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## CITIZEN PETITION

On behalf of Abbott Laboratories (Abbott), the undersigned submit this petition under 21 C.F.R. § 10.30 and section 351 of the Public Health Service Act (PHSA), as amended by the Biologics Price Competition and Innovation Act of 2009 (BPCIA), to request that the Commissioner of Food and Drugs take the action requested below.

### **A. Action Requested**

Abbott requests that FDA confirm that it will not accept for filing, file, approve, or discuss with any company, or otherwise take any action indicating that the agency will consider, any application or any investigational new drug application (IND) for a biosimilar that cites, as its reference product, BLA 125057 for Humira® (adalimumab) or any other product for which the biologics license application (BLA) was submitted to FDA prior to March 23, 2010, the date on which the BPCIA was signed into law.

### **B. Statement of Grounds**

On March 23, 2010, the President signed the BPCIA, which provides FDA with authority to approve biosimilars – biological products that are “highly similar” to previously licensed biological products. Biosimilars will be the subject of abbreviated development programs and license applications, because their sponsors are permitted to rely on FDA’s finding that an earlier licensed biologic (reference product) is safe, pure, and potent.

That finding in turn has been made possible only because the reference product sponsor has invested massive amounts of capital, which studies show often surpasses more than a billion dollars, and has taken great risk to develop, test, and seek a license to market the

reference product.<sup>1</sup> An innovator's resulting license application typically reflects more than a decade of research and contains analytical, preclinical, and clinical data, as well as detailed manufacturing information, most of which qualifies as trade secrets. These trade secrets are the private property of the reference product sponsor and are therefore protected by the Fifth Amendment to the U.S. Constitution.

When 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. Moreover, when Abbott submitted its license application (and accompanying trade secrets) to the agency in 2002 — eight years before passage of the BPCIA — it had no notice, or reasonable expectation, that the agency would use its trade secrets to approve another company's product. To the contrary, Abbott developed and submitted those trade secrets in reasonable reliance on FDA's lack of legal authority to approve biosimilars, confirmed by years of agency statements that it lacked such authority. Other manufacturers who submitted their BLAs prior to enactment of the BPCIA are in the same position as Abbott: they reasonably expected — on the basis of applicable law and agency statements — that the trade secrets contained in their applications would not be used to benefit a competitor.

Under well-established Supreme Court jurisprudence, 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. FDA should not implement the BPCIA in any manner that would raise this constitutional issue. The agency is required to avoid constitutional questions whenever possible, and that imperative is reinforced in this case because these takings would expose the United States to enormous financial liability for just compensation.

Accordingly, Abbott requests that FDA confirm that it will not accept for filing, file, approve, or discuss with any company, or otherwise take any action indicating that the agency will consider, any application or any IND for a biosimilar that cites, as its reference product, BLA 125057 for Humira (adalimumab) or any other product for which the BLA was submitted to FDA prior to March 23, 2010, the date on which the BPCIA was signed into law.

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<sup>1</sup> See *Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the H. Comm. on the Judiciary Subcomm. on Courts and Competition Policy*, 111th Cong. 2 (2009) (statement of Rep. Henry C. Johnson, Jr., Chairman, Subcomm. on Courts and Competition Policy) (stating that some estimates place the average cost of developing a new biologic at "as much as \$1.37 billion") (Exhibit 1); see also Henry Grabowski, *Follow-on biologics: data exclusivity and the balance between innovation and competition*, 7 NATURE REVIEWS DRUG DISCOVERY 479, 482 (2008) (calculating the research and development costs for a new biologic at \$1.24 billion to \$1.33 billion) (Exhibit 2).

FACTUAL AND LEGAL BACKGROUND

**I. The Information in a BLA Is Trade Secret under State and Federal Law.**

A BLA submitted under section 351(a) of the PHSA is typically tens of thousands of pages<sup>2</sup> and contains extensive information about the manufacture of the product as well as extensive analytical, preclinical, and clinical data demonstrating that the proposed product is safe, pure, and potent. A BLA must contain — among other things — (1) all data from the laboratory and preclinical studies that supported initial testing in humans and any other laboratory and preclinical studies performed; (2) all data from clinical studies performed to determine whether the product is safe, pure, and potent; (3) a full description of the manufacturing methods; (4) data from stability testing; and (5) representative samples and summaries of the results of testing on those samples.<sup>3</sup>

A. State law

Whether a particular piece of information qualifies as a trade secret typically is a matter of state law. The long-standing common law protections for trade secrets have been harmonized by the Uniform Trade Secrets Act (UTSA), which has been adopted with minor variations by 45 states (including Maryland and Illinois), as well as the District of Columbia.<sup>4</sup>

The UTSA defines a “trade secret” as information 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.<sup>5</sup>

To establish a trade secret under the UTSA, an owner must therefore show that: (1) the information in question provides the owner with economic value or advantage because the

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<sup>2</sup> See RONALD P. EVENS, *DRUG AND BIOLOGICAL DEVELOPMENT: FROM MOLECULE TO PRODUCT AND BEYOND* 163 (2007) (stating that BLAs are “voluminous, in the tens of thousands of pages, and often surpassing 100,000 pages”) (Exhibit 3).

<sup>3</sup> 21 C.F.R. § 601.2; *see also* 76 Fed. Reg. 20,513, 20,517 (Apr. 13, 2011) (“Manufacturers are required by current regulations to submit all available data, including adverse event reports, with a BLA. . . . [C]urrent regulations, do[] not allow [FDA] to approve an application if the data are not sufficient to establish that the biological product is safe, pure, and potent in relation to the manufacturer’s intended use of the product.”) (Exhibit 4).

<sup>4</sup> Dole, Richard F., *The Uniform Trade Secrets Act -- Trends and Prospects*, 33 *HAMLIN L. REV.* 409, 410 (2010) (Exhibit 5). Abbott is a resident of Illinois. For jurisdictional purposes, FDA resides in Maryland and the District of Columbia.

<sup>5</sup> Unif. Trade Secrets Act § 1 (Exhibit 6).

information is not readily ascertainable by others, and (2) the owner has taken reasonable measures to maintain the secrecy of the information.<sup>6</sup> The manufacturing information and analytical, preclinical, and clinical data in BLAs satisfy both tests.

*First*, maintaining the secrecy of the data and information in a license application gives the submitter an economic advantage, because the license holder's competitors cannot obtain approval of a competing similar product without undertaking an investment of similar magnitude or compensating the innovator for a right to reference that information and data. The trade secrets, if disclosed to a competitor, could provide a significant shortcut to market by giving that competitor free knowledge of the results of the expensive, time-consuming, and risky efforts to comprehensively evaluate the product.<sup>7</sup> FDA has recognized that public disclosure of trade secrets, or FDA's use of trade secrets to provide a similar shortcut to a competitor, would allow a competitor to obtain approval of a similar product in the United States or abroad, which could seriously threaten incentives for creating innovative products:

The agency's policy against use of the pioneer drug manufacturer's proprietary data for approval of a me-too [animal drug] is supported by an important public policy consideration – providing an economic incentive to pioneer manufacturers for drug development and research. If a me-too manufacturer could rely on the pioneer's data to obtain approval for its own product, it would be able to use the benefits of the pioneer's research without having to incur any of the costs associated with that research.<sup>8</sup>

The fact that trade secrets are so closely guarded prevents the shortcut to market, allows an innovative company to maintain a competitive advantage, and protects incentives for innovation.

*Second*, biologics innovators go to great lengths to ensure that the data and other information submitted in their applications are not publicly released, whether inadvertently or

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<sup>6</sup> *Optic Graphics, Inc. v. Agee*, 591 A.2d 578, 586-87 (Md. Ct. Spec. App. 1991) (“[T]here are two requirements for a court to find that information is a ‘trade secret’ . . . : the information must (1) hold independent economic value because it is not generally known to or readily ascertainable by others who stand to benefit economically if they use or disclose it, and (2) be the subject of reasonable efforts to maintain its secrecy.” (internal citations and quotation marks omitted)) (Exhibit 7).

<sup>7</sup> See *Webb v. Dep't of Health & Human Servs.*, 696 F. 2d 101, 103 (D.C. Cir. 1982) (“If a manufacturer's competitor could obtain all the data in the manufacturer's NDA, it could utilize them in its own NDA without incurring the time, labor, risk, and expense involved in developing them independently.”).

<sup>8</sup> Letter to Steven S. Hurvitz, Esq. from Frank E. Young, Commissioner of Food and Drugs, Docket No. 84P-0322 (Dec. 17, 1985), at 13 (Exhibit 8); see also *In re Goodyear Tire & Rubber Co.*, No. 05-10-00485-CV, 2010 WL 2510371, at \*6 (Tex. Ct. App. June 23, 2010) (finding that manufacturing information was trade secret, in part, because: (1) a competitor with access to the information would receive a technical advantage without having to compensate the owner for expenses incurred in developing the information and (2) the competitor's development cost would thus be greatly reduced by access to the manufacturing information, allowing it to obtain an unfair market advantage) (Exhibit 9).

purposefully, or otherwise accessible to potential competitors.<sup>9</sup> For example, employees receive training on proper procedures for handling trade secret and/or confidential commercial information; contractors engaged to support a BLA are required to sign extensive confidentiality agreements; and even internal company documents are frequently marked with trade secret and/or confidential commercial information designations.<sup>10</sup> Access to company trade secret information is limited through password protection and other security measures preventing access by employees who do not need the information to perform their job functions.<sup>11</sup> Biologics innovators typically also have extensive security at their manufacturing facilities and corporate offices to prevent unauthorized access to and release of confidential information.<sup>12</sup> When documents are ultimately submitted to FDA in a license application, many are expressly marked as trade secret and/or confidential information.<sup>13</sup>

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<sup>9</sup> See generally Shanley, Agnes, From the Editor: Best Practices or Trade Secrets? PharmaManufacturing.com, <http://www.pharmamanufacturing.com/articles/2005/267.html> (last visited Mar. 7, 2012) (“Few companies guard intellectual property and trade secrets more zealously than pharmaceutical manufacturers. Their survival depends on it.”) (Exhibit 10). The fact that high-level summaries and conclusions about clinical trial results or other product information are made public through various means (e.g., company press releases, clinical trial databases, FDA release of summary basis of review) does not eliminate the trade secret status of the underlying non-disclosed information. FDA recognized this legal principle in 1972 when it explained that safety and effectiveness data in new drug applications (NDAs) were trade secrets, even though the agency was requiring applicants to submit a summary for public release after approval. 37 Fed. Reg. 9128, 9131 (May 5, 1972) (Exhibit 11); see also 39 Fed. Reg. 44,602, 44,618 (Dec. 24, 1974) (explaining that publishing limited information in a journal does not eliminate trade secret protection for the broader set of information: “[i]f only the product formula appears, only the product formula has been disclosed”) (Exhibit 12).

<sup>10</sup> See *LeJeune v. Coin Acceptors, Inc.*, 849 A.2d 451, 464-65 (Md. 2004) (finding that a company took “reasonable measures to maintain the secrecy” of cost data and manufacturing specifications by using non-disclosure agreements with customers, marking certain documents as confidential, and communicating to employees “the secret nature of its manufacturing processes and business methods”) (Exhibit 13).

<sup>11</sup> *PepsiCo, Inc. v. Redmond*, No. 94 C 6838, 1996 WL 3965, \*16 (N.D. Ill. Jan. 2, 1996) (finding that a beverage company’s “efforts to maintain the secrecy of its trade secret and confidential information were reasonable and more than required” by the Illinois Trade Secrets Act, in part, because the company only “provided confidential and trade secret information to those employees with an actual need to know it”) (Exhibit 14).

<sup>12</sup> *Tabs Associates, Inc. v. Brohawn*, 475 A.2d 1203, 1213 (Md. Ct. Spec. App. 1984) (concluding that the plaintiff had presented sufficient evidence that its operations manual could qualify as a trade secret, in part, by showing that “certain security precautions were taken with respect to the work site [where the manual was held] including a sign in process, and a jobsite security process”) (Exhibit 15).

<sup>13</sup> *Id.* (noting that the manual was marked as “secret”); *PepsiCo*, 1996 WL 3965 at \*16 (finding that a company’s “efforts to maintain the secrecy of its trade secret and confidential information were reasonable and more than required” by the Illinois Trade Secrets Act, in part, because the company “regularly marked information ‘private and confidential’”) (Exhibit 14). The failure to mark all documents submitted to an agency as trade secret or confidential commercial information, however, does not eliminate trade secret status. See *Georgia Dep’t of Natural Res. v. Theragenics Corp.*, 545 S.E.2d 904, 906 (Ga. 2001) (finding that although “it would be a prudent practice for a regulated party . . . who is required to file materials with [an agency] to designate at the outset what materials it considers to be its proprietary trade secrets,” the failure to do so did not mean the submitted materials were unprotected) (Exhibit 16).

B. Federal law

Various federal laws and regulations also define the scope of and provide broad protection to trade secret information. These federal protections for “trade secrets” reach both the manufacturing information and the safety and efficacy data in BLAs. In particular, the Federal Trade Secrets Act (FTSA) makes it a federal crime for any federal employee to disclose “trade secret” information acquired during the course of his or her government duties.<sup>14</sup> Similarly, the Freedom of Information Act (FOIA) exempts trade secrets and confidential commercial or financial information from the information that must be disclosed by agencies upon request.<sup>15</sup> FDA regulations broadly state that 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.”<sup>16</sup> And the federal courts have repeatedly confirmed that “data” submitted to FDA — including analytical, preclinical, and clinical data to support a marketing application — constitute trade secrets.<sup>17</sup>

**II. FDA’s Biosimilar Authority**

On March 23, 2010, the President signed legislation that included the BPCIA. Applications for licensure of “biosimilar” and “interchangeable” biological products will be truncated in comparison with full license applications, because their sponsors may rely on FDA’s

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<sup>14</sup> 18 U.S.C. § 1905; *see also* 18 U.S.C. §§ 1832, 1839 (prohibiting the theft of trade secrets and broadly defining a trade secret as “all forms and types of financial, business, scientific, technical, economic, or engineering information, including patterns, plans, compilations, program devices, formulas, designs, prototypes, methods, techniques, processes, procedures, programs, or codes, whether tangible or intangible, and whether or how stored, compiled, or memorialized physically, electronically, graphically, photographically, or in writing if (A) the owner thereof has taken reasonable measures to keep such information secret; and (B) the information derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable through proper means by, the public”).

<sup>15</sup> 5 U.S.C. § 552(b)(4).

<sup>16</sup> 21 C.F.R. § 20.61(a). FDA regulations thus state explicitly that the manufacturing information in a BLA is trade secret. 21 C.F.R. § 601.51(f).

<sup>17</sup> *Jerome Stevens Pharms., Inc. v. FDA*, 402 F.3d 1249, 1251, 1256, 1258 (D.C. Cir. 2005) (reversing the district court’s dismissal of a drug company’s claims arising from FDA’s publication of “trade secret” information from the company’s NDA); *Webb v. Dep’t of Health & Human Servs.*, 696 F.2d 101, 103 (D.C. Cir. 1982) (noting that premature disclosure of “NDA data” is prohibited by the Trade Secrets Act). The fact that some of the agency statements and court findings on trade secrets cited in this Petition refer to trade secrets in NDAs rather than trade secrets in BLAs is inconsequential. NDAs and BLAs contain largely the same information, and the agency treats them alike in many circumstances. *See, e.g.*, FDA, Guidance for Industry: Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products 6 (May 1998) (“The examples are applicable whether the claim arises in the original filing of an NDA or BLA . . .”); Pub. L. No. 105-115 § 123(f) (directing FDA to take measures to “minimize differences in the review and approval” of products approved through BLAs and those approved through NDAs). Similarly, the value of these data (i.e., their role in securing approval) and company efforts to keep them confidential are also largely the same. Thus as a general matter, FDA’s reasoning regarding the trade secret status of information in NDAs applies with equal force to BLAs.

finding that a previously licensed product is safe, pure, and potent. A biosimilar license application must contain information demonstrating that the product is “biosimilar” to a biological product previously licensed on the basis of a full application. The product is “biosimilar” if the two are “highly similar . . . notwithstanding minor differences in clinically inactive components” and if there are no “clinically meaningful differences” between the products in terms of safety, purity, and potency. The showing of biosimilarity must be based on data from: (1) analytical studies demonstrating that the products are highly similar notwithstanding minor differences in clinically inactive components, (2) animal studies (including the assessment of toxicity), and (3) a clinical study or studies in one condition of use for which the reference product is approved.<sup>18</sup> FDA may waive any of these requirements upon a finding that the data in question are “unnecessary.”<sup>19</sup> The application must also contain “publicly-available information” regarding FDA’s “previous determination that the reference product is safe, pure, and potent.”<sup>20</sup>

FDA has emphasized the importance of early meetings with potential biosimilar applicants and has proposed a special user fee scheme to accommodate those meetings.<sup>21</sup> Although the agency has issued draft guidances on the biosimilar approval pathway, these drafts are written in general terms and do not address class-specific or product-specific development programs. Early one-on-one meetings will instead be the primary source of information for biosimilar applicants seeking to design a development program. In February 2012, one FDA official indicated that the agency had already received 35 requests for pre-IND meetings for proposed biosimilar products for 11 different reference products. The same official indicated that FDA has held 21 pre-IND sponsor meetings to date and has received nine INDs.<sup>22</sup> We believe that some (if not all) proposed biosimilar product applications that have been or will be the subject of such meetings will reference innovator biologic products that were approved via BLAs submitted prior to March 23, 2010. Accordingly, the constitutional issue raised in this petition is both timely and urgent.

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<sup>18</sup> PHS § 351(k)(2).

<sup>19</sup> *Id.*

<sup>20</sup> *Id.* It may also contain other “publicly-available information” regarding the reference product.

<sup>21</sup> See, e.g., Steven Kozlowski, M.D. et al., *Developing the Nation’s Biosimilars Program*, 5 N. ENGL. J. MED. 385, 387 (Aug. 4, 2011) (“Although the agency frequently meets with sponsors before they submit investigational new drug applications, a more extensive product review will be required to determine how much additional data are needed for a biosimilar.”) (Exhibit 17); Biologics Price Competition and Innovation Act of 2009; Options for a User Fee Program for Biosimilar and Interchangeable Biological Product Applications for Fiscal Years 2013 Through 2017; Request for Comments, 76 Fed. Reg. 27,062, 27,063 (May 10, 2011) (“Given that the approval pathway for biosimilar and interchangeable biological products is new, FDA services are most critical . . . during the investigational stage prior to submission of a marketing application.”) (Exhibit 18).

<sup>22</sup> See Rachel E. Sherman, M.D., MPH, *Biosimilar Biological Products*, Biosimilar Guidance Webinar, at slide 11 (Feb. 15, 2012), <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM292463.pdf> (Exhibit 19).

### III. Development and Approval of the Humira License Application

Adalimumab is a recombinant human IgG1 monoclonal antibody specific for human tumor necrosis factor (TNF). The basic molecule was discovered in the 1990s as the result of collaboration between the BASF Corporation and Cambridge Antibody Technology (CAT). The ultimate clinical candidate was created and manufactured at BASF Bioresearch Corporation and taken through much of the drug development process by BASF Knoll, then further developed by Abbott after the latter acquired the pharmaceutical arm of BASF Knoll in 2000. In acquiring this business, Abbott also acquired (and now owns) the trade secrets generated by BASF Knoll with respect to adalimumab.<sup>23</sup>

Abbott's work with TNF began in the mid-1980s. In 1986, Abbott isolated a high-affinity murine antibody that neutralizes TNF alpha named "MAK-195." In 1991, Abbott decided to develop a therapeutic, fully-human, anti-TNF alpha antibody. Abbott initially collaborated with the foremost expert in using human B-cells to make fully human antibodies. After two years of experimentation, however, Abbott and its collaborator were unable to isolate a single high-affinity, neutralizing fully-human anti-TNF alpha antibody.

In 1993, Abbott and CAT collaborated to overcome the weaknesses of the existing phage display technology. Together they worked to create inventive ways to develop better antibodies and antibody fragments with phage display, which in turn increased the chance of finding useful antibodies and antibody fragments. Abbott and CAT also utilized a new technology known as "guided selection" that improved the chances of isolating a high-affinity, fully-human antibody from phage display libraries. Abbott used its own murine antibody, MAK-195, and invested significant time, effort, and resources inventing improved affinity maturation techniques.<sup>24</sup> Abbott and CAT made hundreds if not thousands of failed antibodies during the course of their collaboration. In 1995, Abbott finally completed its goal of developing a high-affinity, neutralizing fully-human anti-TNF alpha antibody, adalimumab. Adalimumab was the first, and to this day the only, FDA-approved high-affinity, neutralizing fully-human anti-TNF alpha antibody developed using phage display. The IND for adalimumab became effective on April 16, 1998. Abbott submitted its BLA for adalimumab, using the trade name Humira, on March 28, 2002.

Abbott invested money to acquire BASF Knoll, expended significant resources to generate the additional trade secrets necessary to support licensure of adalimumab, and incurred the expense of preparing and submitting its license application for Humira. In deciding to make these investments, Abbott relied on the fact that federal law did not authorize FDA to approve any other company's product on the basis of the BLA or underlying trade secrets. Abbott also relied on FDA's repeated formal and informal assurances that the agency had no authority to receive, review, or approve abbreviated biologic license applications.

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<sup>23</sup> Accordingly, any reference to "Abbott" in this Petition includes its predecessor BASF Knoll unless otherwise specifically noted.

<sup>24</sup> Affinity maturation refers to a trial-and-error process of altering the amino-acid sequence of the variable regions of an antibody with the hope of improving its affinity to a target antigen.



FDA approved Humira on December 31, 2002, for “reducing signs and symptoms and inhibiting the progression of structural damage in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs).” After the initial approval, Abbott continued to invest in Humira by conducting numerous studies and analyses as part of its post-approval commitments. Abbott also invested in further clinical testing to explore other potential uses for Humira, which is now approved for six indications and provides a valuable treatment option for hundreds of thousands of patients in the United States and abroad. The last indication for which Humira received approval (treatment of juvenile idiopathic arthritis) was added in February 2008, over two years before the BPCIA was enacted.

Abbott has consistently and carefully protected the trade secrets in its Humira application and subsequent supplements. Abbott takes the precautions described above in Section I.A to guard its trade secrets, but it also goes even further by taking steps that are designed to address the unique challenges that can arise from submitting trade secrets to an agency and from disclosing trade secrets during litigation with other pharmaceutical companies. For example, Abbott has a rigorous publication review process in place to ensure against inadvertent disclosure of trade secrets. Abbott also monitors FDA’s FOIA docket to determine whether any person has requested information related to Humira or other Abbott products. This allows the company to take action if there is a risk that its trade secrets may be disclosed. Abbott also insists upon rigorous protective orders any time that its trade secrets may need to be subject to discovery during litigation. In addition, Abbott avoids submitting trade secrets to foreign national regulatory authorities that do not offer protection to the information that is consistent with international treaties.

Abbott believes that at least three companies have begun preclinical and/or clinical testing of biosimilar adalimumab, but does not know whether FDA is advising any companies about the contents of a biosimilar application citing approval of Humira.<sup>25</sup>

#### **IV. The Takings Clause of the Fifth Amendment**

The Fifth Amendment to the U.S. Constitution prohibits the government from taking private property without providing compensation: “nor shall private property be taken for public use, without just compensation.” The Supreme Court’s jurisprudence has generally

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<sup>25</sup> See Brazil to manufacture biosimilar adalimumab, Generic and Biosimilars Initiative Online (May 13, 2011), <http://www.gabionline.net/Biosimilars/News/Brazil-to-manufacture-biosimilar-adalimumab> (reporting that the Instituto Vital Brazil and PharmaPraxis are developing a version of adalimumab) (Exhibit 20); ClinicalTrials.gov, Pharmacokinetics and Safety Study of BI 695501 in Healthy Subjects, ClinicalTrials.gov Study No. NCT01505491 (reporting that Boehringer Ingelheim Pharmaceuticals, Inc. is conducting a clinical trial to establish the pharmacokinetic equivalence of a new compound to adalimumab) (Exhibit 21); BioCentury Extra (Feb. 24, 2012) (noting that Mylan is developing an adalimumab biosimilar) (Exhibit 22). Through a FOIA request dated July 22, 2011, Abbott inquired whether any potential adalimumab biosimilar applicant was meeting with FDA. The agency rejected this request for information on August 9, 2011, citing the trade secret and confidential commercial information exception to FOIA. See Letter from Frederick J. Sadler, Director, Division of Freedom of Information, to John A. Hughes, DLA Piper, LLP (Aug. 9, 2011) (Exhibit 23).

divided takings of private property into *per se* and regulatory takings.<sup>26</sup> A *per se* taking occurs where the government action (1) “requires an owner to suffer a permanent physical invasion of her property” or (2) “completely deprive[s] an owner of all economically beneficial” uses of the property.<sup>27</sup> In contrast, a “regulatory taking” occurs when the government’s action does not effect a permanent physical occupation of private property or entirely destroy the property’s economically beneficial uses.

To determine whether a regulatory taking has occurred, the courts consider three factors laid out by the Supreme Court in *Penn Central*: (1) whether the government action “interfered with distinct investment-backed expectations,” (2) the economic impact of the government’s action on the property owner, and (3) the nature of the government action.<sup>28</sup> As the First Circuit has noted, however, “the Supreme Court has frequently found that one of the *Penn Central* factors is dispositive.”<sup>29</sup> Specifically, whether the property owner had a reasonable, investment-backed expectation “can be dispositive on the issue of whether or not there is a compensable taking.”<sup>30</sup>

Information that qualifies under state law as a trade secret, including data submitted in license applications, is private property for purposes of the Fifth Amendment.<sup>31</sup> *Monsanto*, the leading regulatory takings case, holds that when an applicant submits trade secret data as part of a license application, at a time when the government has provided assurances through law, regulation, and/or agency guidance that the data will not be used by the agency to benefit a competitor of that applicant, later “consider[ation of] those data [by the agency] in

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<sup>26</sup> Land use exactions constitute a third category of takings claims, but are not relevant to this petition. *See Lingle v. Chevron U.S.A. Inc.*, 544 U.S. 528, 546 (2005).

<sup>27</sup> *Id.* at 538.

<sup>28</sup> *Penn Cent. Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978).

<sup>29</sup> *Philip Morris, Inc. v. Reilly*, 312 F.3d 24, 34 n.5 (1st Cir. 2002) (citing *Hodel v. Irving*, 481 U.S. 704, 716 (1987) (concluding that the character of the government action involved was determinative)); *see also id.* at 36 (“[I]n some regulatory takings cases, one factor is frequently dispositive.”).

<sup>30</sup> *Mehaffy v. United States*, No. 09-860L, 2012 WL 51687, at \*7 (Fed. Cl. Jan. 10, 2012) (citing *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1005-06 (1984) (Exhibit 24); *see also Good v. United States*, 189 F.3d 1355, 1360 (Fed. Cir. 1999) (noting that because the court found “the expectations factor dispositive,” it would “not further discuss the character of the government action or the economic impact of the regulation”); *Am. Commerce Nat’l Bank v. United States*, 38 Fed. Cl. 271, 273 (Fed. Cl. 1997) (declining to address the economic impact of an alleged taking “because other considerations,” including the reasonable, investment-backed expectation, “[were] dispositive of this case”).

<sup>31</sup> *See Monsanto*, 467 U.S. at 1003-04 (“We therefore hold that to the extent that Monsanto has an interest in its health, safety, and environmental data cognizable as a trade-secret property right under Missouri law, that property right is protected by the Taking Clause of the Fifth Amendment.”); *see also id.* at 1003 (“That intangible property rights protected by state law are deserving of the protection of the Taking Clause has long been implicit in the thinking of this Court.”). FDA has acknowledged that companies have a “property right” in their trade secrets. *See* 39 Fed. Reg. 44,602, 44,611, 44,612 (Dec. 24, 1974) (Exhibit 12).

evaluating the application of a subsequent applicant” would frustrate the applicant’s “reasonable investment-backed expectation” that the data would, instead, remain inviolate.<sup>32</sup>

In *Monsanto*, the Supreme Court applied the *Penn Central* factors to determine whether the Environmental Protection Agency’s (EPA’s) use of data submitted under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) to support registration of pesticides constituted a taking. The Court focused on the first factor — whether EPA’s action interfered with Monsanto’s reasonable, investment-backed expectation — ultimately finding that this analysis alone “dispose[d] of the taking question regarding [Monsanto’s] data.”<sup>33</sup> Monsanto had submitted trade secret data in support of its applications to register pesticides. EPA later considered Monsanto’s data in connection with applications filed by other companies seeking to register their own pesticides. Monsanto argued that EPA’s consideration of these data was a taking under the Fifth Amendment.

Three versions of FIFRA were relevant to the case:

- From enactment in 1947 until 1972, FIFRA was primarily a licensing and labeling statute. If EPA so requested, applicants were required to submit data supporting claims on the product label. The statute explicitly prohibited disclosure of “any information relative to formulas of products” but did not prohibit the disclosure of the health and safety data submitted with an application.<sup>34</sup>
- In 1972, Congress created a new registration procedure and rules for the public disclosure of information submitted through the registration process. The agency was permitted to consider data submitted by one applicant in determining whether to approve another application, if the subsequent applicant offered to compensate the owner of the submitted data. A pesticide applicant, however, could designate any portions of the submitted material it believed to be “trade secrets or commercial or financial information.” EPA was prohibited both from publicly disclosing that information and from using that information in evaluating a registration application of another company.<sup>35</sup>
- FIFRA was again amended in 1978 to grant a 10-year period of exclusive use for data relating to new active ingredients in pesticides registered after September 30, 1978. In addition, all other data submitted after December 31, 1969 could be cited and considered in support of a subsequent application for 15 years after the date of submission if the subsequent applicant offered to compensate the owner of the submitted data. All other data (i.e., data that did not qualify under either of these two provisions) could be considered by EPA without limitation. In addition,

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<sup>32</sup> *Monsanto*, 467 U.S. at 1011.

<sup>33</sup> *Id.* at 1005.

<sup>34</sup> *Id.* at 991.

<sup>35</sup> *Id.* at 991-93.

after 1978, EPA was permitted to disclose almost all health, safety, and environmental data to qualified parties.<sup>36</sup>

The *Monsanto* Court first acknowledged that trade secrets are property protected by the Fifth Amendment's prohibition on taking private property for public use without just compensation.<sup>37</sup> The Court then held that no taking occurred with respect to data submitted after the 1978 amendments, as "Monsanto could not have had a reasonable, investment-backed expectation that EPA would keep the data confidential beyond the limits prescribed in the amended statute itself."<sup>38</sup> This is because "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."<sup>39</sup>

Moving next to FIFRA as enacted in 1947 and until 1972, the Court held that Monsanto had not established that it had an "investment-backed expectation that its information would remain inviolate in the hands of EPA."<sup>40</sup> To the contrary, the Court found evidence that "the practice of using data submitted by one company during consideration of the application of a subsequent applicant was widespread and well known" under FIFRA at the time.<sup>41</sup> Accordingly, EPA's use of these data did not constitute a taking.

Finally, the Court addressed the statutory scheme in effect from 1972 to 1978, finding that the scheme gave Monsanto "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 trade secrets."<sup>42</sup> Monsanto had a reasonable, investment-backed expectation that the agency would not use data submitted to EPA during this time frame for the benefit of a competitor. Government action that interfered with this expectation constituted a taking.

The *Monsanto* case, decided in 1984, remains the law and has been followed in subsequent federal and state cases.<sup>43</sup> The principles set out in *Monsanto* establish that FDA would take property, and the government would be required to pay just compensation, were FDA to use trade secrets, submitted in a reference product BLA before the BPCIA's enactment, in the course of evaluating and approving a biosimilar application. In order to avoid this constitutional issue, and also to avoid imposing immense financial liability on the United States, FDA should not accept for filing, file, approve, or discuss with any company, or otherwise take any action

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<sup>36</sup> *Id.* at 994-97.

<sup>37</sup> *Id.* at 1003-04.

<sup>38</sup> *Id.* at 1006.

<sup>39</sup> *Id.*

<sup>40</sup> *Id.* at 1008.

<sup>41</sup> *Id.* at 1009 n.14.

<sup>42</sup> *Id.* at 1011.

<sup>43</sup> See, e.g., *Philip Morris, Inc.*, 312 F.3d at 33; *Tri-Bio Labs., Inc. v. United States*, 836 F.2d 135, 141 (3d Cir. 1987); *Syngenta Crop Prot., Inc. v. Helliker*, 138 Cal. App. 4th 1135, 1146-48 (Cal. Ct. App. 2006) (Exhibit 25).

indicating that the agency will consider, any application or any IND for a biosimilar that cites, as its reference product, BLA 125057 for Humira (adalimumab) or any other product for which the BLA was submitted to FDA prior to March 23, 2010, the date on which the BPCIA was signed into law.

## ANALYSIS AND DISCUSSION

### **I. Approval of a Biosimilar Application Uses the Trade Secrets that Supported the Reference Product License.**

Any FDA approval of a biosimilar application necessarily uses the trade secrets that were submitted in support of the BLA that the biosimilar is referencing.<sup>44</sup> Such a use occurs even though the BPCIA directs FDA to base approval of the biosimilar product only on information in the biosimilar application and directs the biosimilar applicant to include in its application only publicly available information regarding FDA's prior finding of safety, purity, and potency for the reference product. The approval of a biosimilar necessarily relies on and uses the trade secrets that the innovator sponsor submitted in support of the BLA. Were it not for those trade secrets — generated at great effort and expense by the sponsor — there would be no pioneer biologic for the biosimilar sponsor to reference.

In the past, FDA has attempted to distinguish between relying on a prior finding of safety and effectiveness for a reference product and relying on the underlying trade secrets, briefly stating that the prior finding does not constitute the trade secrets.<sup>45</sup> But the agency has never explained this distinction and has never responded to the various legal arguments made to the contrary over the years. In fact, FDA's purported distinction between reliance on the finding and use of the underlying trade secrets does not withstand scrutiny for several reasons.

*First*, reliance on a prior finding causes a substantial injury to the owner of the trade secrets supporting that finding, and this is sufficient under settled trade secret jurisprudence to establish use of the trade secrets. *Second*, also under settled trade secret jurisprudence, where one company's previously submitted trade secrets relieve a subsequent company from producing and submitting similar information, the former's trade secrets are used — *even if* the government

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<sup>44</sup> This petition refers largely to FDA's use of trade secrets in BLAs. Other information in BLAs may be confidential commercial or financial information and would for that reason be protected under federal law. *See* 5 U.S.C. § 552(b)(4); 21 C.F.R. § 20.61(b). Any such confidential business information would be protected by the Fifth Amendment against an uncompensated taking. *See Carpenter v. United States*, 484 U.S. 19, 26 (1987) (“Confidential business information has long been recognized as property.”) (citing *Monsanto*, 467 U.S. at 1001-04). Thus, just as FDA's use of innovators' trade secrets in approving biosimilars would constitute a taking for which compensation is required, so would FDA's use of any confidential commercial information in BLAs.

<sup>45</sup> *See, e.g.*, Letter of Steven K. Galson, M.D., M.P.H., Director, CDER, to Kathleen M. Sanzo, Esq., Morgan, Lewis & Bockius LLP; Stephan E. Lawton, Esq., BIO; and Stephen J. Juelsgaard, Esq., Genentech, Docket No. 2004P-0231, PDN1 (May 30, 2006), at 38 n.70 (“Because approval of Omnitrope has been accomplished without reference to trade secret or confidential commercial information belonging to other applicants, we need not address the argument made by Genentech that reliance by FDA on trade secret or confidential commercial information would constitute a *taking* under the Fifth Amendment to the Constitution.”) (Exhibit 26).

does not actually re-examine the initially submitted trade secrets. As the cases discuss, the mere fact that a shortcut exists evidences use because without some use of the trade secrets no shortcut to approval would be possible. *Third*, the prior finding for a reference product is inseparable from the trade secrets contained in the license application supporting that finding. Indeed, as discussed more fully below, FDA has previously conceded the inseparability of approval of a follow-on product and the underlying trade secrets embodied in the reference product's approval.

A. Agency reliance on a prior finding injures the trade secret owner in a way that establishes use under settled trade secret jurisprudence.

As explained by the Restatement of the Law (Third) Unfair Competition, “[t]here are no technical limitations on the nature of the conduct that constitutes ‘use’ of a trade secret.”<sup>46</sup> Under well-settled trade secret law, “any exploitation of the trade secret that is likely to result in injury to the trade secret owner . . . is a ‘use.’”<sup>47</sup> This test — whether there is exploitation of the trade secret likely to result in injury to the trade secret owner — is easily met when FDA considers and approves a biosimilar application. FDA’s reliance on its earlier finding that the reference product is safe, pure, and potent — to grant another company a license to market a competing biosimilar product — diminishes the economic value of the reference product sponsor’s trade secrets that made the finding possible. The trade secrets generated at great risk and expense by the first entrant lose value and provide a diminished competitive advantage if the government can simply proceed with approving competitor products on the basis of subsequent applications that omit trade secrets comparable to those required of the reference product sponsor. The shortcut to market for subsequent applicants inflicts a significant injury on the company who submitted the trade secrets. This injury is sufficient to establish use of the trade secrets in question under the Restatement and case law.

FDA has previously maintained that its reliance on a prior finding constitutes only “indirect reliance” on the trade secrets in that prior application.<sup>48</sup> The agency’s distinction, however, between direct and indirect reliance is meaningless with respect to the resulting injury

<sup>46</sup> Restatement (Third) of Unfair Competition § 40, cmt. c (Exhibit 27).

<sup>47</sup> *Id.*; see also *Bohnsack v. Varco, L.P.*, No. 10-20741, 2012 WL 171900, at \*13 (5th Cir. Jan. 23, 2012) (noting the “broad definition of use” in the Restatement and finding that the plaintiff had demonstrated use because a reasonable juror could conclude that the defendant’s actions were “likely to result in injury to the trade secret owner” by lowering the market value of the plaintiff’s invention, even though the defendant did not take the underlying trade secrets for the invention and use them to create a competitor invention or divulge them to a third party) (Exhibit 28).

<sup>48</sup> See Letter from Janet Woodcock, M.D., Director, CDER, to Katherine M. Sanzo, Esq. and Lawrence S. Ganslaw, Esq., Morgan, Lewis & Bockius, LLP; Jeffrey B. Chasnow, Esq., Pfizer; Stephan E. Lawton, Esq. and Gillian R. Woollett, Ph.D., BIO; and William R. Rakoczy, Esq., Lord, Bissell & Brook LLP, Docket No. 2001P-0323, PDN 1, at 10 n. 14 (Oct. 14, 2003) (“[R]eliance on an FDA finding of safety and effectiveness for an NDA is certainly indirect reliance on the data submitted in the original NDA . . .”) (Exhibit 29); see also Letter of Steven K. Galson, M.D., M.P.H., Director, CDER, to Kathleen M. Sanzo, Esq., Morgan, Lewis & Bockius LLP; Stephan E. Lawton, Esq., BIO; and Stephen J. Juelsgaard, Esq., Genentech, Docket No. 2004P-0231, PDN1 (May 30, 2006), at 31 (admitting that FDA’s approval of Omnitrope<sup>®</sup> was based on the “finding of safety and effectiveness for Genotropin,” which was, “in turn, based upon additional adequate and well-controlled studies” in the Genotropin<sup>®</sup> NDA) (Exhibit 26).

because both reliance on a prior finding of safety and effectiveness and reliance on the underlying privately owned trade secrets result in loss of the competitive advantage that the secrets afford. Thus, under the Restatement and trade secret cases, FDA’s reliance on a prior finding for the reference biologic in approving a biosimilar is a “use” of the trade secrets in the innovator’s BLA.<sup>49</sup>

B. Where one company’s trade secrets relieve a subsequent company from producing and submitting similar information to an agency, the agency uses the first company’s trade secrets.

The purpose of the BPCIA is to allow subsequent entrants to file “abbreviated” applications – applications for licensure to market a biological product that contain fewer data (and thus, cost less to prepare and submit) than the reference product application contained. Indeed, the statute expressly permits FDA to waive for a biosimilar applicant some or all supporting analytical, preclinical, and clinical data.<sup>50</sup> Put another way, because of the trade secrets submitted by the innovator, and *only* because of those trade secrets, the biosimilar applicant will be relieved of the obligation that would otherwise attach: to generate and submit in a full application its own trade secrets demonstrating *de novo* the safety, purity, and potency of its product for every proposed indication.<sup>51</sup>

When 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, the agency is using the original applicant’s trade secrets – even if it does not actually look at the previously submitted data again. This was the case in *Syngenta Crop Protection*.<sup>52</sup> Syngenta had submitted trade secrets to the California Department of Pesticide Regulation to support state registration of its pesticide products.<sup>53</sup> Gustafson, a subsequent applicant, sought to register a pesticide product with the same active ingredient. Gustafson did not re-submit the Syngenta data, nor did it refer to the data or claim a license or any other sort of authorization from Syngenta to rely on them. Nor did the Department review Syngenta’s data again. Instead, like FDA reviewing a biosimilar application, the Department registered Gustafson’s product in mere reliance on the fact that it had granted

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<sup>49</sup> Both types of reliance (e.g., direct and indirect) are also inconsistent with the purpose of trade secret law, which is to “encourage innovation and development.” *American Can Co., v. Mansukhani*, 742 F.2d 314, 329 (7th Cir. 1984). FDA’s direct use of the trade secrets to approve a biosimilar would harm incentives for innovation because the trade secret owners would face competition from companies that received a very significant shortcut to market. FDA’s indirect use of the trade secrets, through reliance on the prior finding, would have the same impact.

<sup>50</sup> PHSA § 351(k)(2).

<sup>51</sup> See Thomas M. Burton & Jonathan D. Rockoff, *FDA Sets Path for Biotech Drug Copies*, WALL ST. J., Feb. 10, 2012 (quoting FDA Associate Director for Medical Policy Rachel Sherman as stating that “[i]nstead of starting from scratch, these [biosimilar] companies will be starting in the middle of the process”) (Exhibit 30).

<sup>52</sup> See *Syngenta Crop Protection, Inc. v. Helliker*, 138 Cal. App. 4th 1135, 1146-48 (Cal. Ct. App. 2006) (Exhibit 25).

<sup>53</sup> The trade secrets in question concerned the health and environmental effects of the active ingredients in those products. *Id.* at 1147.

registration to Syngenta.<sup>54</sup> This fact “fill[ed] the data gaps” in Gustafson’s application.<sup>55</sup> “[B]y taking into account its prior evaluation of an active ingredient based on data submitted by another applicant,” the Department relieved the subsequent applicant of “the expense of producing or otherwise acquiring similar data” and thus “use[d]’ the data to the benefit of” the subsequent applicant.<sup>56</sup> To our knowledge, no court has reached a different result under the Uniform Trade Secrets Act or questioned the reasoning of the *Syngenta* court.

The Supreme Court in *Monsanto* similarly focused on the shortcut available to subsequent entrants, and the resulting harm to the trade secret owner, when it found that the federal pesticide registration scheme in place from 1972 to 1978 caused a taking of proprietary data. Although the statutory scheme expressly authorized the agency to use the first entrant’s data — which the PHSA does not and which the California Department of Pesticide Registration in *Syngenta* did not — the Court’s ruling did not turn on this fact. Rather, the *Monsanto* Court’s analysis focused on the impact of the scheme: “it is the fact that the operation of the data-consideration or data-disclosure provisions will allow a competitor *to register more easily its product . . . that may constitute a taking.*”<sup>57</sup> The BPCIA allows a biosimilar applicant to register more easily its competing product and thus requires FDA to use the reference product sponsor’s trade secrets.

- C. The finding that the reference product is safe, pure, and potent is inseparable from the trade secrets in the license application that supported the finding, and reliance on the finding therefore constitutes use of the trade secrets.

The PHSA directs FDA to rely, in approving a biosimilar, on publicly available information regarding the agency’s determination that the reference product is safe, pure, and potent. That determination in turn constitutes a formal decision by FDA that the trade secrets and other information owned and submitted by the first company demonstrate that the company’s product is safe, pure, and potent when used under the conditions described in the labeling and that the product therefore may be lawfully marketed in the United States.<sup>58</sup> Both as a matter of law and as a practical matter, FDA could not make that determination had the reference product sponsor not first submitted its trade secrets to the agency in a BLA.

The biosimilarity demonstration must be supported by analytical, preclinical, and clinical testing, unless FDA exercises its waiver authority. But when the biosimilar applicant

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<sup>54</sup> *Id.* at 1147, 1163-64, 1182.

<sup>55</sup> *Id.* at 1182.

<sup>56</sup> *Id.* at 1172.

<sup>57</sup> *Monsanto*, 467 U.S. at 1011 n.15 (emphasis added).

<sup>58</sup> See *Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the H. Comm. on Energy & Commerce Subcomm. on Health*, 110th Cong. 55 (2007) (statement of Dr. Janet Woodcock, M.D., Deputy Commissioner, Chief Medical Officer, Food and Drug Administration) (stating that FDA relies, in part, on the trade secret data contained in a BLA when finding that the biologic is safe, pure, and potent) (Exhibit 31).



conducts that testing, and when it files its application for approval of the biosimilar, the safety, purity, and potency of the reference product is established by a file housed at FDA that contains not only the originally submitted trade secrets, but also subsequent supplemental applications by the reference product sponsor, safety reports, annual reports, and often information from postmarket studies and trials. These applications themselves generally contain new trade secrets. In other words, the initial agency determination that the reference product was safe, pure, and potent has relevance when the biosimilar applicant submits its application only to the extent that the determination is subsequently maintained by the reference product sponsor.

The inseparable nature of a government license and the information and data supporting that license was explained by the Ninth Circuit in *G.S. Rasmussen & Associates, Inc. v. Kalitta Flying Service, Inc.*<sup>59</sup> Rasmussen had been granted a supplemental Type Certificate (STC) from the Federal Aviation Administration (FAA) for an aircraft design. An STC allows changes to aircraft designs that have already themselves been approved. An STC applicant must present engineering and test data sufficient to establish the airworthiness of the proposed modification. The Ninth Circuit noted that an STC “is granted upon the presentation of certain documentation, which normally can be obtained only through expensive and time-consuming design, experimentation, and testing.” In addition, “an STC is issued to a particular individual and entitles the holder to specific privileges.” And it “is transferable and it may be licensed.”<sup>60</sup> In all of these respects, it is very much like a biologics license.

Rasmussen sued Kalitta after the latter copied the changes that Rasmussen had made to his aircraft design and presented a photocopied version of Rasmussen’s STC to the FAA, which then certified Kalitta’s design as airworthy. Because Rasmussen sued for unjust enrichment and conversion, the issue before the Ninth Circuit was whether he had a property right in the STC. But the Ninth Circuit’s analysis also establishes the more fundamental proposition — relevant here — that a license supported by testing data *has value* to its owner *because* of the data that were generated and submitted at great risk and expense to support issuance of the license.

The court first noted that the STC “has value *only* because it helps secure a government privilege to do something that would otherwise be forbidden. The time, money and effort Rasmussen devoted to obtaining his STC would largely be wasted but for the fact that they generated the data necessary to satisfy the requirements of the Federal Aviation Act and the Code of Federal Regulations.”<sup>61</sup> The Court then made three key findings. *First*, “[t]he nature and extent of the rights afforded by an STC are capable of precise definition: It enables an airplane owner to obtain an airworthiness certificate for a particular design modification without the delay, burden and expense of proving to the FAA that a plane so modified will be safe.” *Second*, there were no “conceptual or practical difficulties in restricting the right to the holder of the STC, or to someone who is a transferee or licensee.” Instead, “the federal regulations contemplate exactly that. Rasmussen’s interest is thus precisely defined and capable of exclusive

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<sup>59</sup> 958 F.2d 896 (9th Cir. 1992).

<sup>60</sup> *Id.* at 901.

<sup>61</sup> *Id.* at 900-01.

possession.” *Third*, Rasmussen had established “a legitimate claim to exclusivity.” Specifically, he “expended considerable time and effort in research and design; he conducted the appropriate tests and compiled the necessary data; he prepared an operations manual and lined up an instrument manufacturer; he convinced the FAA that the modification is safe; and he obtained a certificate which results in preferential rights in the issuance of airworthiness certificates by the FAA.” The Ninth Circuit explained: “[w]ithout Rasmussen’s efforts, the STC Kalitta relied on simply would not exist.” It then used the language of *Monsanto*: “Rasmussen has the type of reasonable investment-backed expectations that give rise to a legitimate claim of exclusive control over the STC.”<sup>62</sup>

The same three points apply to an approved BLA and the accompanying agency finding that the biologic in question is safe, pure, and potent. *First*, a BLA allows a company to introduce the biologic into U.S. interstate commerce. *Second*, a BLA is under the exclusive control of the sponsor. The sponsor, for example, has the exclusive right to transfer or sell the license. *Finally*, a biologic sponsor has expended substantial resources to procure the license. Without the company’s efforts to create the trade secrets in the BLA, the license “simply would not exist.” FDA’s reliance on the finding accompanying the license is therefore reliance on the underlying trade secrets and frustrates the license holder’s “reasonable investment-backed expectation” of “exclusive control” over the license. FDA may not, in other words, separate the “public finding” from the underlying data. Abbott has a “legitimate claim of exclusive control” with respect to both. The finding is inseparable from the trade secrets that supported the finding.

Not surprisingly, federal courts that have described approval of follow-on applications submitted to FDA view as interchangeable the agency’s reliance on its finding that the reference product was safe and effective and the agency’s reliance on the data that supported the finding.<sup>63</sup> And the agency itself has at times conceded that it relies on the underlying data,

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<sup>62</sup> *Id.* at 903.

<sup>63</sup> Compare *Andrx Pharms., Inc. v. Bioavail Corp. Int’l*, 256 F.3d 799, 802 (D.C. Cir. 2001) (describing abbreviated new drug applications (ANDAs) as applications relying “on the FDA’s previous determination that the drug is safe and effective”); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1063 (D.C. Cir. 1998) (finding that an ANDA “relies on the FDA’s previous determination that the drug is safe and effective”), with *Purepac Pharm. Co. v. Torpharm, Inc.*, 354 F.3d 877, 879 (D.C. Cir. 2004) (describing ANDAs as applications “that ‘piggyback’ on the safety-and-effectiveness information that the brand-name manufacturers submitted in their NDAs”); *Am. Bioscience, Inc. v. Thompson*, 243 F.3d 579, 580 (D.C. Cir. 2001) (observing that ANDA applicants are “relying on the NDA filed by the original manufacturer”); *Zenith Labs, Inc. v. Abbott Labs.*, No. 96-1661, 1997 U.S. Dist. LEXIS 23954, at \*3 (D.N.J. Oct. 3, 1997) (describing the ANDA process as “permit[ting] a generic drug manufacturer to rely on the safety and effectiveness data compiled and submitted by the pioneer drug manufacturer in connection with its NDA”) (Exhibit 32); *Merck & Co., Inc. v. Kessler*, 80 F.3d 1543, 1546 (Fed. Cir. 1996) (describing the ANDA process as permitting a “generic producer of the fully tested drug to rely on the safety and efficacy data of a prior applicant”) (citations omitted); *Granotec, Inc. v. Shalala*, No. 97-1873, 1998 U.S. App. LEXIS 6685, \*4-5 (4th Cir. Apr. 3, 1998) (Exhibit 33); *Am. Bioscience, Inc. v. Thompson*, 141 F. Supp. 2d 88, 91 (D.D.C. 2001) (“In other words, the generic manufacturer is allowed to rely on the safety and effectiveness data submitted in the pioneer’s NDA.”); *Am. Bioscience, Inc. v. Shalala*, 142 F. Supp. 2d 1, 4 (D.D.C. 2000) (same); *In re Terazosin Hydrochloride Antitrust Litigation*, 164 F. Supp. 2d 1340, 1343-44 (S.D. Fl. 2000) (“Geneva’s ANDA relied on data concerning Hytrin’s safety and efficacy. . . .”); *Teva Pharms. USA, Inc. v. FDA*, No. 99-67-CCK, 1999 U.S. Dist. LEXIS 14575, \*4 (D.D.C. Aug. 19, 1999) (same) (Exhibit 34); *Pfizer v. FDA*, 753 F. Supp. 171, 172 (D. Md. 1989) (explaining (continued...))

rather than the finding.<sup>64</sup> In a recent statement, for example, an FDA official stated that the development and approval of biosimilars will involve “an abbreviated pathway that will depend on existing *data*” that supported approval of the reference product.<sup>65</sup> Similarly, in one of the draft biosimilar guidance documents recently released by the agency, FDA states that it is generally unnecessary for a biosimilar applicant to conduct a “clinical study to assess . . . cardiac repolarization (a QT/QTc study) or a drug-drug interaction study” because “a proposed biosimilar product may rely upon the reference product’s clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential and drug-drug interactions.”<sup>66</sup> In sum, FDA’s own statements with regard to biosimilars and other products approved through an abbreviated pathway establish that there is no difference between relying on the underlying data and trade secrets and relying on the prior finding.

Indeed, such reliance on the underlying trade secrets should be viewed as inevitable, given FDA’s access and familiarity with the trade secrets in the reference product’s BLA. Following the Restatement, courts infer use of trade secrets where a party has knowledge of trade secrets and then becomes involved with new processes or products that are substantially similar to the product or process to which those trade secrets pertain.<sup>67</sup> Here, FDA “is in possession of [Abbott’s] confidential information and is in a position to use it.”<sup>68</sup> And the agency has in fact acknowledged as much, stating in a hearing before Congress that it is realistically impossible to eliminate reliance on internal knowledge of information in a prior application.<sup>69</sup>

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that ANDA applicants are “permitted . . . to rely on the safety and effectiveness data submitted by the ‘pioneer’ drug manufacturer with its NDA”); *Glaxo v. Heckler*, 623 F. Supp. 69, 72 (E.D.N.C. 1985) (stating that ANDA applicants “may rely on existing data and information on file with the FDA in order to satisfy the safety and efficacy requirements of federal food and drug law”).

<sup>64</sup> For instance, when FDA reviewed a 505(b)(2) application for a follow-on version of Paxil<sup>®</sup>, FDA stated in its chemistry review that the follow-on applicant “is relying on clinical, statistical, pharmacology/toxicology and biopharmaceutics *data* contained in NDA 20-031 [for] Paxil<sup>®</sup> . . . to support approval.” CDER, Chemistry Review #1 for NDA 21-299 (Apr. 3, 2001), at 3 (emphasis added). The medical review of the application further notes that FDA allowed the follow-on applicant to proceed with its stated plan to “file an NDA under section 505(b)(2) of the [FDCA] for paroxetine mesylate based [in part] on the safety and efficacy *data* for the hydrochloride salt, which is marketed in the U.S. as Paxil.” CDER, Review and Evaluation of Clinical Data (Mar. 21, 2001), at 2 in Medical Review for NDA 21-299 (emphasis added).

<sup>65</sup> Thomas M. Burton & Jonathan D. Rockoff, *FDA Sets Path for Biotech Drug Copies*, WALL ST. J., Feb. 10, 2012 (emphasis added) (Exhibit 30).

<sup>66</sup> FDA, Draft Guidance for Industry on Biosimilars: Q & As Regarding Implementation of the BPCI Act of 2009: Questions and Answers Part I (Feb. 2012).

<sup>67</sup> Restatement (Third) of Unfair Competition § 40 cmt. c (“Although the trade secret owner bears the burden of proving unauthorized use, proof of the defendant’s knowledge of the trade secret together with substantial similarities between the parties’ products or processes may justify an inference of use by the defendant.”) (Exhibit 27).

<sup>68</sup> *Rugen v. Interactive Bus. Systems, Inc.*, 864 S.W. 2d 548, 552 (Tex. 1993) (Exhibit 35).

<sup>69</sup> *The Law of Biologic Medicine: Hearing Before the Sen. Comm. on the Judiciary*, 108th Cong. 66 (2004) (written statement by Lester M. Crawford, D.V.M., Ph.D., Acting Commissioner of Food and Drugs) (stating that “reviewers (continued…)”).

The U.S. government has in at least one other context — international trade rules related to the protection of pharmaceutical test data — treated use of data and reliance as synonymous concepts. Article 39.3 of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), for example, requires World Trade Organization members, including the United States, to protect “data” submitted for approval of pharmaceutical products from “unfair commercial use.”<sup>70</sup> It is well-accepted in the international trade context that this obligation to protect data from unfair commercial use is satisfied through a regulatory non-reliance framework. For its part, the U.S. government has typically suggested that its schemes for regulatory exclusivity (for example, in the Hatch-Waxman provisions) constitute compliance with TRIPS Article 39.3.<sup>71</sup> This exclusivity prohibits FDA from relying for a certain period of time on its prior finding that a product was safe and effective. Subsequent U.S. bilateral free trade agreements have typically included even more explicit non-reliance provisions. These provisions are intended to be consistent with Article 39.3 as well as current U.S. law, and they make it clear that in order to protect data from unfair commercial use as required by TRIPS Article 39.3, a regulatory agency may not rely on a prior approval or the underlying data.<sup>72</sup> The U.S. government’s position in international trade negotiations — which we assume is informed by FDA’s views — is that both ways of describing follow-on review have the same meaning.

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are sometimes unavoidably conscious of information in a prior application, even without physically consulting the application, simply because they recall the information from having worked on the earlier review”) (Exhibit 36).

<sup>70</sup> TRIPS art. 39.3 (emphasis added) (Exhibit 37).

<sup>71</sup> For example, during the 1994 Statement of Administrative Action for The Uruguay Round Agreements Act, the U.S. government noted that TRIPS “requires few changes in U.S. law and regulations.” The Uruguay Round Agreements Act, Statement of Administrative Action (1994), reprinted in 1994 U.S.C.C.A.N. 4040, 4280 (Exhibit 38); *see also id.* at 4040 (“It should be noted that this Statement does not, for the most part, discuss those many instances in which U.S. law or administrative practice will remain unchanged under the Uruguay Round agreements. In many cases, U.S. laws and regulations are already in conformity with the obligations imposed by those agreements.”).

<sup>72</sup> *See* United States-Australia Free Trade Agreement art. 17.10 (“If a Party requires, as a condition of approving the marketing of a new pharmaceutical product, the submission of undisclosed test or other data concerning safety or efficacy of the product, the Party shall not permit third persons, without the consent of the person who provided the information, to market the same or a similar product *on the basis of that information, or the marketing approval granted to the person who submitted such information*, for at least five years from the date of marketing approval by the Party.” (emphasis added)) (Exhibit 39); *see also* Report of the Industry Sector Advisory Committee for Chemicals and Allied Products on the Free Trade Agreement Between the United States and Australia (Mar. 12, 2004), at 10 (describing the reliance provision as serving to “clarify the obligations contained in TRIPS Article 39.3” and as not “imposing any additional obligations above those contained in TRIPS Article 39.3”) (Exhibit 40); Report of the Industry Functional Advisory Committee on Intellectual Property on the U.S.-Australia Free Trade Agreement (Mar. 12, 2004), at 14 (stating that “[t]o give effect to the data exclusivity obligations of Article 39.3 of TRIPS, [the agreement] imposes an obligation of ‘non-reliance’ on either the pioneer approval or the pioneer data package itself”) (Exhibit 41).

## II. Use of Trade Secrets Submitted in a BLA Prior to Enactment of the BPCIA Would Constitute a Taking under *Monsanto*.

Under *Monsanto*, the government effects a taking — for which just compensation is required — if it interferes with a property owner’s “reasonable investment-backed expectation” regarding government use of its property. This factor “focuses on reasonable, objective expectations, rather than a claimant’s subjective expectations or hopes for a property.”<sup>73</sup> In this case, the relevant consideration is the expectation of the property owner at the time the data were submitted to the agency.<sup>74</sup>

As explained below, when Abbott submitted its application to market Humira in 2002, the company had a reasonable, investment-backed expectation — grounded in the plain language of the statute and FDA regulations and consistent agency practice — 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.<sup>75</sup> This expectation, and the binding authority of *Monsanto*, compels the conclusion that approval of biosimilar versions of Humira or other biologics approved via BLAs submitted before enactment of the BPCIA constitutes a taking for which just compensation is required. FDA should not implement the BPCIA in a way that would require compensation, because doing so would expose the United States to enormous liability.

### A. Abbott had a reasonable, investment-backed expectation that the trade secrets in its application would not be used for the benefit of competitors.

1. *The PHSA and FDA’s implementing regulations, and FDA’s consistent practice in applying these provisions, gave Abbott a reasonable expectation that its trade secrets would not be used to support another company’s application or released to competitors to guide their research efforts.*

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<sup>73</sup> *McGuire v. United States*, 97 Fed. Cl. 425, 441 (Fed. Cl. 2011).

<sup>74</sup> See *Monsanto*, 467 U.S. at 1013 n.17 (“While the 1975 amendments to FIFRA purported to carry backward the protections against data consideration and data disclosure to submissions of data made on or after January 1, 1970, . . . the relevant consideration for our purposes is the nature of the expectations of the submitter at the time the data were submitted.”).

<sup>75</sup> See *Monsanto*, 467 U.S. at 1008-11; *id.* at 1009 n.14 (discussing the evidence of EPA’s policy on using submitted data); *Tri-Bio Labs.*, 836 F.2d at 140-41 (holding that an FDA “regulation provided pioneer animal drug manufacturers with a[] . . . reasonable investment-backed expectation that the FDA would refrain from nonconsensual use of research material”); *id.* at 141 (finding that FDA’s “consistent interpretation” of an agency regulation entitled an innovator to rely on it); *Chevron Chemical Co. v. Costle*, 641 F.2d 104, 115 (3d Cir. 1981) (discussing whether a company that submitted data to EPA has an expectation that the agency would not use the data for the benefit of a competitor and noting that prior to 1972, a statute and “agency practice defined the scope of that expectation”); *Petrolite Corp. v. U.S. Environmental Protection Agency*, 519 F. Supp. 966, 971 (D.D.C. 1981) (dismissing a takings claim where the plaintiff presented “no evidence indicating that the development and submission of this data preceded in time the adoption of the agency practice of using the data in subsequent applications”).

Since 1902, federal law has required a government-issued license in order to market a biological product in the United States.<sup>76</sup> This requirement was incorporated into section 351(a) of the PHSA in 1944. Moreover, from 1944 until enactment of the BPCIA in 2010, section 351(a) provided the exclusive means to obtain a biologics license in the United States.

Section 351(a) does not, on its face, allow FDA to rely on a finding that one company's biologic is safe, pure, and potent (or that company's trade secrets) to approve any other company's application. Instead it requires FDA to issue a biologics license only if the sponsor demonstrates in the license application that the biological product "is safe, pure, and potent." This language parallels section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA), which requires an applicant to submit in its application full reports of the investigations performed to show whether the drug is safe and effective. Neither section 351(a) of the PHSA nor section 505(b)(1) of the FDCA refers to studies performed by another applicant or to approval or licensure of another company's product.

Both provisions, however, stand in sharp contrast to the drug approval provisions in sections 505(b)(2) and 505(j) of the FDCA. Section 505(b)(2) authorizes an applicant to rely on investigations "not conducted by or for the applicant," and section 505(j) directs the applicant to cite, and compare its proposed drug to, another drug "previously approved" as safe and effective. The absence of remotely similar language in the PHSA gave Abbott, at the time it submitted the Humira BLA to FDA, a reasonable, investment-backed expectation that its trade secrets and the Humira license that embodies those trade secrets would not be used to approve another company's application.

FDA's regulations, as interpreted and applied by the agency, similarly gave Abbott a reasonable expectation that its trade secrets would not be released in order to guide a competitor's research efforts (or to support that company's "me too" product). Section 601.51 of the agency's regulations states that the manufacturing information in a BLA cannot be released by the agency unless it is no longer trade secret.<sup>77</sup> Although the same regulation provides that safety and efficacy data in a BLA can be released following approval of the application unless extraordinary circumstances exist,<sup>78</sup> that phrase has long been understood to mean that the relevant data will in fact be protected so long as they remain trade secrets. Long before Abbott submitted the Humira application, the agency explained in statements before Congress, in the *Federal Register*, and in federal court litigation that "extraordinary circumstances" exist whenever the safety and efficacy data retain competitive value.<sup>79</sup> Moreover, in the context of

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<sup>76</sup> 32 Stat. 728 (1902).

<sup>77</sup> 21 C.F.R. § 601.51(f)(1).

<sup>78</sup> *Id.* § 601.51(e)(1).

<sup>79</sup> 130 Cong. Rec. 24,977-78 (Sept. 12, 1984) (statement of Sen. Hatch) (reading into the record a letter from Frank E. Young, M.D., Ph.D., Commissioner of Food and Drugs explaining that the FDA definition of "extraordinary circumstances" for data disclosure purposes encompassed situations where the data or information retain their status as trade secrets) (Exhibit 42); 39 Fed. Reg. 44,602, 44,613 (Dec. 24, 1974) (stating that information about past manufacturing methods will not be released "[i]f a manufacturer can show in a particular case that, because of (continued...)

this regulation, it explicitly tied the question of release and competitive value to whether “me too” applications from subsequent applicants are feasible. Specifically, when FDA issued this regulation in 1974, it explained that the regulation permitted release of the safety and efficacy data only because “all biological products are required to undergo clinical testing in order to demonstrate safety, purity, potency, and effectiveness prior to licensing, regardless whether other versions of the same product are already marketed or standards for the product have been adopted by rule making . . . . There is no such thing as a ‘me-too’ biologic.”<sup>80</sup> In other words, the data were available for release solely because they could not be used by a competitor to support approval of a follow-on application. Conversely, however, where the data retained competitive value (i.e., could be used by a competitor to obtain a shortcut to market), FDA’s scheme precluded their release. This gave innovative sponsors like Abbott a reasonable, investment-backed expectation that their trade secrets would not be released or used to benefit competitors.

Decades of consistent FDA practice in applying its statutory authority and implementing regulations also gave Abbott a reasonable expectation that the agency would not approve biosimilars based, in whole or in part, on the prior finding for a reference product, or otherwise use an innovator’s trade secrets to assist its competitors. We are aware of no instance in which FDA released trade secrets from a BLA to a competitor to guide that company’s research efforts and no instance in which it released safety and efficacy data that retained competitive value (i.e., that still qualified as trade secrets). The one relevant administrative precedent we have found, discussed below, indeed proves the opposite: that under the law in place prior to enactment of the BPCIA, it was agency policy to *refuse* disclosure requests if the data in question were trade secrets.

In 1996, Berlex Laboratories asked FDA to release safety and efficacy data contained in Biogen’s approved BLA for Avonex (interferon beta-1a). Biogen had previously shared manufacturing information with Dr. Rentschler Biotechnologie under a joint venture agreement, and Rentschler subsequently entered into an affiliation arrangement with Berlex. Biogen argued to FDA that the data should not be released because access to the data would

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extraordinary circumstances, these data will provide a future competitive advantage”) (Exhibit 12); *id.* at 44,633 (“Should a specific instance arise in which a competitive advantage can be demonstrated in concrete terms, a manufacturer is permitted to support nondisclosure of such information under the ‘extraordinary circumstances’ exemption provided in the final regulations.”); Final Brief for Appellant Food & Drug Administration, *Pub. Citizen Health Research Grp. v. Food & Drug Admin.*, 1999 WL 34833581 (D.C. Cir. Mar. 29, 1999) (stating that under FDA’s “long-standing construction” of the regulation governing release of IND safety and efficacy data, a showing of “extraordinary circumstances” sufficient to prevent release of otherwise available information from an application requires “a showing that there is a likelihood of substantial competitive harm to the submitter through public disclosure”) (Exhibit 43).

<sup>80</sup> 39 Fed. Reg. 44,602, 44,641 (Dec. 24, 1974) (Exhibit 12). This statement was made in a preamble, and, except in rare circumstances, FDA’s preambles are binding on the agency. A “statement of policy or interpretation” made in a preamble constitutes an FDA advisory opinion. An agency advisory opinion “obligates the agency to follow it until it is amended or revoked. The Commissioner may not recommend legal action against a person or product with respect to an action taken in conformity with an advisory opinion which has not been amended or revoked.” *See* 21 C.F.R. § 10.85.

allow Rentschler and Berlex to obtain approval for their competing product.<sup>81</sup> FDA accepted this reasoning and permitted Biogen to significantly limit the information that could be released to Berlex by inviting Biogen to identify information that “‘Berlex, Rentschler, or their affiliate could use . . . to obtain approval of their own interferon-beta product in the United States or in specific foreign markets.’”<sup>82</sup> The agency thus accepted Biogen’s argument that extraordinary circumstances under section 601.51 existed because these data from the Avonex BLA retained competitive value.

The Berlex precedent 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). FDA’s consistent implementation of its trade secret regulations supported the reasonable, investment-backed expectation of Abbott that the trade secrets in a BLA would not be released or used in any way to assist or guide competitors’ development efforts.<sup>83</sup>

2. *FDA’s repeated statements in both formal and informal settings that it lacked legal authority to approve biosimilar applications gave Abbott a reasonable expectation that its trade secrets would remain inviolate.*

Until enactment of the BPCIA in 2010, the agency consistently and publicly maintained that it lacked authority to approve biosimilars. FDA adopted this view in formal hearing testimony before Congress,<sup>84</sup> in written submissions to Congress,<sup>85</sup> in *Federal Register* preambles,<sup>86</sup> and in numerous speeches to industry<sup>87</sup> from the early 1970s until the 2010 passage

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<sup>81</sup> Comment, Robert A. Long, Jr., Docket No. 2004P-0171, C7 (July 13, 2005), at 6 (Exhibit 44).

<sup>82</sup> *Id.*

<sup>83</sup> See *Tri-Bio Labs.*, 836 F.2d at 141 (“At the time Schering sent its data to the FDA, the regulation had been in effect for some years and had received a consistent interpretation by the FDA, thus entitling Schering to rely on it. Accordingly, the FDA’s regulation — as published and implemented — had created for Schering a property interest in its data.”).

<sup>84</sup> *Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the H. Comm. on Energy & Commerce Subcomm. on Health*, 110th Cong. 20 (2007) (statement of Dr. Janet Woodcock, M.D., Deputy Commissioner, Chief Medical Officer, Food and Drug Administration) (“[A]n abbreviated pathway, though, does not exist for copies of protein products that are approved under the Public Health Service Act.”) (Exhibit 31).

<sup>85</sup> Letter from Frank M. Torti, M.D., M.P.H., FDA Principal Deputy Commissioner and Chief Scientist, to the Hon. Frank Pallone, Jr., Chairman, H. Subcomm. on Health, at 7 (Sept. 18, 2008) (“Currently, the PHSA does not contain an abbreviated approval pathway for biological products licensed under the PHSA that is analogous to the abbreviated approval pathways under sections 505(b)(2) or section 505(j) of the FD&C Act.”) (Exhibit 45); Letter from Michael Leavitt, Sec’y of Health & Human Services to Sen. Edward Kennedy, at 1 (June 26, 2007) (“There is no approval pathway for biological products licensed under the PHSA that is analogous to section 505(b)(2) or section 505(j) of the FDCA.”) (Exhibit 46).

<sup>86</sup> See, e.g., 39 Fed. Reg. 44,602, 44,641 (Dec. 24, 1974) (Exhibit 12); 57 Fed. Reg. 17,950, 17,951 (Apr. 28, 1992) (stating that the Hatch-Waxman procedures are “inapplicable to antibiotics (which are approved under section 507 of the act) and biological drug products licensed under 42 U.S.C. 262”) (Exhibit 47).



of the BPCIA. These statements of agency interpretation came both before Abbott submitted its original application for a Humira license and in the years following when the company continued to supplement the application with trade secrets. For example, in 2001, Director of the Center for Drug Evaluation and Research (CDER) Janet Woodcock stated that there is no “statutory framework” for the approval of biosimilars.<sup>88</sup> Similarly, in May 2004, then-Acting Director of CDER Steven Galson stated that “FDA does not have the legal authority to reference information in an innovator company’s BLA submission” in order to approve follow-on biologics.<sup>89</sup> One month later, then-Acting Commissioner of Food and Drugs Lester Crawford stated that FDA did not have the authority to approve a follow-on application under the PHSA “that relies on the prior approval of the biological product or on data submitted by another sponsor.”<sup>90</sup>

In sum, prior to enactment of the BPCIA, Abbott had a reasonable expectation that the trade secrets in the Humira BLA would not be released or used to approve biosimilar competitors. Abbott made a massive investment in developing Humira on the basis of that expectation.<sup>91</sup> Use of the Humira BLA to approve a biosimilar now would upset this expectation and therefore effect a taking.

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<sup>87</sup> See, e.g., *McClellan Outlines ‘Generic’ Biologics Proposal*, DICKINSON’S FDA REVIEW 5 (March 2004) (reporting that “the agency still believes that the current law does not generally permit generic biologics”) (Exhibit 48); *McClellan: Legislation Will Be Needed for Generic Biologics*, FDA Enforcement Manual 5 (June 2003) (quoting the FDA Commissioner as stating that biosimilars are ““going to require a lot more science and more legislation before we can get close to it”) (Exhibit 49).

<sup>88</sup> *Recent Developments Which May Impact Consumer Access to, and Demand for, Pharmaceuticals*, Hearing Before the H. Subcomm. on Health of the H. Comm. on Energy and Commerce, 107th Cong. 33 (2001) (statement of Dr. Janet Woodcock) (Exhibit 50).

<sup>89</sup> “Follow-On” Biologics Guidance Will Limit Use of Data to “Public Domain,” THE PINK SHEET, May 10, 2004, at 3 (Exhibit 51).

<sup>90</sup> *The Law of Biologic Medicine: Hearing Before the Sen. Comm. on the Judiciary*, 108th Cong. 134 (2004) (written statement by Lester M. Crawford, Acting Commissioner of Food and Drugs) (Exhibit 36). In addition to FDA statements that the agency did not have the legal authority to approve biosimilars prior to 2010, in the 1990s (when Humira was being developed) the agency made clear that it was not pursuing a biosimilar pathway and had no immediate plans to do so. For example, in 1998, the nominee for (and subsequent) Commissioner of Food and Drugs told Congress that FDA “has no plans to allow submissions of abbreviated applications for biological products.” *Henney FDA Will Be “Open, Timely and Responsive,” Nominee Says*, THE PINK SHEET (Aug. 31, 1998), at 3, 4 (Exhibit 52). Well into the 2000s, the agency expressed significant doubt regarding whether the science of the time supported abbreviated approvals for biologics and indicated that the development of a biosimilar approval pathway was, as a scientific matter, some time away. For example, in May 2004, the Acting Director of CDER stated that “[t]he development and potential submission of applications for most potential follow-on biologics is really many years away.” *Follow-On” Biologics Guidance Will Limit Use of Data to “Public Domain,”* THE PINK SHEET (May 10, 2004), at 3, 5 (Exhibit 51).

<sup>91</sup> See *Monsanto*, 467 U.S. at 1011 (holding that because the statute “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 trade secrets” doing so “would frustrate Monsanto’s reasonable investment-backed expectation with respect to its control over the use and dissemination of the data it had submitted”).

B. The economic impact of the use in question, and the government action constituting the use in question, further support finding a “taking” under *Monsanto*.

As discussed above, under *Monsanto*, the strength of Abbott’s investment-backed expectation that its trade secrets in the Humira BLA would not be used by FDA to approve a competitor product alone establishes a taking of Abbott’s property. Nonetheless, the second and third prongs of the *Penn Central* test (economic impact and nature of the government action, respectively), while not necessary to the analysis, also support a finding that approving a biosimilar of Humira effects a taking. The *Monsanto* decision establishes that where the government uses one company’s trade secrets to approve another company’s product (even where the trade secrets are not disclosed), the economic impact of the use 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.<sup>92</sup> Thus, it is “the fact that operation of the *data-consideration or data-disclosure provisions* will allow a competitor to register more easily its product or to use the disclosed data to improve its own technology that may constitute a taking.”<sup>93</sup> Similarly, the economic value of the trade secrets in Abbott’s Humira BLA lies in the competitive advantage over others that Abbott earned by virtue of those trade secrets. FDA’s use of those trade secrets, if it were to consider and/or approve a biosimilar application that cites the Humira BLA, would destroy that competitive edge.<sup>94</sup>

The nature of the government action (the third *Penn Central* factor) also supports the conclusion that use of Abbott’s trade secrets would constitute a taking. Where the government use of property is unrelated to a public harm caused by the property owner, this weighs in favor of finding a taking.<sup>95</sup> Here, Abbott’s marketing of Humira does not inflict any

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<sup>92</sup> *Id.* at 1011-12.

<sup>93</sup> *Id.* at 1011 n.15 (emphasis added).

<sup>94</sup> FDA’s use of trade secrets included in a pre-BPCIA BLA could also be viewed as a *per se* taking. At least one court of appeals has framed the issue in these terms, suggesting that application of the *Penn Central* framework to intellectual property leads to a kind of *per se* approach. See *Philip Morris, Inc.*, 312 F.3d at 35 (“[A]pplying the *Penn Central* regulatory takings framework is not practically different from utilizing *per se* rules. Functionally, these *per se* rules are simply shortcuts.”); see also *id.* at 50-51 (Selya, J. concurring) (urging courts to “take the next logical step” and apply a *per se* analysis to trade-secret takings). Some commentators have also explored this approach to analyzing takings in this context. See, e.g., Richard A. Epstein, *The Constitutional Protection of Trade Secrets and Patents Under the Biologics Price Competition and Innovation Act of 2009*, 66 FOOD & DRUG L.J. 285, 297-98 (2011) (arguing that a *per se* analysis is more appropriate in takings cases involving intangible property rights such trade secrets, including those taken under the BPCIA) (Exhibit 53); William P. Barr, Henry Weissmann, & John P. Frantz, *The Gild that Is Killing the Lily: How Confusion over Regulatory Takings Doctrine Is Undermining the Core Protections of the Takings Clause*, 73 GEO. WASH. L. REV. 429, 487 (2005) (arguing that “when the government seeks to use, or to allow a third party to use, the owner’s intellectual property rights, a *per se* taking occurs”) (Exhibit 54). A court may conclude, therefore, that FDA has taken trade secrets submitted by an innovator before the BPCIA was enacted even without applying the *Penn Central* analysis. In any event, whether a court applies the three-factor regulatory takings test or a *per se* standard, the result should be the same.

<sup>95</sup> See *Eastern Enters. v. Apfel*, 524 U.S. 498, 537 (1998) (“[T]he nature of the governmental action in this case is quite unusual. That Congress sought a legislative remedy for what it perceived to be a grave problem in the funding (continued...)”).

harm on the U.S. public, but instead offers a valuable treatment option to thousands of patients.<sup>96</sup> Moreover, to the extent that the government seeks to facilitate lower prices in the biologics market, there are other potential avenues that would not require the use of trade secrets belonging to Abbott and other pre-enactment sponsors.<sup>97</sup> The government could, for example, increase the incentive to undertake research on biologics or enact incentives for voluntary data-sharing, which could help facilitate entry into the biologics market.

C. FDA should not apply the BPCIA to pre-enactment BLAs because doing so would call the statute’s constitutionality into question.

The canon of “constitutional avoidance” calls for interpretation and implementation of federal statutes in a way that would avoid raising substantial questions about their constitutionality.<sup>98</sup> The courts have repeatedly applied this rule in the context of takings claims, particularly when interpreting a statute one way would have the effect of taking property from an identifiable class and impose very large financial liability on the United States.<sup>99</sup>

Agencies too must consider possible constitutional infirmities, including takings imposing large liabilities on the United States, in selecting among possible interpretations of a statute.<sup>100</sup> Because approving biosimilars of pre-enactment reference products would take the trade secret property of an identifiable class (i.e., pre-enactment reference product sponsors) and

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of retired coal miners’ health benefits is understandable; complex problems of that sort typically call for a legislative solution. When, however, that solution singles out certain employers to bear a burden that is substantial in amount, based on the employers’ conduct far in the past, and unrelated to any commitment that the employers made *or to any injury they caused*, the governmental action implicates fundamental principles of fairness underlying the Takings Clause.” (emphasis added); *Atlas Corp. v. United States*, 895 F.2d 745, 757 (Fed. Cir. 1990) (finding that a taking did not occur, in part, because the government “action [did] not invade or permanently appropriate [the plaintiff’s] property for public use” but rather safeguarded the public health by requiring the property owner to take certain actions); *Brace v. United States*, 72 Fed. Cl. 337, 356 (Fed. Cl. 2006) (“[T]he absence of a nuisance certainly cuts in favor of a finding of a taking . . .”).

<sup>96</sup> *Huntleigh USA Corp. v. United States*, 63 Fed. Cl. 440, 448-49 (Fed. Cl. 2005) (finding that the character of the government action could support a takings claim even though the statute was enacted to serve a legitimate public purpose where the plaintiff conducted its business “in compliance with the law, and in no way presented a danger to the public” and where “the entire expense” of pursuing the public purpose was placed on the plaintiff).

<sup>97</sup> See *Philip Morris, Inc.*, 312 F.3d at 45; *Pennsylvania Coal Co. v. Mahon*, 260 U.S. 393, 414 (1922) (finding that preventing a coal company from mining property to which it had a right in order to protect the safety of an individual homeowner would constitute a taking, in part, because the goal could be achieved by providing notice to the homeowner).

<sup>98</sup> See, e.g., *NLRB v. Catholic Bishop of Chicago*, 440 U.S. 490, 507 (1979).

<sup>99</sup> See, e.g., *United States v. Security Indus. Bank*, 459 U.S. 70, 78 (1982) (applying “the ‘cardinal principle that this Court will first ascertain whether a construction of the statute is fairly possible by which the constitutional question may be avoided’” (quoting *Lorillard v. Pons*, 434 U.S. 575, 577 (1978)); *Bell Atl. Tel. Cos. v. FCC*, 24 F.3d 1441 (D.C. Cir. 1994).

<sup>100</sup> See, e.g., *Nat’l Treasury Employees Union v. Federal Labor Relations Authority*, 986 F.2d 537, 540 (D.C. Cir. 1993) (requiring an agency to consider the possible invalidity of the statute in selecting between readings).

impose a very large financial liability on the United States, retrospective application of the BPCIA would call the statute's constitutionality into question. FDA should therefore apply the BPCIA prospectively only.

In *United States v. Security Industrial Bank*, for example, the Supreme Court relied on these principles to reject a retrospective reading of an amendment to the Bankruptcy Code.<sup>101</sup> The amendment permitted individual debtors to avoid liens on their household items. The Court explained that “there is substantial doubt whether the retroactive destruction of the appellees’ liens in this case comports with the Fifth Amendment.”<sup>102</sup> That doubt was enough, the Court determined, for it to “decline to construe the Act” retrospectively, for doing so “could in turn call upon the Court to resolve difficult and sensitive questions arising out of the guarantees of the Takings Clause.”<sup>103</sup> Although the taking at issue was a regulatory taking and therefore typically subject to a fact-specific inquiry, the Court held that because the statute would constitute a taking of the lienholders’ property in every case, the lienholders comprised an identifiable class.<sup>104</sup> Because the statute provided no ready mechanism to compensate this class for the takings, the Court applied the canon of constitutional avoidance, holding that Congress could not have intended the statute to apply retroactively.<sup>105</sup>

Similarly, in *Bell Atlantic Telephone Companies v. FCC*, the D.C. Circuit addressed the FCC’s interpretation of a statute that would require telephone exchange companies to permit a small physical intrusion into their facilities by competing service providers.<sup>106</sup> Following *Security Industrial Bank*, the court held that when “administrative interpretation of a statute” creates an “identifiable class of cases in which application of a statute will necessarily constitute a taking,” *Chevron* deference is inapplicable and the avoidance canon requires interpreting the statute to avoid the taking of property.<sup>107</sup> Reasoning that the agency’s interpretation of the statute would constitute a taking in “all the cases to which the interpretation would be applied,” the court set aside the agency’s interpretation.<sup>108</sup> Moreover, when a court or agency-rendered interpretation of a statute exposes the United States to large amounts of

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<sup>101</sup> 459 U.S. 70 (1982).

<sup>102</sup> *Id.* at 78.

<sup>103</sup> *Id.* at 82 (quoting *NLRB v. Catholic Bishop of Chicago*, 440 U.S. 490, 507 (1979)).

<sup>104</sup> *See* 459 U.S. at 75-76.

<sup>105</sup> *Id.* at 78-82; *see also United States v. Riverside Bayview Homes, Inc.*, 474 U.S. 121, 128 n.5 (noting that constitutional avoidance approach followed in *Security Industrial Bank* is “sensible where it appears that there is an identifiable class of cases in which application of a statute will necessarily constitute a taking”).

<sup>106</sup> 24 F.3d 1441 (D.C. Cir. 1994).

<sup>107</sup> *Id.* at 1445 (internal quotation marks omitted).

<sup>108</sup> *Id.* at 1446-47.

monetary liability for takings, Congress cannot be presumed to have intended for the statute to apply in the proposed manner.<sup>109</sup>

These principles apply squarely here and require FDA to interpret the BPCIA to apply prospectively only. Retrospective application of the BPCIA would take property of “an identifiable class” of property owners — companies whose BLAs were approved before enactment of the BPCIA — and would expose the United States to billions of dollars of liability. Congress cannot have intended this result.

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Following this well-settled law, FDA should not accept for filing, file, approve, or discuss with any prospective applicant, or otherwise take any action whatsoever indicating that the agency will consider for approval, any application or any IND for a product, filed under section 351(k) of the PHSA that cites, as its reference product, BLA 125057 for Humira (adalimumab) or any other product for which the BLA was submitted prior to March 23, 2010, the date on which the BPCIA was signed into law. FDA should, instead, interpret the BPCIA as applying only to post-enactment reference products, thereby avoiding both significant constitutional questions and significant governmental liability.

### **C. Environmental Impact**

The actions requested herein are subject to categorical exclusion under 21 C.F.R. § 25.30 and 21 C.F.R. § 25.31.

### **D. Economic Impact**

Pursuant to 21 C.F.R. § 10.30(b), an economic impact statement will be submitted only at the request of the Commissioner.

### **E. Certification**

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

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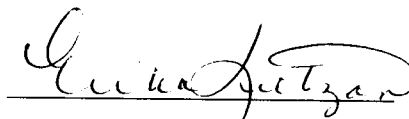
<sup>109</sup> See *Nat'l Mining Assoc. v. Kempthorne*, 512 F.3d 702, 712 (D.C. Cir. 2008) (where there is evidence that the “government would be on the hook for a ‘massive and unforeseen sum,’ paid out ... as just compensation,” constitutional avoidance is appropriate); *Bell Atl. Tel. Cos.*, 24 F.3d at 1445 (“*Chevron* deference to agency action that creates a broad class of takings claims, compensable in the Court of Claims, would allow agencies to use statutory silence or ambiguity to expose the Treasury to liability both massive and unforeseen.”).

Respectfully submitted,

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