)(I) is unnecessary in an application submitted under this subsection.
(iii) Additional information An application submitted under this subsection—
(I) shall include publicly-available information regarding the Secretary's previous determination that the reference product is safe, pure, and potent; and
(II) may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.
(B) Interchangeability
An application (or a supplement to an application) submitted under this subsection may include information demonstrating that the biological product meets the standards described in paragraph (4).
(3) Evaluation by Secretary
Upon review of an application (or a supplement to an application) submitted under this subsection, the Secretary shall license the biological product under this subsection if—
(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product—
(i) is biosimilar to the reference product; or
(ii) meets the standards described in paragraph (4), and therefore is interchangeable with the reference product; and
(B) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).
(4) Safety standards for determining interchangeability
Upon review of an application submitted under this subsection or any supplement to such application, the Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application (or a supplement to such application) is sufficient to show that—
(A) the biological product—
(i) is biosimilar to the reference product; and
(ii) can be expected to produce the same clinical result as the reference product in any given patient; and
(B) for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

[26] The Waxman-Hatch Act (Drug Price Competition and Patent Term Restoration Act of 1984) established an abbreviated pathway for the registration of so-called generic medicines. As long as the follow-on generic can establish that the active ingredient in its product has the same chemical structure, dosage, mode of administration, and bioavailability when administered to healthy volunteers as the innovator's product then the generic equivalent can be registered without independent clinical trial evidence. *See*, 21 U.S.C. § 355(j).

that trade agreement language discussing data exclusivity for pharmaceutical products containing new or previously unapproved chemical entities does not apply to biologics.

This interpretation is reinforced by the FDA's regulatory definitions "new chemical entities," which is a special category. As previously discussed, traditional data exclusivity in existing US FTAs is limited to pharmaceutical products involving a new chemical entity or a chemical entity that has not been used in a pharmaceutical product previously in that country. The term, "new chemical entity" is not separated defined in these agreements. However, the FDA has defined a "new chemical entity" for purposes of data exclusivity as "a drug that contains no active moiety that has been approved by the FDA in any other application submitted under section 505(b) [21 U.S.C. §355(j)] of the Act. 21 C.F.R. § 314.08(a). The FDA in turn defines an "active moiety" in terms that applies only to chemicals:

> *Active moiety* means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

Id. Pursuant to this definition, the current data exclusivity provisions in US FTAs logically apply only to traditional small-molecule, chemically synthesized medicines and not to biologics.

Conclusion – the practical significance for TPP negotiators

The thrust of this analysis is that countries, including Parties to the TPP negotiation, are not required by any relevant trade agreement to grant any form of data exclusivity with respect to biologics. Even Peru is granted reprieve from a biologics provision in the EU- Peru/Columbia TA so long as it provides protection "against disclosure and the practices that are contrary to honest commercial practices, in accordance with Article 39.2 of the TRIPS Agreement, in absence of specific legislation regarding thereof."[27] Likewise, US-Singapore's data exclusivity is at least implicitly limited to pharmaceutical products involving chemical entities. Admittedly, some countries may have unilaterally adopted data exclusivity or interpreted existing data exclusivity legislation to apply to biologics. However, the absence of binding treaty commitments means that TPP negotiators can and should apply their minds to potential costs of treaty-mandated biologic exclusivity, which extends the period of monopoly protections for the entire class of essential biopharmaceutical products. Moreover, these data monopolies would arise even if the biologic innovator had neglected to file for patent protection in a particular Party. Negotiators might also consider alerting the U.S. and its public to fact that twelve years of data exclusivity for biologics in the TPP would bind the hands of Congress in the future – it would lock-in an excessive period of data exclusivity through secret, closed-door negotiations, even while the Obama Administration and certain members of Congress are reconsidering wisdom of the existing legislation. Given the opportunity for public debate, a well-informed Congress might well determine – in accordance with prior advice from the U.S. Federal Trade Commission – that extended periods of data exclusivity are not needed to incentivize biologic research and development.[28] That policy space

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[27] EU- Peru/Columbia TA, *supra* note 14, Article 231.

[28] Federal Trade Commission, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION: A FEDERAL TRADE COMMISSION REPORT (2009), *available at*: http://www.ftc.gov/os/2009/06/P083901biologicsreport.pdf.
The Commission's Report states that competition by follow-on biologics (FOBs) is unlikely to be similar to branded-generic drug competition because:

- The substantial costs involved in obtaining FDA approval, plus the substantial costs to develop manufacturing capacity, will limit the number of FOB competitors;
- The lack of automatic substitution between an FOB drug and a pioneer biologic drug will slow the rate at which FOBs can acquire market share;
- An FOB drug also may have difficulty gaining market share due to concerns about safety and efficacy differences with the pioneer biologic drug;
- Biologic drugs currently are not reimbursed according to strategies that insurers often use to encourage the use of lower-priced drugs;

would be lost or seriously curtailed if the U.S. hard-wires twelve years of biologic data exclusivity into the TPP.

The U.S. is making many excessive demands concerning intellectual property rights in the protracted and on-going TPP negotiation. Right now, it is also using the false threat of an illusory deadline – the end of 2013 – to coerce negotiation partners into accepting heightened intellectual property rights and enforcement measures, including investor-state dispute resolution provisions that specifically include IPRs. Although the U.S. has not formally discussed its IP demands for nearly two years, it is apparently hoping to freeze seasoned and knowledgeable trade negotiators out of the final decision-making process, hoping that trade-hungry politicians from the home capitals will make ill-advised concessions in the hope of capturing a temporary share of the U.S.'s shrinking import market.[29] But U.S. trade deficits cannot continue to mount year-after-year and the U.S. is also seeking to solidify its cross-Atlantic trading relationship with Europe.[30] Will the hope of greater access to U.S. markets materialize, or will TPP partners wake-up with buyer's remorse? Will the false gold of streamlined market access and trade facilitation buy poor health and delayed access to affordable biologic medicines for residents of the Pacific rim?

Data exclusivity for biologics, especially extra-long data exclusivity, is a fool's gamble. Most of the countries involved in the TPP are smaller and relatively poorer than the U.S. so that there are already scarce incentives for biosimilar manufacturers to invest in product development and registration in those countries. By all means TPP Parties should establish biosimilar pathways and encourage the development of biosimilar industries, but they should not do so at the cost of extending data monopolies that will primarily serve the interest of U.S. multinational biotechs.

- As a result of these factors, FOB entry, although important, will be less-dramatic than generic drug competition. FOB entry is likely only in biologic drug markets larger than $250 million in annual sales. Only two or three FOB manufacturers are likely to attempt entry for a given pioneer drug product. These entrants are unlikely to introduce their drugs at discounts any larger than between 10 and 30 percent of the pioneer product's price;
- The effect on pioneer manufacturers also will be different. They are expected to respond and offer competitive discounts to maintain market share and are likely to retain 70 to 90 percent of their market share and will continue to reap substantial profits, even after FOB entry.

[29] *See* "Froman Says TPP In 'End Game;' Ministers To Provide Political Direction At Next Round," Inside US Trade (August 9, 2013).

[30] *See* USTR, *Press Release: U.S., EU Announce Decision to Launch Negotiations on a Transatlantic Trade and Investment Partnership* (February 13, 2013), *available at*: http://www.ustr.gov/about-us/press-office/press-releases/2013/february/statement-US-EU-Presidents; USTR, *Press Release: Negotiations for the Transatlantic Trade and Investment Partnership Have Begun* (July 8, 2013), *available at*: http://www.ustr.gov/about-us/press-office/blog/2013/july/TTIP-negotiations-begin; Shayerah I. Akhtar & Vivian C. Jones, Proposed Transatlantic Trade and Investment Partnership (TTIP): In Brief, Congressional Research Service (July 23, 2013), *available at*: http://www.fas.org/sgp/crs/row/R43158.pdf.

APPENDIX 1
SAMPLE US FTA PROVISIONS ON DATA PROTECTION/EXCLUSIVITY

NAFTA Arts. 1711: Measures Related to Certain Regulated Products

5. If a Party requires, as a condition for approving the marketing of ***pharmaceutical*** or agricultural chemical ***products that utilize new chemical entities***, the submission of undisclosed test or other data necessary to determine whether the use of such products is safe and effective, the Party shall protect against disclosure of the data of persons making such submissions, where the origination of such data involves considerable effort, except where the disclosure is necessary to protect the public or unless steps are taken to ensure that the data is protected against unfair commercial use.
6. Each Party shall provide that for data subject to paragraph 5 that are submitted to the Party after the date of entry into force of this Agreement, no person other than the person that submitted them may, without the latter's permission, rely on such data in support of an application for product approval during a reasonable ***period of time*** after their submission. For this purpose***, a reasonable period shall normally mean not less than five years from the date on which the Party granted approval to the person that produced the data for approval to market its product, taking account of the nature of the data and the person's efforts and expenditures in producing them***. Subject to this provision, there shall be no limitation on any Party to implement abbreviated approval procedures for such products on the basis of bioequivalence and bioavailability studies.
7. Where a Party relies on a marketing approval granted by another Party, ***the reasonable period of exclusive use of the data submitted in connection with obtaining the approval relied on shall begin with the date of the first marketing approval relied on***.

CAFTA

Article 15.10: Measures Related to Certain Regulated Products

1. (a) If a Party requires, as a condition of approving the marketing of a ***new pharmaceutical*** or agricultural chemical ***product***, the submission of undisclosed data concerning safety or efficacy, the Party shall not permit third persons, without the consent of the person who provided the information, to market a product on the basis of (1) the information, or (2) the approval granted to the person who submitted the information ***for at least five years for pharmaceutical products*** and ten years for agricultural chemical products from the date of approval in the Party.[15]

   (b) If a Party permits, as a condition of approving the marketing of a ***new pharmaceutical*** or agricultural chemical ***product***, third persons to submit evidence concerning the safety or efficacy of a product that was previously approved in another territory, such as evidence of prior marketing approval, the Party shall not permit third persons, without the consent of the person who previously obtained such approval in the other territory, to obtain authorization or to market a product on the basis of (1) evidence of prior marketing approval in the other territory, or (2) information concerning safety or efficacy that was previously submitted to obtain marketing approval in the other territory, ***for at least five years for pharmaceutical products*** and ten years for agricultural chemical products from the date approval was granted in the Party's territory to the person who received approval in the other territory. In order to receive protection under this subparagraph, a Party may require that the person providing the information in the other territory seek approval in the territory of the Party within five years after obtaining marketing approval in the other territory.

   (c) ***For purposes of this paragraph, a new product is one that does not contain a chemical entity that has been previously approved in the territory of the Party***.

   …

15 Where a Party, on the date it implemented the TRIPS Agreement, had in place a system for protecting pharmaceutical or agricultural chemical products not involving new chemical entities from unfair commercial use that conferred a period of protection shorter than that specified in paragraph 1, that Party may retain such system notwithstanding the obligations of paragraph 1.

US-Peru FTA

Article 16.10: Measures Related to Certain Regulated Products

Pharmaceutical Products

2. (a) If a Party requires, as a condition for approving the marketing of a ***pharmaceutical product that utilizes a new chemical entity***, the submission of undisclosed test or other data necessary to determine whether the use of such products is safe and effective, the Party shall protect against disclosure of the data of persons making such submissions, where the origination of such data involves considerable effort, except where the disclosure is necessary to protect the public or unless steps are taken to ensure that the data are protected against unfair commercial use.

(b) Each Party shall provide that for data subject to subparagraph (a) that are submitted to the Party after the date of entry into force of this Agreement, no person other than the person that submitted them may, without the latter's permission, rely on such data in support of an application for product approval ***during a reasonable period of time after their submission. For this purpose, a reasonable period shall normally mean five years from the date on which the Party granted approval to the person that produced the data for approval to market its product, taking account of the nature of the data and person's efforts and expenditures in producing them***. Subject to this provision, there shall be no limitation on any Party to implement abbreviated approval procedures for such products on the basis of bioequivalence or bioavailability studies.

(c) Where a Party relies on a marketing approval granted by the other Party, and grants approval within six months of the filing of a complete application for marketing approval filed in the Party, ***the reasonable period of exclusive use of the data submitted in connection with obtaining the approval relied on shall begin with the date of the first marketing approval relied on***.

(d) A Party need not apply the provisions of subparagraphs (a), (b), and (c) with respect to ***a pharmaceutical product that contains a chemical entity*** that has been previously approved in the territory of the Party for use in a pharmaceutical product.

US-Korea FTA

Article 18.9: Measures Related To Certain Regulated Products

1. (a) If a Party requires or permits, as a condition of granting marketing approval for a ***new pharmaceutical*** or new agricultural chemical ***product***, the submission of ***information*** concerning safety or efficacy of the product, the origination of which involves a considerable effort, the Party shall not, without the consent of a person that previously submitted such safety or efficacy information to obtain marketing approval in the territory of the Party, authorize another to market a same or a similar product based on:
    (i) the safety or efficacy information submitted in support of the marketing approval; or
    (ii) evidence of the marketing approval,

    for at least five years for pharmaceutical products and ten years for agricultural chemical products from the date of marketing approval in the territory of the Party.

(b) If a Party requires or permits, in connection with granting marketing approval for ***a new pharmaceutical*** or new agricultural chemical ***product***, the submission of evidence concerning the safety or efficacy of a product that was previously approved in another territory, such as evidence of prior marketing approval in the other territory, the Party

shall not, without the consent of a person that previously submitted the safety or efficacy information to obtain marketing approval in the other territory, authorize another to market a same or a similar product based on:

(i) the safety or efficacy information submitted in support of the prior marketing approval in the other territory; or

(ii) evidence of prior marketing approval in the other territory,

for at least five years for pharmaceutical products and ten years for agricultural chemical products from the date of marketing approval of the new product in the territory of the Party.24

(c) For purposes of this Article, a ***new pharmaceutical product is one that does not contain a chemical entity that has been previously approved in the territory of the Party for use in a pharmaceutical product***, and a new agricultural chemical product is one that contains a chemical entity that has not been previously approved in the territory of the Party for use in an agricultural chemical product.

2. (a) If a Party requires or permits, as a condition of granting marketing approval for a ***pharmaceutical product that includes a chemical entity that has been previously approved for marketing in another pharmaceutical product***, the submission of new clinical information that is essential to the approval of the pharmaceutical product containing the previously approved chemical entity, other than information related to bioequivalency, the Party shall not, without the consent of a person that previously submitted such new clinical information to obtain marketing approval in the territory of the Party, authorize another to market a same or a similar product based on:

(i) the new clinical information submitted in support of the marketing approval; or

(ii) evidence of the marketing approval based on the new clinical information,

for at least three years from the date of marketing approval in the territory of the Party.

(b) If a Party requires or permits, in connection with granting marketing approval for a ***pharmaceutical product*** of the type specified in subparagraph (a), the submission of evidence concerning new clinical information for a product that was previously approved based on that new clinical information in another territory, other than evidence of information related to bioequivalency, such as evidence of prior marketing approval based on the new clinical information, the Party shall not, without the consent of the person that previously submitted such new clinical information to obtain marketing approval in the other territory, authorize another to market a same or a similar product based on:

(i) the new clinical information submitted in support of the prior marketing approval in the other territory; or

(ii) evidence of prior marketing approval based on the new clinical information in the other territory,

for at least three years from the date of marketing approval based on the new clinical information in the territory of the Party.

US-Singapore FTA

ARTICLE 16.8 : CERTAIN REGULATED PRODUCTS

1. If a Party requires the submission of information concerning the safety and efficacy of a ***pharmaceutical*** or agricultural chemical ***product*** prior to permitting the marketing of such product, the Party shall not permit third parties not having the consent of the party providing the information to market the same or a similar product on the basis of the approval granted to the party submitting such information for ***a period of at least five years from*** the date of approval for a pharmaceutical product and ten years from the date of approval for an agricultural chemical product.[16-14]

2. If a Party provides a means of granting approval to market ***a product specified in paragraph 1*** on the basis of the grant of an approval for marketing of the same or similar product in another country, the Party shall defer the date of any such approval to third parties not having the consent

of the party providing the information in the other country ***for at least five years*** from the date of approval for a pharmaceutical product and ten years from the date of approval for an agricultural chemical product in the territory of the Party or in the other country, whichever is later.

[16-14] Where a Party, on the date of its implementation of the TRIPS Agreement, had in place a system for protecting ***pharmaceutical*** or agricultural chemical ***products not involving new chemical entities*** from unfair commercial use that conferred a different form or period of protection shorter than that specified in paragraph 1 of Article 16.8, that Party may retain such system notwithstanding the obligations of that paragraph.

US Trans-Pacific Partnership IP Chapter Proposal

ARTICLE 9: Measures Related to Certain Regulated Products
...

Pharmaceutical Products

Submission of Information of Evidence Concerning the Safety or Efficacy of a New Pharmaceutical Product
2.

(a) If a Party requires or permits, as a condition for granting marketing approval for a ***new pharmaceutical product***, the submission of ***information*** concerning the safety or efficacy of the product, the origination of which involves a considerable effort, the Party shall not, without the consent of a person previously submitting such safety or efficacy information to obtain marketing approval in the territory of the Party, authorize a third person to market a same or a similar product based on:

(i) the safety or efficacy information previously submitted in support of the marketing approval; or

(ii) evidence of the existence of the marketing approval

for at least five years from the date of marketing approval of the new pharmaceutical product in the territory of the Party.

(b) If a Party requires or permits, in connection with granting marketing approval for a ***new pharmaceutical product***, the submission of evidence concerning the safety or efficacy of a product that was previously approved in another territory, such as evidence of prior marketing approval in the other territory, the Party shall not, without the consent of a person previously submitting the safety or efficacy information to obtain marketing approval in the other territory, authorize a third person to market a same or similar product based on:

(i) the safety or efficacy information submitted in support of a prior marketing approval in the other territory; or

(ii) evidence of the existence of a prior marketing approval in the other territory,

for at least five years from the date of marketing approval of the new pharmaceutical product in the territory of the Party.

Submission of New Clinical Information or Evidence relating to a Pharmaceutical Product that Includes a Chemical Entity that has been Previously Approved for Marketing in Another Pharmaceutical Product

(c) If a Party requires or permits, as a condition of granting marketing approval for a ***pharmaceutical product that includes a chemical entity that has been previously approved for marketing in another pharmaceutical product***, the submission of new clinical information that is essential to the approval of the pharmaceutical product containing the previously approved chemical entity, other than information related to bioequivalency, the Party shall not, without the consent of a person previously submitting such new clinical information to obtain marketing approval in the territory of the Party, authorize a third person to market a same or a similar product based on:

(i) the new clinical information previously submitted in support of the marketing approval; or

(ii) evidence of the existence of the marketing approval that was based on the new clinical information,

for at least three years form the date of marketing approval based on the new clinical information in the territory of the Party.

(d) If a Party requires or permits, in connection with granting marketing approval for a ***pharmaceutical product of the type specified in subparagraph (c)***, the submission of evidence concerning new clinical information for a product that was previously approved based on that new clinical information in another territory, other than evidence of information related to bioequivalency, such as evidence of prior marketing approval based on new clinical information, the Party shall not, without the consent of a person previously submitting such new clinical information to obtain marketing approval in the other territory, authorize a third person to market a same or a similar product based on:

(i) the new clinical information submitted in support of a prior marketing approval in the other territory; or

(ii) evidence of the existence of a prior marketing approval that was based on the new clinical information in the territory of the Party.

for at least three years from the date of marketing approval based on the new clinical information in the territory of the Party.

…

9. [Placeholder for specific provision applying to biologics].

General Provisions relating to Pharmaceutical Products and Agricultural Chemical Products

10. For purposes of this Article, ***a new pharmaceutical product means a product that does not contain a chemical entity that has been previously approved in the territory of the Party for use in a pharmaceutical product***.[6] For purposes of this Article, a new agricultural chemical product is one that contains a chemical entity that has not been previously approved in the territory of the Party for use in an agricultural chemical product.

[6] For greater certainty, the Parties understand that ***the term "pharmaceutical product" as used in this Chapter includes biologic products***.