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SEP 23 2016

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Re: Docket No. FDA-2012-P-0317

Dear Mr. Hester:

This letter responds to a Citizen Petition received on April 2, 2012 (Petition) and submitted on behalf of Abbott Laboratories (Abbott).¹ As described below, the Petition requests that FDA (FDA or Agency) not implement the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) as to “any application or any investigational new drug application (IND) for a biosimilar product that cites, as its reference product,” biologics license application (BLA) 125057 for Humira (adalimumab)² or any other product for which the BLA was submitted to FDA prior to the enactment of the BPCI Act.³ The Petition claims that permitting a biosimilar to reference a BLA submitted before the effective date of the BPCI Act would constitute a taking under the Fifth Amendment to the U.S. Constitution.⁴

FDA has carefully considered the issues that you have raised, other submitters’ comments to the citizen petition docket, and the relevant legal authorities. For the reasons set forth below, the Petition is denied.

I. SUMMARY OF THE PETITION

The Petition requests that FDA “confirm that it will not accept for filing, file, approve or discuss

¹ On January 2, 2013, Abbott announced that it had completed the separation of its research-based pharmaceuticals business, which became AbbVie Inc. (AbbVie). In this response, “Abbott” refers to both Abbott and AbbVie, collectively or individually.

² AbbVie holds the BLA for Humira.

³ Petition at 1.

⁴ See, e.g., *id.* at 2.

with any company” any application or any IND for a biosimilar product that references BLA 125057 for Humira (adalimumab) “or any other product for which a BLA was submitted to FDA prior to March 23, 2010, the date on which the BPCI Act was signed into law.”⁵ FDA approved the BLA for Humira on December 31, 2002.⁶ The Petition asserts that a BLA contains “analytical, preclinical, and clinical data, as well as detailed manufacturing information, most of which qualifies as trade secrets” or confidential commercial or financial information.⁷ The Petition claims that “[w]hen FDA approves a biosimilar biological product on the grounds that the reference product has been shown safe, pure, and potent, it uses these trade secrets.”⁸ The Petition states that the “approval of a biosimilar necessarily relies on and uses the trade secrets that the innovator sponsor submitted in support of the BLA” because, “[w]ere it not for those trade secrets[,] . . . there would be no pioneer biologic for the biosimilar sponsor to reference.”⁹

The Petition claims that Abbott and other manufacturers who submitted their BLAs to FDA prior to enactment of the BPCI Act “reasonably expected — on the basis of applicable law and agency statements — that the trade secrets and confidential commercial information contained in their applications would not be used to benefit a competitor” through approval of another company’s product.¹⁰ The Petition further claims that

FDA’s use of the trade secrets in pre-enactment sponsors’ BLAs to support approval of competitor products would frustrate these sponsors’ investment-backed expectation regarding their property and would constitute a taking under the Fifth Amendment to the U.S. Constitution that requires just compensation.¹¹

The Petition asserts that FDA should not implement the BPCI Act in any manner that would raise this constitutional issue and claims that the alleged takings “would expose the United States to enormous financial liability for just compensation.”¹²

II. BACKGROUND

A. The BPCI Act and the Biosimilar Pathway

The BPCI Act was enacted as part of the Affordable Care Act¹³ on March 23, 2010. The BPCI

⁵ Petition at 1.

⁶ The Petition (at 9) states that the last indication for which Humira received approval was in February 2008, over two years before the BPCI Act was enacted. We note that the Humira (adalimumab) injection product labeling currently lists ten indications, two of which were approved since September 2015 (See product labeling for Humira, approved June 30, 2016, available at <https://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>).

⁷ Id. at 2 & 13 n.44.

⁸ Id. at 2 (emphasis omitted).

⁹ Id. at 13.

¹⁰ Id. at 2.

¹¹ Id.

¹² Id.

¹³ Public Law 111-148, 124 Stat. 119, 804-21, tit. VII (sections 7001-7003).

Act creates an abbreviated approval pathway for biological products demonstrated to be biosimilar to, or interchangeable with, a reference product. The BPCI Act also grants exclusivity to sponsors of BLAs approved under section 351(a) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(a)).

Section 351(k) of the PHS Act, added by the BPCI Act, sets forth the requirements for an application for a proposed biosimilar product and an application or a supplement for a proposed interchangeable product. Section 351(i) of the PHS Act defines *biosimilarity* to mean “that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components” and that “there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.”¹⁴ The BPCI Act also amended the definition of *biological product* to include “protein (except any chemically synthesized polypeptide).”¹⁵

FDA will approve a BLA submitted under section 351(k) of the PHS Act if FDA “determines that the information submitted in the application . . . is sufficient to show that the biological product is biosimilar to the reference product . . .” and if “the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application.”¹⁶ An application submitted under section 351(k) of the PHS Act must contain, among other things, information demonstrating that “the biological product is biosimilar to a reference product based upon data derived from”:

- Analytical studies that demonstrate that the proposed biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components
- Animal studies (including the assessment of toxicity); and
- A clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency in one 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 proposed biological product.¹⁷

An application must also demonstrate that:

- The proposed biological product and reference product utilize the same mechanism of action for the conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent that the mechanism of action is known for the reference

¹⁴ 42 U.S.C. 262(i)(2)(A) and (B).

¹⁵ 42 U.S.C. 262(i)(1).

¹⁶ 42 U.S.C. 262(k)(3)(A) and (B).

¹⁷ 42 U.S.C. 262(k)(2)(A)(i)(I). The Agency has the discretion to determine that any of these elements is unnecessary in a section 351(k) application. 42 U.S.C. 262(k)(2)(A)(ii).

product

- The conditions of use prescribed, recommended, or suggested in the proposed labeling have been previously approved for the reference product
- The route of administration, dosage form, and strength of the proposed biological product are the same as those of the reference product; and
- The facility where the proposed biological product is manufactured, processed, packed, or held meets standards designed to assure that the product continues to be safe, pure, and potent.¹⁸

An application must include publicly available information regarding the Agency's previous determination that the reference product is safe, pure, and potent, and may include any additional information in support of the application, including publicly available information about the reference product or another biological product.¹⁹

Further, the BPCI Act provides exclusivity to sponsors of BLAs approved under section 351(a) of the PHS Act. The BPCI Act added section 351(k)(7) to the PHS Act, which specifies periods of time in which a 351(k) sponsor is not permitted to submit and FDA is not permitted to approve a 351(k) BLA. More specifically, approval of a section 351(k) application may not be made effective until 12 years after the date of first licensure of the reference product, which under the statute excludes the date of licensure of supplements and of certain other applications.²⁰ In addition, a section 351(k) application may not be submitted for review until 4 years after the date of first licensure of the reference product.²¹ The BPCI Act also adds section 351(m) to the PHS Act, which provides additional exclusivity to sponsors who conduct pediatric studies that meet certain requirements for pediatric exclusivity.²²

FDA has finalized several guidance documents describing aspects of FDA's implementation of the BPCI Act.²³

Congress created the biosimilar pathway after many years of discussions about the need for an abbreviated approval pathway for biological products that would be modeled in some respects on

¹⁸ 42 U.S.C. 262(k)(2)(A)(i)(II)-(V).

¹⁹ 42 U.S.C. 262(k)(2)(A)(iii).

²⁰ 42 U.S.C. 262(k)(7)(A) and (C).

²¹ 42 U.S.C. 262(k)(7)(B).

²² 42 U.S.C. 262(m). The BPCI Act also contains provisions relating to patents. See 42 U.S.C. 262(l); 7002(c) of the BPCI Act (conforming amendments relating to patents).

²³ For example, see the guidance for industry *Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009*. We update guidances periodically. For the most recent version of a guidance, check the FDA Drugs guidance Web page at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>. FDA's policies and procedures for developing, issuing, and using guidance documents (good guidance practices) are addressed in 21 CFR 10.115.

the abbreviated new drug application (ANDA) approval process for generic drugs.²⁴ This earlier pathway for generic drugs was created under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments).²⁵

Similar to the Hatch-Waxman Amendments, the BPCI Act was enacted with the intent of “balancing innovation and consumer interests.”²⁶ Accordingly, the BPCI Act provides both a new biosimilar approval pathway as well as substantial periods of exclusivity for sponsors of reference products. Citing the Hatch-Waxman Amendments, the Federal Circuit has recently observed of the biosimilar pathway that “this is not the first time that Congress has allowed generic applicants to benefit from the early work of innovators. That was a decision that Congress was entitled to make and it did so.”²⁷

B. The Protection of Trade Secrets

Trade secrets are subject to protection under both state and federal law. The Petition cites the Uniform Trade Secrets Act (UTSA), which, according to the Petition, has been adopted with minor variations by 45 states (including Maryland and Illinois), as well as the District of Columbia. The UTSA defines a *trade secret* as:

[I]nformation, including a formula, pattern, compilation, program, device, method, technique, or process, that:

- (i) derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use, and
- (ii) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.²⁸

²⁴ See, e.g., See Schmickel, D, 1999, The Biotechnology Industry Organization’s View on Hatch-Waxman Reform, Food Drug Law J, 54:241, 241-42; Behrendt, KE, 2002, The Hatch-Waxman Act: Balancing Competing Interests or Survival of the Fittest?, Food Drug Law J, 57:247, 269. The discussion, prior to enactment of the BPCI Act, of potential pathways for approval of biosimilar products is discussed further in section III.C.1. For the purpose of this response, the term *generic drug* refers to a new drug product for which approval is sought in an ANDA submitted under section 505(j) of the FD&C Act.

²⁵ Public Law 98-417. The Hatch-Waxman Amendments amended the Federal Food, Drug, and Cosmetic (FD&C Act) to add section 505(j) (21 U.S.C. 355(j)).

²⁶ Public Law 111-148, sec. 7001(b). The Hatch-Waxman Amendments reflect Congress’s efforts to balance the need to “make available more low cost generic drugs by establishing a generic drug approval procedure” with new incentives for drug development in the form of exclusivity and patent term extensions. See House Report No. 98-857, part 1, at 14-15 (1984), reprinted in 1984 U.S.C.C.A.N. 2647 at 2647-2648.

²⁷ *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1361 n.6 (Fed. Cir. 2015) (citations omitted) (rejecting an argument brought by Amgen (the sponsor of the reference product) that it was entitled to state law damages from Sandoz (the biosimilar applicant) for “wrongfully benefitting from Amgen’s establishment of the safety and efficacy” of its drug).

²⁸ National Conference of Commissioners, 1986, Uniform Trade Secrets Act with 1985 Amendments, § 1(4), available at http://www.uniformlaws.org/shared/docs/trade%20secrets/utsa_final_85.pdf.

The Petition also cites the Federal Trade Secrets Act, which makes it a criminal offense for a Federal employee to “publish[], divulge[], disclose[], or make[] known in any manner or to any extent not authorized by law any information coming to him in the course of his employment or official duties” that, among other things, “concerns or relates to” trade secrets.²⁹

In addition, the Freedom of Information Act (FOIA)³⁰ and FDA’s information disclosure regulations protect trade secrets and confidential commercial or financial information from disclosure, as discussed below.

C. Takings Under the Fifth Amendment

The Fifth Amendment to the U.S. Constitution prohibits the Government from taking private property for public use without just compensation.³¹ A taking cannot arise in the absence of a valid property interest.³² A taking gives rise to an entitlement to compensation *per se*, where the Government effects “a physical ‘invasion’” of real property or “where regulation denies all economically beneficial or productive use of land.”³³ In other circumstances, such as those presented here, the Supreme Court “engages in essentially ad hoc, factual inquiries” in determining whether a given regulation effects an uncompensated taking.³⁴

In *Penn Central Transportation Co. v. City of New York*, 438 U.S. 104 (1978), the Supreme Court identified three principal factors that “aim[] to identify regulatory actions that are functionally equivalent to the classic taking in which government directly appropriates private property or ousts the owner from his domain.”³⁵ These factors thus “focus[] directly upon the severity of the burden that government imposes upon private property rights,”³⁶ specifically:

- (1) “the extent to which the regulation has interfered with distinct investment-backed expectations”
- (2) “the economic impact of the regulation on the claimant”
- (3) “the character of the governmental action”³⁷

²⁹ 18 U.S.C. 1905.

³⁰ 5 U.S.C. 552.

³¹ U.S. CONST. amend. V.

³² See *Ruckelshaus v. Monsanto*, 467 U.S. 986, 1001-04 (1984); *Air Pegasus of D.C., Inc. v. United States*, 424 F.3d 1206, 1212-13 (Fed. Cir. 2005).

³³ *Lucas v. S.C. Coastal Council*, 505 U.S. 1003, 1015 (1992).

³⁴ *Penn Cent. Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978); see *Lingle v. Chevron U.S.A. Inc.*, 544 U.S. 528, 538-39 (2005).

³⁵ *Lingle*, 544 U.S. at 538-39 (2005) (citing *Penn Cent. Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978)).

³⁶ *Id.*

³⁷ *Penn Cent.*, 438 U.S. at 124.

The Supreme Court applied the *Penn Central* factors to an alleged taking of trade secrets in *Ruckelshaus v. Monsanto*, 467 U.S. 986 (1984). In the *Monsanto* case, Monsanto claimed that the provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) allowing the Environmental Protection Agency (EPA) to consider data from one application in evaluating a subsequent application and governing the disclosure of application data effected an unconstitutional taking.

In *Monsanto*, the Court focused on certain provisions of FIFRA that had changed as the statute was amended. In the version of the statute that was in effect from 1972 until 1978, FIFRA provided that a party submitting data to the EPA could designate materials as “trade secrets or commercial or financial information.”³⁸ That version of FIFRA expressly prohibited EPA from publicly disclosing information that it judged to contain or relate to “trade secrets or commercial or financial information.”³⁹ In addition, the 1972 to 1978 version of FIFRA expressly authorized EPA to consider data submitted by one applicant for registration in support of another application relating to a similar chemical, provided that the subsequent applicant offered to compensate the applicant who originally submitted the data.⁴⁰ Finally, the version of FIFRA in effect from 1972 until 1978 provided that any data that the original applicant had designated as “trade secrets or commercial or financial information” could not be considered by EPA to support another registration application unless the original submitter consented.⁴¹

A 1978 amendment to FIFRA modified this scheme by granting new registrants a 10-year period of exclusive use for data on new active ingredients and by providing a 15-year period of compensation for data submitted in prior registrations.⁴² The 1978 amendment also “provide[d] for disclosure of all health, safety, and environmental data to qualified requesters, notwithstanding the prohibition against disclosure of trade secrets.”⁴³ The Court observed that after the effective date of the 1978 amendment, “Monsanto was on notice of the manner in which EPA was authorized to use and disclose any data turned over to it by an applicant for registration.”⁴⁴

Monsanto held, first, that the Takings Clause of the Fifth Amendment would protect any trade secret property right that Monsanto had under state law.⁴⁵ Next, the Court analyzed the first *Penn Central* factor: the degree to which FIFRA interfered with “reasonable investment-backed expectations.”⁴⁶ The Court concluded that a taking could arise from EPA’s “consideration or disclosure of health, safety, and environmental data” only if Monsanto had submitted the data to

³⁸ *Monsanto*, 467 U.S. at 992 (quoting FIFRA § 10(a), 86 Stat. 989).

³⁹ *Id.* (quoting FIFRA § 10(b), 86 Stat. 989).

⁴⁰ *Id.* (citing FIFRA § 3(c)(1)(D)), 86 Stat. 989).

⁴¹ *Id.* at 993 (quoting FIFRA § 10(c), 86 Stat. 989).

⁴² *Id.* at 994-95 (citing FIFRA § 3(c)(1)(D)(i) and (ii), 92 Stat. 820-822).

⁴³ *Id.* at 995-96 (citing FIFRA § 10(d), 7 U.S.C. 136h(d)).

⁴⁴ *Id.* at 1006.

⁴⁵ *Id.* at 1003-04.

⁴⁶ *Id.* at 1005 (quoting *PruneYard Shopping Ctr. v. Robins*, 444 U.S. 74, 83 (1980)).

EPA between 1972 and 1978, the period when FIFRA contained an “explicit assurance of confidentiality or exclusive use.”⁴⁷ The Court found that at no other time did FIFRA provide an “explicit governmental guarantee” that would support a reasonable investment-backed expectation.⁴⁸ This reasoning applied both to FIFRA after the 1978 amendments and also to FIFRA before 1972, when the statute was “silent with respect to EPA’s authorized use and disclosure of data submitted to it in connection with an application for registration.”⁴⁹

As discussed below, *Monsanto* supports the conclusion that, to the extent Abbott has any property interest in the information in its BLA for Humira, there is no taking effected by FDA’s approval of a biosimilar to Humira.

D. FDA’s Information Disclosure Regulations

FDA implemented FOIA through regulations that include both general provisions (currently codified at part 20 (21 CFR part 20)) and specific provisions that apply to certain categories of information.⁵⁰

One general provision states that “[e]xcept where specifically exempt pursuant to the provisions of [part 20], all [FDA] records shall be made available for public disclosure.”⁵¹ A specific exemption provides that “[d]ata and information submitted or divulged to the [FDA] which fall within the definitions of a trade secret or confidential commercial or financial information are not available for public disclosure.”⁵² Part 20 implements a FOIA exemption for “trade secrets and commercial or financial information obtained from a person and privileged or confidential.”⁵³ Part 20 defines a *trade secret* as follows:

A trade secret may consist of any commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort. There must be a direct relationship between the trade secret and the productive process.⁵⁴

In addition, part 20 defines *confidential commercial or financial information* as follows:

Commercial or financial information that is privileged or confidential means valuable data or information which is used in one’s business and is of a type customarily held in

⁴⁷ Id. at 1013.

⁴⁸ Id. at 1011-13.

⁴⁹ Id. at 1008-10.

⁵⁰ See 39 FR 44602 (Dec. 24, 1974).

⁵¹ § 20.20(b); see 39 FR 44602, 44605 (Dec. 24, 1974).

⁵² § 20.61(c).

⁵³ See 5 U.S.C. 552(b)(4); 39 FR 44602, 44611-12 (Dec. 24, 1974).

⁵⁴ § 20.61(a); accord *Public Citizen v. FDA*, 704 F.2d 1280, 1289 (D.C. Cir. 1983).

strict confidence or regarded as privileged and not disclosed to any member of the public by the person to whom it belongs.⁵⁵

FDA's specific disclosure regulation for biological products (§ 601.51 (21 CFR 601.51)) defines a *biological product file* as "all data and information submitted with or incorporated by reference in any application for a biologics license, IND's incorporated into any such application, master files, and other related submissions" and provides that the "availability for public disclosure of any record in the biological product file shall be handled in accordance with the provisions of this section."⁵⁶

Under that regulation, the contents of a biological product file (and the existence of the file) remain confidential prior to approval of a BLA, provided that "the existence of a biological product file has not been publicly disclosed or acknowledged."⁵⁷

After the BLA is approved, the regulation makes the following eight categories of information in the biological product file "immediately available for public disclosure unless extraordinary circumstances are shown":⁵⁸

- "All safety and effectiveness data and information"⁵⁹
- "A protocol for a test or study, unless it is shown to fall within the exemption established for trade secrets and confidential commercial or financial information in § 20.61"
- "Adverse reaction reports, product experience reports, consumer complaints, and other similar data and information, after deletion of" names and similar identifying information
- "A list of all active ingredients and any inactive ingredients previously disclosed to the public, as defined in § 20.81"
- "An assay method or other analytical method, unless it serves no regulatory or compliance purpose and it is shown to fall within the exemption established in § 20.61" for trade secrets and confidential commercial information
- "All correspondence and written summaries of oral discussions relating to the biological product file"
- All records showing the manufacturer's testing of a particular lot, after deletion of data or information that would show the volume of the drug produced, manufacturing procedures

⁵⁵ § 20.61(b).

⁵⁶ § 601.51(a).

⁵⁷ § 601.51(b) & (c).

⁵⁸ § 601.51(e).

⁵⁹ Id. Safety and effectiveness data is defined in § 601.51(g) to "include all studies and tests of a biological product on animals and humans and all studies and tests on the drug for identity, stability, purity, potency, and bioavailability."

and controls, yield from raw materials, costs, or other material falling within §20.61”

- “All records showing the testing of and action on a particular lot by” FDA⁶⁰

After approval of a BLA, the following three categories of information in a biological product file remain unavailable for public disclosure unless the information was previously disclosed to the public or “relate[s] to a product or ingredient that has been abandoned” and “no longer represent[s] a trade secret or confidential commercial or financial information”:

- “Manufacturing methods or processes, including quality control procedures”
- “Production, sales, distribution, and similar data and information, except that” a compilation of these data may be available for public disclosure provided that it does not reveal confidential data or information
- “Quantitative or semiquantitative formulas”⁶¹

As FDA explained in the preamble to the final rule, these three categories of information generally include trade secrets or confidential commercial or financial information.⁶²

III. DISCUSSION

A. Abbott Lacks a Protected Property Interest in Information Available to the Public

The Fifth Amendment does not protect information that Abbott describes as trade secrets but that was available for public disclosure under FDA’s information disclosure regulations after the Agency approved the Humira BLA in 2002. Such publicly available information cannot satisfy the second element under the UTSA definition of a *trade secret*, i.e., that the information “is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.”⁶³

Under FDA’s regulations, FDA must make “[a]ll safety and effectiveness data and information” submitted in a BLA “immediately available for public disclosure unless extraordinary circumstances are shown” following approval of a BLA.⁶⁴ The phrase *safety and effectiveness data* includes “all studies and tests of a biological product on animals and humans and all studies and tests on the drug for identity, stability, purity, potency, and bioavailability.”⁶⁵ This

⁶⁰ § 601.51(e).

⁶¹ § 601.51(f).

⁶² 39 FR 44602, 44640 (Dec. 24, 1974).

⁶³ UTSA, *supra* note 28, at § 1(4).

⁶⁴ § 601.51(e)(1).

⁶⁵ § 601.51(g).

definition encompasses the analytical, preclinical, and clinical data that Abbott now characterizes as trade secrets.⁶⁶

The “extraordinary circumstances” exception in FDA’s disclosure regulation would not have prevented the Agency from disclosing Abbott’s analytical, preclinical, and clinical data in response to a FOIA request. In promulgating the final disclosure regulation in 1974, FDA made clear that the extraordinary circumstances provision “creates a strong presumption of disclosure and requires any person who believes that a specific record...should not be disclosed bears the burden of overcoming that presumption by showing *unusual circumstances* that justify nondisclosure.”⁶⁷ FDA thus explained that the burden for demonstrating extraordinary circumstances rests with the person wishing to prevent disclosure.⁶⁸ FDA also explained that it expected the person wishing to prevent disclosure to articulate extraordinary circumstances “in concrete terms” to justify non-disclosure.⁶⁹ Moreover, FDA anticipated that extraordinary circumstances would be found only “on rare occasions” where “circumstances may arise that cannot be foreseen at this time.”⁷⁰

When the Humira BLA was submitted and approved in 2002, Abbott did not show — and still has not shown — any extraordinary circumstances, i.e., “unusual circumstances,” that justify nondisclosure of the safety and effectiveness data and information of the Humira BLA.⁷¹ Because no extraordinary circumstances were shown, § 601.51(e) required FDA to make Abbott’s safety and effectiveness data and information available for public disclosure immediately following FDA’s approval of the Humira BLA in 2002.⁷²

⁶⁶ See Petition at 2.

⁶⁷ 39 FR 44602, 44603 (Dec. 24, 1974) (emphasis added).

⁶⁸ *Id.*

⁶⁹ *Id.* at 44633. Case law confirms this expectation, emphasizing that “[c]onclusory and generalized allegations” of competitive harm could not support nondisclosure under the FOIA exemption for trade secrets and confidential commercial information. *Pub. Citizen Health Research Grp.*, 185 F.3d 898, 906 (D.C. Cir. 1999) (quoting *Pub. Citizen Health Research Grp. v. FDA*, 704 F.2d 1280, 1291 (D.C. Cir. 1983)); see also *Gov’t Accountability Project v. U.S. Dep’t of Health & Human Servs.*, 691 F. Supp. 2d 170, 175-76 (D.D.C. 2010) (discussing specific safety and effectiveness data and stating that “[d]efendants have proffered only vague and conclusory allegations in support of their claim that release of the information at issue will likely cause competitive harm”).

⁷⁰ *Id.* at 44632. Abbott cites a single case in which, Abbott states, FDA found extraordinary circumstances on specific facts where, in light of a prior commercial relationship between two parties, the release of information could have been used to obtain approval for a competing product. Petition at 23-24. Abbott has not identified any other instance in which the Agency has withheld information that otherwise would be available for public disclosure under § 601.51(e) based upon an explicit finding of extraordinary circumstances. In fact, FDA has repeatedly disclosed safety and effectiveness information from approved BLAs, consistent with applicable statutory and regulatory provisions, including 21 CFR § 601.51(e).

⁷¹ 39 FR 44602, 44603 (Dec. 24, 1974). We note that Abbott only appears to be challenging the alleged “use” of the data and information in its BLA to approve other biosimilar applications as described in its petition and does not appear to be alleging any specific disclosure of its data or information.

⁷² This was true at the time of approval of Abbott’s BLA, and the result would be the same today after the creation of a biosimilars pathway under the BPCI Act. The possibility that a biological product may be approved under section 351(k) of the PHS Act is not inherently an “extraordinary circumstance” that would justify a departure from the requirement that FDA make safety and effectiveness data and information available for public disclosure upon

As the Supreme Court observed in *Monsanto*, “the property right [in a trade secret] is defined by the extent to which the owner of the secret protects his interest from disclosure to others.”⁷³ The information in Humira’s BLA that was subject to public disclosure following approval cannot meet the requirement, under the UTSA, that a trade secret be “the subject of efforts that are reasonable under the circumstances to maintain its secrecy.” This requirement is not satisfied where information is disclosed to the Government without a mechanism to ensure that secrecy is maintained.⁷⁴ In the absence of a protected property right, Abbott cannot establish a taking as to that data and information.⁷⁵

Our conclusion is the same to the extent that Abbott claims that the safety and effectiveness data and information is confidential commercial information, rather than trade secrets, under FDA’s disclosure regulations. FDA’s disclosure regulations implement and adopt the language of FOIA,⁷⁶ and information must be secret to qualify for the FOIA exemption for trade secrets and confidential commercial and financial information (i.e., Exemption 4).⁷⁷ That secrecy does not exist where information is subject to disclosure by the Government, even if the Government never actually releases the information.⁷⁸

Because the analytical, preclinical, and clinical data submitted by Abbott were available for public disclosure immediately following the approval of the Humira BLA, they are not property entitled to protection under the Fifth Amendment.⁷⁹

approval of a BLA. The utility of such safety and effectiveness data and information to a potential competitor is not inherently greater if the competitor seeks licensure for its biological product under section 351(k) of the PHS Act rather than under section 351(a). Furthermore, public availability of the safety and effectiveness data and information supporting approval of the reference product by itself does not necessarily reduce the burden on the biosimilar applicant to provide data, including from analytical and clinical studies, to support approval of a biosimilar under section 351(k). Accordingly, FDA continues to evaluate claims of extraordinary circumstances on a case-by-case basis and will assess whether such claims describe, in concrete terms, unusual circumstances that justify nondisclosure.

⁷³ *Monsanto*, 467 U.S. at 1002.

⁷⁴ *Laing v. BP Expl. & Prod. Inc.*, No. 8:13-cv-1041-T-23TGW, 2014 WL 272846, at *4 (M.D. Fla. Jan. 23, 2014) (applying the Florida Uniform Trade Secrets Act and stating that “[c]lear authority holds that an idea is not reasonably maintained in requisite secrecy if disclosed to a government official without an accompanying mechanism to maintain secrecy” (internal quotation omitted)); see also *Cubic Transp. Sys., Inc. v. Miami-Dade County*, 899 So.2d 453, 454 (Fla. Dist. Ct. App. 2005) (holding that plaintiff failed to take “reasonable” measures to preserve confidentiality where it submitted documents to a local government without marking the documents as “confidential” (quoting *Sepro Corp. v. Fla. Dep’t of Env’tl. Prot.*, 839 So.2d 781, 783-84 (Fla. 1st DCA 2003)); cf. *Awards.com, LLC v. Kinko’s, Inc.*, 834 N.Y.S.2d 147, 156 (N.Y. App. Div. 2007) (apparently applying Restatement of Torts § 757 Comment b in holding that plaintiffs waived any trade secret protection as to material publicly filed in court because “[p]rotection against the misappropriation of trade secrets still requires a substantial element of secrecy”).

⁷⁵ See *Monsanto*, 467 U.S. at 1001-04; *Air Pegasus*, 424 F.3d at 1212-13.

⁷⁶ See, e.g., 39 FR 44602 (Dec. 24, 1974).

⁷⁷ *Herrick v. Garvey*, 298 F.3d 1184, 1193-94 (10th Cir. 2002) (applying FOIA Exemption 4).

⁷⁸ *Id.*

⁷⁹ We note that Abbott’s Petition does not purport to establish the specific elements of a trade secret or confidential commercial information for each piece of information that Abbott claims is protected. There may be additional reasons why the information at issue does not constitute trade secrets or confidential commercial information. For

B. Even Assuming a Property Interest Could be Identified, Abbott Fails to Identify a Use of Its Information by FDA That Would Give Rise to a Taking

Even assuming that Abbott could establish a property interest in any information in its BLA for Humira, Abbott fails to identify any use by FDA of its information that would give rise to a taking. We note that Abbott does not base its takings argument upon any direct use by FDA of any particular trade secret in Abbott's BLA or approval of a biosimilar application. Specifically, Abbott has not identified any particular trade secret that has been "used" but instead argues that *all* of the trade secrets in the reference product's BLA are used when a biosimilar is approved.⁸⁰

Abbott relies on a very broad conception of actionable "use" that is not supported by the law: that it would represent a taking for FDA to rely on its prior determination that the reference product is safe, pure, and potent because that determination by the Agency was based on consideration of Abbott's trade secrets. Abbott alleges that "[a]ny FDA approval of a biosimilar application necessarily uses the trade secrets that were submitted in support of the BLA that the biosimilar is referencing" because, "[w]ere it not for those trade secrets[,] . . . there would be no pioneer biologic for the biosimilar sponsor to reference."⁸¹ Abbott further argues that there is a "use" where "an agency relieves a follow-on applicant of the obligation to submit supporting data for a product, because a prior applicant for a similar product has already submitted relevant trade secrets to the agency."⁸² However, as we discuss in Section III.C, Abbott's argument that there was any "use" of its information that amounts to a taking is directly at odds with *Monsanto* because here there was no "explicit guarantee of exclusive use" as would be necessary to create a reasonable expectation that might support a takings claim.⁸³

FDA disagrees with Abbott's contention that the Agency's reliance on FDA's prior finding that the reference product is safe, pure, and potent constitutes a "use" of Abbott's information that could give rise to a taking.⁸⁴ Abbott has no protected property interest in FDA's finding regarding the safety, purity, and potency of the reference product. The BPCI Act requires biosimilar applications to include "*publicly-available* information regarding [FDA's] previous determination that the reference product is safe, pure, and potent."⁸⁵ There is no property interest, including any interest that Abbott could assert, in publicly available information about

example, Abbott's alleged trade secrets and confidential commercial information may be publicly available through other means and in other jurisdictions. Technical information concerning adalimumab has been disclosed in more than 200 U.S. patents and applications assigned to either Abbott or its corporate affiliates.

⁸⁰ Petition at 13.

⁸¹ *Id.*

⁸² *Id.* at 15-16 (citing *Syngenta Crop Protection, Inc. v. Helliker*, 138 Cal. App. 4th 1135, 1146-48 (Cal. Ct. App. 2006)); see also Petition at 14 (claiming that "subsequent applications . . . omit trade secrets comparable to those required of the reference product sponsor"). Abbott does not cite, nor have we identified, any additional authority in support of the theory of the "use" of a trade secret set forth in *Syngenta*.

⁸³ *Monsanto*, 467 U.S. at 1009 n.14; see *id.* at 1008-1010.

⁸⁴ See Petition at 14-15.

⁸⁵ 42 U.S.C. 262(k)(2)(A)(iii)(I) (emphasis added). The BPCI Act also provides that a biosimilar application "may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product." 42 U.S.C. 262(k)(2)(A)(iii)(II).

FDA's prior determination regarding the reference product.⁸⁶ Where there is no property interest, there cannot be a taking.⁸⁷

Other than Abbott's broad and unsupported conception of "use," which we reject, Abbott has not identified any specific "use" of its trade secrets that would constitute a taking.⁸⁸ A biosimilar applicant must submit its own comparative information about the biosimilar product and the reference product to meet the statutory requirements for approval.⁸⁹ In addition, the biosimilar applicant does not rely on any manufacturing process information submitted for the reference product but, instead, must generate and submit its own information to establish that the manufacturing process for the biosimilar product is acceptable.⁹⁰

Thus, Abbott does not identify any "use" of its information that would amount to a taking.

C. There Is No Regulatory Taking Under the *Penn Central* Analysis

As discussed above, because Abbott's analytical, preclinical, and clinical data were available for public disclosure immediately following the approval of the Humira BLA, they are not property entitled to protection under the Fifth Amendment. Further, Abbott has not identified a "use" of its information that would amount to a taking. However, even if Abbott were to identify both (1) property that is eligible for Fifth Amendment protection and (2) a use of that property by FDA when FDA approved a biosimilar product, the *Penn Central* factors demonstrate that FDA's approval of a biosimilar product that references a BLA approved before the enactment of the BPCI Act does not give rise to a regulatory taking. We address each of the following three *Penn Central* factors in turn: (1) "the extent to which the regulation has interfered with distinct investment-backed expectations," (2) "the economic impact of the regulation on Abbott," and (3) "the character of the governmental action."⁹¹

⁸⁶ Publicly available information cannot satisfy the second element under the UTSA definition of a *trade secret*, i.e., that the information "is the subject of efforts that are reasonable under the circumstances to maintain its secrecy." UTSA, *supra* note 28, at § 1(4); see also *Monsanto*, 467 U.S. at 1002. We note that in the context of ANDAs submitted under section 505(j) of the FD&C Act and new drug applications (NDAs) submitted under section 505(b)(2) of the FD&C Act, FDA has stated that "[r]eliance on FDA's *finding* or conclusion that an approved drug is safe and effective does not involve disclosure to the ANDA or 505(b)(2) applicant — or to the public — of the data in the listed drug's NDA. Instead, it permits the ANDA or 505(b)(2) applicant to rely on the fact that FDA found a drug product with certain characteristics to be safe and effective . . ." May 30, 2006, response to Kathleen M. Sanzo, Stephan E. Lawton, and Stephen G. Juelsgaard re: Docket Nos. FDA-2004-P-0339, FDA-2003-P-0003, FDA-2004-P-0214, and FDA-2004-N-0059 (emphasis in original). (Original Docket Nos. 2004P-0231/CP1 & SUP1, 2003P-0176/CP1 & EMC1, 2004P-0171/CP1, and 2004N-0355 were changed as a result of FDA's transition to its new docketing system (Regulations.gov) in January 2008.)

⁸⁷ See *Monsanto*, 467 U.S. at 1001-04; *Air Pegasus*, 424 F.3d at 1212-13.

⁸⁸ See Petition at 15.

⁸⁹ *E.g.* 42 U.S.C. 262(k)(2)(A)(i)(I)-(IV) (describing information about the reference product and proposed biosimilar product that a biosimilar applicant must submit).

⁹⁰ See 42 U.S.C. 262(k)(2)(A)(i)(V); see, generally, guidance for industry *Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product*, at 4-5..

⁹¹ *Penn Cent.*, 438 U.S. at 124.

1. *FDA's Approval of a Biosimilar Product Referencing a Pre-Enactment BLA Does Not Interfere With Any Reasonable Investment-Backed Expectations*

We begin our analysis with the *Penn Central* factor that the Supreme Court held to be decisive in rejecting an alleged taking of a trade secret: the absence of any interference with reasonable investment-backed expectations.⁹²

Abbott has failed to establish that when it submitted its BLA to FDA in 2002, Abbott had a reasonable investment-backed expectation “that the trade secrets in that application would not be used by the agency in any manner to support approval of another company’s product or disclosed to other applicants to guide their research efforts.”⁹³ Nowhere in the Petition does Abbott identify an “explicit governmental guarantee” that may “form the basis of a reasonable investment-backed expectation.”⁹⁴ Instead, Abbott claims that it based its expectation upon: (1) the absence, prior to the enactment of the BPCI Act, of language in the PHS Act expressly authorizing an applicant to reference a previously approved BLA; (2) FDA’s disclosure regulation and the Agency’s application of that regulation; and (3) statements by FDA officials, prior to the enactment of the BPCI Act, that FDA lacked authority to approve biosimilars.⁹⁵ None of these facts supports a reasonable investment-backed expectation for the reasons set forth below.

First, *Monsanto* holds that statutory silence cannot support a reasonable investment-backed expectation, so the absence of statutory language expressly authorizing a proposed biosimilar product to reference a previously licensed BLA at the time the Abbott BLA was submitted does not provide the foundation for the expectation that Abbott claims. In *Monsanto*, the Supreme Court analyzed three versions of FIFRA: the statute enacted in 1947, FIFRA as amended in 1972, and FIFRA as amended in 1978. The Court held that only the 1972 version of FIFRA “explicitly guaranteed to Monsanto and other registration applicants an extensive measure of confidentiality and exclusive use.”⁹⁶ That version “gave Monsanto explicit assurance that EPA was prohibited from disclosing publicly, or considering in connection with the application of another, any data submitted by an applicant if both the applicant and EPA determined the data to constitute secrets.”⁹⁷ Thus, only the 1972 version included an “explicit governmental guarantee [that] formed the basis of a reasonable investment-backed expectation.”⁹⁸

By contrast, the Court emphasized that the 1947 statute “was silent with respect to EPA’s authorized use and disclosure of data submitted to it in connection with an application for registration,” and held that therefore “Monsanto could not have had a ‘reasonable investment-

⁹² *Monsanto*, 467 U.S. at 1005.

⁹³ Petition at 21.

⁹⁴ *Monsanto*, 467 U.S. at 1011.

⁹⁵ Petition at 21-25.

⁹⁶ *Monsanto*, 467 U.S. at 1011.

⁹⁷ *Id.* (citing FIFRA § 10, 86 Stat. 989).

⁹⁸ *Id.*

backed expectation' that EPA would maintain those data in strictest confidence and would use them exclusively for the purpose of considering the Monsanto application in connection with which the data were submitted."⁹⁹ The Court indicated that even if EPA had a practice of not using the data to examine other applications, there was no "explicit guarantee of exclusive use" as would be necessary to create a "reasonable expectation that...EPA would not use the data...when examining the application of another."¹⁰⁰

The statute at issue here — the PHS Act as of 2002 — is analogous to the 1947 version of FIFRA in that the PHS Act did not explicitly guarantee that a follow-on biological product referencing a previously approved BLA never would be approvable. *Monsanto* holds that such statutory silence cannot support a reasonable investment-backed expectation of the type that Abbott claims.

Second, FDA's disclosure regulation, promulgated in 1974,¹⁰¹ could not support a reasonable investment-backed expectation because that regulation is silent with respect to any use of data by FDA and makes the analytical, preclinical, and clinical data in a BLA available for public disclosure upon the approval of the BLA. Abbott claims that the exception to the disclosure regulation for extraordinary circumstances would have barred disclosure and asserts that the Agency's application of that exception in response to a 1996 request from Berlex Laboratories "demonstrates that FDA has consistently taken the position that the agency would not release safety and efficacy data where these data retained competitive value (i.e., could be used by a competitor)."¹⁰²

In the Berlex matter — the only example Abbott cites as an application of the extraordinary circumstances exception for a BLA — Abbott describes unique facts that the BLA holder presented to FDA to establish the potential for competitive harm.¹⁰³ Abbott does not present any analogous facts that would have applied to the information in the Humira BLA in 2002 or subsequent years.

When Abbott argues that the extraordinary circumstances exception to FDA's disclosure regulation supported a reasonable expectation that the safety and effectiveness information in the Humira BLA would not be made available for public disclosure,¹⁰⁴ Abbott disregards that this exception, by its very terms, arises only in unusual circumstances.¹⁰⁵ Absent a showing of

⁹⁹ Id. at 1008, 1010.

¹⁰⁰ Id. at 1009 n.14.

¹⁰¹ 39 FR 44602 (Dec. 24, 1974).

¹⁰² Petition at 24.

¹⁰³ See id. at 23-24.

¹⁰⁴ See id. at 22-24.

¹⁰⁵ See § 601.51(e). The Petition cites prior FDA statements characterizing the operation of "extraordinary circumstances" provision. See Petition at 22 n.79. The statements cited by Abbott emphasize that a manufacturer may support nondisclosure by showing "in a particular case, because of extraordinary circumstances, [disclosure of data] will provide a future competitive advantage." Id. (quoting 39 FR 44602, 44613). These statements could not have supported the reasonable expectation that Abbott claims because Abbott did not ever show that extraordinary

extraordinary circumstances, FDA's disclosure regulations made Abbott's safety and effectiveness data immediately available for public disclosure at the time the BLA was approved in 2002.¹⁰⁶ Abbott never showed that extraordinary circumstances existed for the Humira BLA and could not have reasonably expected that its analytical, preclinical, and clinical data would not be made available for public disclosure upon approval of the Humira BLA, as is required by FDA's regulation.¹⁰⁷

Third, Abbott claims that it relied upon statements by FDA officials that the Agency lacked authority to approve a biosimilar product prior to the enactment of the BPCI Act. None of those statements, however, suggests that FDA never would have such authority. Nor does Abbott cite any legal support for the claim that such Agency statements amount to "an explicit governmental guarantee [that] formed the basis of a reasonable investment-backed expectation."¹⁰⁸

Instead, Abbott cites a case that highlights the absence of any explicit governmental guarantee here. In *Tri-Bio Laboratories, Inc. v. United States*, 836 F.2d 135 (3d Cir. 1987), the Third Circuit held that the following provision in an FDA regulation supported a reasonable investment-backed expectation that the Agency would refrain from nonconsensual use of information: "Any reference to information furnished by a person other than the applicant may not be considered unless its use is authorized in a written statement signed by the person who submitted it."¹⁰⁹ The regulation at issue in *Tri-Bio Laboratories* related to applications for new animal drugs and Abbott cites no analogous statutory or regulatory provision applicable to BLAs.

In fact, it would have been unreasonable for Abbott to expect that the information in its BLA would never "be used by the agency in any manner to support approval of another company's

circumstances existed for the Humira BLA. Furthermore, Abbott does not appear to be challenging any specific disclosure of its data or information.

¹⁰⁶ In promulgating the disclosure regulations in 1974, FDA noted that "unlike the situation for new drugs," no competitor could utilize the safety and effectiveness data to "gain approval" for a biological product because "[t]here is no such thing as a 'me-too' biologic," 39 FR 44602, 44641 (Dec. 24, 1974) (noting further that "biologics never became 'old drugs' and [could not] be marketed solely on the basis of an existing product standard published in the *Federal Register*"). Abbott alleges that this statement provided "a reasonable, investment-backed expectation that [a sponsor's] trade secrets would not be released or used to benefit competitors." Abbott's emphasis on this preamble statement is misplaced. First, we note that Abbott does not appear to be challenging any specific disclosure of its data or information. Second, substantial discussion of potential biosimilar approval pathways had already occurred by the time Abbott submitted its BLA for Humira in 2002 and therefore Abbott should have known at that time of the potential for approval of a biosimilar. (This issue is discussed in more detail in this response, below.) Third, to the extent Abbott suggests that certain statements in a preamble to a disclosure regulation can be interpreted as a promise that the law would not change (e.g., by the enactment of a statutory approval pathway for biosimilar products), we note that the preamble provided no such promise, nor would it have been reasonable for Abbott to interpret it as such.

¹⁰⁷ In *Monsanto*, the Supreme Court concluded that when a party submitting data to the government "is aware of the conditions under which the data are submitted, and the conditions are rationally related to a legitimate Government interest, a voluntary submission of data by an applicant in exchange for the economic advantages of a registration can hardly be called a taking." 467 U.S. at 1007.

¹⁰⁸ *Monsanto*, 467 U.S. at 1011.

¹⁰⁹ *Tri-Bio Labs.*, 836 F.2d at 140-41 (quoting 21 CFR 514.1(a) (1987)).

product or disclosed to other applicants to guide their research efforts.”¹¹⁰ As a general matter, a firm that does business in a heavily regulated field, like pharmaceuticals and biotechnology, must expect regulatory change.¹¹¹ And here, Abbott could and should have foreseen the advent of biosimilars when it submitted its BLA in 2002. In the late 1990s, there was considerable discussion in the pharmaceutical and biotechnology industry about potential pathways for approval of biosimilar products. In 1998, the CEO of generic drug maker Barr Laboratories, Inc., said that a top priority of the generic industry was the development of a pathway for the approval of follow-on biologics.¹¹²

The following year, the *Food and Drug Law Journal* published two articles about the possibility of generic biologics.¹¹³ An article published in the same journal in 2001 called for “[a]ny legislative changes to the treatment of biological products (e.g., contemplating ‘generic biologics’) [to] be given close scrutiny” and for “[t]he protection of innovators’ clinical data, as framed in the FDA’s data exclusivity rules, [to] be seriously evaluated for greater protection.”¹¹⁴ The next year, the same journal published an article noting that “it is possible to foresee the patents for several biotech drugs expiring; thus, necessitating the need for review and approval of generic biologics. Accordingly, an abbreviated approval process for generic biotech drugs is necessary.”¹¹⁵

The creation of a pathway for approval of generic biologics also gained attention in Congress in the early 2000s. In 2002, Senator Orrin Hatch stated:

¹¹⁰ Petition at 21.

¹¹¹ *Connolly v. Pension Benefit Guar. Corp.*, 475 U.S. 211, 227 (1986) (“Those who do business in a regulated field cannot object if the legislative scheme is buttressed by subsequent amendments to achieve the legislative end.” (quoting *Fed’l Housing Admin. v. The Darlington, Inc.*, 358 U.S. 84, 91 (1958))); see also *Franklin Mem’l Hosp. v. Harvey*, 575 F.3d 121, 128 (1st Cir. 2009) (noting that a hospital’s “investment-backed expectations are tempered by the fact that it operates in the highly regulated hospital industry”). We note that the creation of the approval pathway for biosimilar products is only a recent example of how FDA’s regulation of biological products has evolved to keep pace with scientific advances. FDA once required that the licensee of a product control and supervise the entire manufacturing process. In 1983, however, FDA established a policy permitting a licensee to produce certain monoclonal antibody products from a partially processed monoclonal antibody obtained from another licensee. See 48 FR 50,795-03 (Nov. 3, 1983). In 1996, FDA concluded that in certain cases, a manufacturer may make changes to the manufacturing process without conducting new clinical testing. FDA guidance *Demonstration of Comparability of Human Biological Products, Including Therapeutic Biotechnology-Derived Products*. This policy was upheld in *Berlex Labs., Inc. v. FDA*, 942 F. Supp. 19 (D.D.C. 1996).

¹¹² See Waxman/Hatch Should be Expanded to Cover Generic Biologics, F-D-C Rep. (“The Pink Sheet”), Nov. 16, 1998, at 3.

¹¹³ See Schmickel, D, 1999, The Biotechnology Industry Organization’s View on Hatch-Waxman Reform, *Food Drug Law J*, 54:241 (“Generic companies have voiced a desire to have a generic biologic Superficially, generic competition seems inevitable”); Raines, L, 1999, Biotechnology and Patent Term Extension Issues, *Food Drug Law J*, 54:237, 239 (1999) (“It is unclear . . . whether an ANDA or paper NDA process can or will be used for biotechnology products that are regulated as drugs. This is one of the most significant and unresolved issues confronting the industry.”).

¹¹⁴ See Schroeder, RG and P Papas, 2001, Protecting the Balance of Hatch-Waxman: Understanding the Industry’s New Dynamics for the 21st Century, *Food Drug Law J*, 56:19, 26.

¹¹⁵ Behrendt, KE, 2002, The Hatch-Waxman Act: Balancing Competing Interests or Survival of the Fittest?, *Food Drug Law J*, 57:247, 269 (citation omitted).

one of the highest priorities of the next Commissioner of Food and Drugs will be to make certain that the leadership of FDA's Center for Biologics is committed . . . to identifying the issues and attempting to find solutions to the many issues that need to be resolved in order to make generic biologics.¹¹⁶

Abbott also could have foreseen that any new regulatory pathway would allow biosimilar products to reference BLAs approved prior to enactment. Each article cited above analogized biosimilars to generic drugs approved under the 1984 Hatch-Waxman Amendments, which are approved based on reference to previously approved drug products and which did not bar generic applicants from referencing pre-enactment innovator drugs.¹¹⁷

For these reasons, Abbott lacked a reasonable investment-backed expectation that the information in its BLA “would not be used by the agency in any manner to support approval of another company's product or disclosed to other applicants to guide their research efforts.”¹¹⁸

2. *The Economic Impact of the Regulation*

Rather than describe any actual economic harm, Abbott asserts that the economic impact of FDA's purported “use” of Abbott's trade secrets is inherently sufficient to support the finding of a taking. This is because the “right to exclude others” is central to the property interest at issue and because — according to Abbott — FDA's purported “use” of Abbott's trade secrets would destroy Abbott's competitive edge.¹¹⁹

Abbott's effort to invoke a presumption of economic harm contradicts its statements to investors that the approval of a biosimilar to Humira will not result in material economic harm. The Chief Financial Officer of AbbVie Inc. (AbbVie) has repeatedly reported to Wall Street analysts that AbbVie does not expect an immediate and significant adverse financial impact from the approval of a biosimilar version of Humira.¹²⁰ He provided the following prediction in June 2014:

We've been very clear to the market that this Humira biosimilar event, when it comes in 2017 — this is not going to be anything like a small molecule. We think that Humira is going to be a very, very durable, important cash flow generator well after 2017.¹²¹

Three months earlier, he made a similar statement about the prospects for Humira following the introduction of competing biosimilar products:

[W]e also don't think this is a brand that is going to be experiencing the type of generic curve that you see with a small molecule. In fact, we think it will be a relatively slow

¹¹⁶ 148 Cong. Rec. 15,678 (Aug. 1, 2002) (statement of Sen. Hatch).

¹¹⁷ See supra note 26 and accompanying text.

¹¹⁸ Petition at 21.

¹¹⁹ Id. at 26.

¹²⁰ AbbVie appears to anticipate competition from biosimilar versions of Humira following patent expiration.

¹²¹ 6/11/14 FD (Fair Disclosure) Wire 14:40:00, AbbVie Inc. at Goldman Sachs Healthcare Conference – Final.

controlled degradation and the reality is when you look at the size of Humira out at that point in time, it is going to be generating meaningful, meaningful cash to AbbVie, much more than it is today.¹²²

During a Barclays Healthcare conference call in March 2015, AbbVie's Chairman and Chief Executive Officer stated:

We built this very robust pipeline that ultimately can deliver significant growth going forward. We built a biosimilar strategy that we've had in place and we have a lot of confidence in...the fact that Humira will be a durable performing asset for us going forward. And we positioned ourselves well to be able to be able to deliver on that expectation that we set for the Company.¹²³

Abbott's expectations regarding the continued market performance of Humira directly contradict Abbott's argument that an approval of a biosimilar to Humira would "destroy [the] competitive edge" Abbott has enjoyed.¹²⁴ Consistent with Abbott's expectations, the Federal Trade Commission predicted that "pioneer manufacturers are likely to retain 70 to 90 percent of their market share and, therefore, will likely continue to reap substantial profits years after entry by [follow-on biological] drugs."¹²⁵ We also note that Abbott has already brought suit, in a patent case, against an applicant for a biosimilar to Humira.¹²⁶ This suit raises the possibility that an injunction or damages could, at least for the life of the relevant patents, prevent any economic impact from the biosimilar.

Any analysis of economic impact must also consider that the BPCI Act provides a new opportunity for Abbott, as a sophisticated biological products manufacturer, to develop biosimilars that reference its competitors' products.¹²⁷ Multiple manufacturers of biological products licensed under section 351(a) of the PHS Act (or their subsidiaries) have stated publicly that they are developing biosimilars for approval under section 351(k).¹²⁸ Indeed, where a regulation results in "a significant, concrete, and disproportionate benefit on the burdened party," this weighs against finding a taking.¹²⁹ This *Penn Central* factor weighs against finding a taking

¹²² 3/5/14 FD (Fair Disclosure) Wire 13:40:00, AbbVie Inc. at Cowen Health Care Conference – Final.

¹²³ Statement of Richard Gonzalez, Chairman and Chief Executive Officer of AbbVie, during the Barclays Healthcare conference call (Mar. 12, 2015) (transcript available at <http://seekingalpha.com/article/2998306-abbvies-abbv-ceo-rick-gonzalez-on-barclays-healthcare-conference-call-transcript?part=single>).

¹²⁴ Petition at 26.

¹²⁵ Federal Trade Commission, *Emerging Health Care Issues: Follow-On Biologic Drug Competition* (June 2009), at 7, available at <http://www.ftc.gov/sites/default/files/documents/reports/emerging-health-care-issues-follow-biologic-drug-competition-federal-trade-commission-report/p083901biologicsreport.pdf>.

¹²⁶ *AbbVie Inc. v. Amgen Inc.*, No. 1:16-cv-00666-SLR (D. Del.) (complaint filed Aug. 4, 2016).

¹²⁷ See *Penn Cent.*, 438 U.S. at 137 (concluding that transferable development rights "undoubtedly mitigate whatever financial burdens the law has imposed on appellants and, for that reason, are to be taken into account in considering the impact of regulation").

¹²⁸ E.g., Sandoz, "Sandoz: Unrivalled Biosimilars Pipeline" (available at <http://www.sandoz-biosimilars.com/en/aboutus/biosimilars-pipeline.shtml>); Amgen Inc., "Our Pipeline" (available at <http://www.amgenbiosimilars.com/our-products/our-pipeline/>).

¹²⁹ *Colorado Springs Prod. Credit Ass'n v. Farm Credit Admin.*, 967 F.2d 648, 654 (D.C. Cir. 1992) (citing, among other cases, *Leonard & Leonard v. Earle*, 279 U.S. 392, 396 (1929) (rejecting oyster packers' objection to state's

given both that Abbott does not predict significant economic injury from the approval of a biosimilar version of Humira and that the BPCI Act offers a new market opportunity for Abbott.¹³⁰

3. *The Character of the Government Action*

The Supreme Court has described the final *Penn Central* factor, the “character of the governmental action,” as a way to assess whether the challenged action “amounts to a physical invasion or instead merely affects property interests through ‘some public program adjusting the benefits and burdens of economic life to promote the common good.’”¹³¹

A key inquiry under this *Penn Central* factor is “how any regulatory burden is distributed among property owners.”¹³² A challenged regulation is more likely to resemble a physical invasion, and thus give rise to the need for compensation, when its impact is concentrated on an individual or on a small number of parties.¹³³ In addition, a regulation that promotes public health or safety is less likely to be found to effect an unconstitutional taking.¹³⁴

Both of these considerations lead to the conclusion that the BPCI Act, as applied to pre-enactment reference products, “adjust[s] the benefits and burdens of economic life to promote the common good,”¹³⁵ rather than “directly appropriates private property or ousts the owner from his domain.”¹³⁶ Congress expressly intended the BPCI Act to establish a “biosimilars pathway balancing innovation and consumer interests.”¹³⁷ Moreover, Abbott alone would not bear the alleged economic impact of the biosimilars program. Any such burden is shared by the numerous holders of BLAs approved before the enactment of the BPCI Act.¹³⁸ The final *Penn Central* factor thus weighs against finding an unconstitutional taking.

seizure of 10% of oyster shells when the shells are used to reseed oyster beds and are therefore “used greatly to advantage the business of packing”).

¹³⁰ Cf. *ViroPharma, Inc. v. Hamburg*, 898 F. Supp. 2d 1, 27-28 (D.D.C. 2012) (finding no irreparable harm from generic entry that would support a preliminary injunction where “ViroPharma’s claims [of economic injury] are belied by its own statements” to investors).

¹³¹ *Lingle*, 544 U.S. at 538-39 (quoting *Penn Cent.*, 438 U.S. at 124).

¹³² *Lingle*, 544 U.S. at 542.

¹³³ See, e.g., *Me. Educ. Ass’n Benefits Tr. v. Cioppa*, 695 F.3d 145, 158 (1st Cir. 2012); *Rose Acre Farms, Inc. v. United States*, 559 F.3d 1260, 1279 (Fed. Cir. 2009); *Tenn. Scrap Recyclers Ass’n v. Bredesen*, 556 F.3d 442, 457 (6th Cir. 2009).

¹³⁴ *Rose Acre Farms*, 559 F.3d at 1281 (“There is little doubt that it is appropriate to consider the harm-preventing purpose of a regulation in the context of the character prong of a *Penn Central* analysis.”).

¹³⁵ See *Lingle*, 544 U.S. at 539 (quoting *Penn Cent.*, 438 U.S. at 124).

¹³⁶ See *id.*

¹³⁷ Public Law 111-148, sec. 7001(b).

¹³⁸ Moreover, many of these sponsors stand to benefit from the exclusivity periods in section 351(k)(7) of the PHS Act.

To summarize section III.C, none of the three *Penn Central* factors suggests that FDA's approval of a biosimilar product that references a BLA approved before the enactment of the BPCI Act would give rise to a taking.

IV. CONCLUSION

In summary, we conclude that there is no merit to the takings argument set forth in the Petition. For the reasons set forth above, the Petition is denied.

Sincerely,



Janet Woodcock, M.D.

Director

Center for Drug Evaluation and Research

C: Neal Parker, AbbVie, Inc. (formerly Abbott Laboratories, Inc.)