

COVINGTON & BURLING

1201 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004-2401
TEL 202.662.6000
FAX 202.662.6291
WWW.COV.COM

WASHINGTON
NEW YORK
SAN FRANCISCO
LONDON
BRUSSELS

July 13, 2005

BY E-MAIL AND FIRST CLASS MAIL

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2004P-0171/CP & 2003P-0176/CP

Introduction and Summary

The Pharmaceutical Research and Manufacturers of America (“PhRMA”) has asked me to analyze whether use by the Food and Drug Administration (“FDA”) of previously-submitted proprietary data to approve follow-on biologics would violate the Takings Clause of the United States Constitution. I conclude that such use of proprietary data without payment of compensation would amount to an unconstitutional taking of property in violation of the Takings Clause.¹

In conducting this analysis, I have reviewed the October 21, 2004 submission of Professor John C. Yoo in this docket.² While I agree that Professor Yoo has identified some of

¹ I am a partner in the law firm of Covington & Burling and head of the firm’s Appellate and Supreme Court Practice Group. In the course of my law practice, I litigate constitutional cases and advise clients on constitutional issues, including issues arising under the Takings Clause. I have served as an Assistant to the Solicitor General of the United States and as a law clerk to Justice Lewis F. Powell, Jr., of the U.S. Supreme Court and Judge John Minor Wisdom of the U.S. Court of Appeals for the Fifth Circuit. I am an Adjunct Professor of Law at Georgetown University, a Lecturer in Law at the University of Virginia, a Fellow of the American Academy of Appellate Lawyers, and a member of the American Law Institute. In preparing this opinion, I consulted with leading experts in FDA’s regulation of biological products, including my colleague Richard F. Kingham of the law firm of Covington & Burling.

² See Letter of John C. Yoo to FDA Docket No. 2004P-0171/CP & 2003P-0176/CP (October 21, 2004).

2004P-0171

C7

Division of Dockets Management

July 13, 2005

Page 2

the pertinent Supreme Court decisions, I disagree with his constitutional analysis. In particular, Professor Yoo ignores differences between biological products and traditional small-molecule drugs that are relevant to the takings analysis. In addition, his analysis fails to take account of longstanding FDA regulations and policies that establish a reasonable, investment-backed expectation of protection for data submitted to FDA by biologics innovators. Professor Yoo also fails to recognize the strength of the constitutional argument that approval of follow-on biologics would amount to a *per se* violation of the Takings Clause.

In this submission I present the constitutional analysis in three stages: *first*, by examining the law that governs trade secrets in the context of biologics applications; *second*, by setting out the constitutional framework of takings law; and *third*, by applying the constitutional principles to the existing regulatory scheme to demonstrate that unconstitutional takings would occur if the FDA were to reverse its longstanding regulations and practices and use innovator data to approve follow-on biologics.³

Because of the unique and complex nature of biologics, any follow-on application would require the FDA to use and disclose the manufacturing methods and process information submitted by innovators in their applications for marketing approval. Such use and disclosure would constitute a taking under binding Supreme Court precedent. For over 30 years, explicit FDA regulations have prohibited the disclosure of biologic innovators' manufacturing methods and process information as trade secrets. The FDA consistently has protected this trade secret information from use and disclosure. In addition, the FDA has maintained a consistent policy against approval of follow-on biologics.

I therefore conclude that the FDA's longstanding practice of protecting innovator data in biologics applications is well-grounded. For the reasons discussed in this letter, an effort to approve follow-on biologics would result in an unconstitutional taking of property under the Fifth Amendment.

I. Biological Drugs: Scientific And Regulatory Background

The complexity of biological products as distinct from small-molecule drugs has been described in PhRMA's Scientific Comments to FDA's Docket No. 2004N-0355. *See* Attachment A (Scientific Comments) to PhRMA Submission of November 12, 2004, FDA Docket No. 2004N-0355 ("Scientific Considerations Related To Developing Follow-On Protein Products"). PhRMA's Scientific Comments also address the close relationship between a biologic's manufacturing process and its clinical attributes. *See id.*

³ The constitutional takings issue would not arise if the innovator were to authorize use or disclosure of its data in connection with approval of a follow-on biologic.

Division of Dockets Management

July 13, 2005

Page 3

In submissions to the same docket, PhRMA has described the statutory provisions governing the submission of biological license applications (“BLAs”) under section 351 of the Public Health Service Act (“PHSA”),⁴ as well as the provisions of section 505 of the Federal Food, Drug, and Cosmetic Act (“FFDCA”)⁵ under which certain biological products have been approved through the submission of new drug applications (“NDAs”). *See* Attachment B (Comments in Support of Citizen Petition Submitted By Genentech Inc. (Docket No. 2004P-0171)) to PhRMA Submission of November 12, 2004, FDA Docket No. 2004N-0355. PhRMA’s previous submissions have also detailed the close integration of manufacturing data with safety and effectiveness data in BLA and NDA submissions for biological products. *See id.*

These prior PhRMA submissions provide the regulatory and scientific background for the constitutional analysis in this submission.

II. Trade Secret Protections For Data Submitted To FDA By Biologic Innovators

A. Definition of “Trade Secret” Under State Law and FDA Regulations

1. State Law

Trade secrets are recognized and protected by state law. *See Ruckleshaus v. Monsanto*, 467 U.S. 986, 1003-04 (1984). The scope of trade secret protection is quite broad. “A trade secret may consist of any formula, pattern, device or compilation of information which is used in one’s business, and which gives him the opportunity to obtain an advantage over competitors who do not know or use it.” *Restatement (Second) of Torts* § 757 cmt. b (1977); *see also Restatement (Third) Unfair Competition* § 39 (1995) (“A trade secret is any information that can be used in the operation of a business or other enterprise that is sufficiently valuable and secret to afford an actual or potential economic advantage over others.”).

These definitions are readily applicable to the manufacturing process and method data submitted to FDA by biologic innovators under either a BLA or an NDA. For example, a federal court of appeals recently confirmed the trade secret status of manufacturing process data associated with Premarin, a conjugated estrogen product manufactured by Wyeth. *See Wyeth v. Natural Biologics, Inc.*, 395 F.3d 897, 900 (8th Cir. 2005). State-law definitions of trade secrets are also applicable to innovators’ safety and effectiveness data.⁶

⁴ *See* 42 U.S.C. §§ 201 *et seq.*

⁵ *See* 21 U.S.C. §§ 301 *et seq.*

⁶ FDA acknowledged in the 1974 preamble to its FOIA regulations that clinical data could “properly be considered” to fall within the definition of a trade secret. *See* 39 Fed. Reg. 44602, 44613 (Dec. 24, 1974) (rejecting argument that “the Restatement definition of a trade secret is (continued...)”).

Division of Dockets Management

July 13, 2005

Page 4

2. FDA Regulations

FDA regulations accord trade secret status to the innovator's manufacturing data. 21 C.F.R. §§ 601.51(f), 314.430(g).⁷ FDA has taken the position that most safety and effectiveness data submitted by biologic innovators are not trade secrets, but this determination was based solely on the fact that safety and effectiveness data submitted by biologic innovators has no economic value for competitors: "[U]nlike the situation with new drugs, no competitor can utilize [the innovator's safety and effectiveness data] to gain approval for his product." 39 Fed. Reg. 44602, 44641 (Dec. 24, 1974). As discussed below, *infra* Part II.B.3, FDA has had a longstanding policy against approval of follow-on biologics. If FDA were to change this policy, it would invalidate the agency's conclusion that biologics innovators' safety and effectiveness data have no economic value in the marketplace. Accordingly, FDA would be obliged to revisit its regulations to recognize the trade secret status of these data.

B. *FDA Law and Policy Affecting Release Of Biologic Innovators' Data*

Under the Federal Trade Secrets Act, it is a criminal offense for a U.S. government employee to disclose any trade secret or other confidential commercial information received "in

far too broad"). Subsequently, in *Public Citizen Health Research Group v. FDA*, 704 F.2d 1280 (D.C. Cir. 1983) (the "*Intraocular Lens Case*"), the D.C. Circuit held that the Restatement's broad definition should not be used to define "trade secret" for FOIA purposes, and further held that certain safety and effectiveness data related to approval of a medical device could not be withheld from disclosure under the FOIA trade secret exemption. *See* 704 F.2d at 1288-90. The holding in *Intraocular Lens* applies to an exemption under FOIA, and thus leaves open the question whether safety and effectiveness data may constitute trade secrets as defined by state law. *See id.* at 1290 n.27. Moreover, the basis on which the *Intraocular Lens* case denied trade secret status to the safety and effectiveness data at issue – namely, the lack of a "relationship" between the data and the "productive process," *see id.* at 1290 – does not apply to the safety and effectiveness data contained in a biologics application, which are closely integrated with the manufacturing data. *See* Attachment B (Comments in Support of Citizen Petition Submitted By Genentech Inc. (Docket No. 2004P-0171)) to PhRMA Submission of November 12, 2004, FDA Docket No. 2004N-0355, at 16-17.

⁷ FDA regulations define "trade secret" as any "commercially valuable plan, formula, process, or device" that is used to make, prepare, compound, or process trade commodities, and that is "the end product of either innovation or substantial effort." 21 C.F.R. § 20.61(a). *See* 39 Fed. Reg. at 44614 (FDA's definition of trade secret "is intended to serve as a general definition, and not to catalog all information that may have trade secret status"). FDA has defined "confidential commercial information" to include "valuable data or information" that is "customarily held in strict confidence" by the innovator and "not disclosed to any member of the public." *Id.* § 20.61(b).

the course of his employment or official duties.” 18 U.S.C. § 1905. Under section 301(j) of the FFDCFA, all persons are prohibited from “using to [their] own advantage, or revealing . . . any information . . . concerning any method or process which as a trade secret is entitled to protection,” or causing any of those acts. 21 U.S.C. § 331(j).

In order to give full effect to the protections embodied in the Trade Secrets Act and in FFDCFA § 301(j), FDA has implemented a policy prohibiting “any discretionary release of documents that fall within the trade secret and confidential commercial information exemption to the Freedom of Information Act.” 39 Fed. Reg. at 44612.⁸ In practice, FDA has significantly limited the release of *any* data submitted in an innovator file – including both manufacturing data and safety and effectiveness data – particularly when there is a potential that the information will be used to the advantage of a competitor.

1. Regulatory Protections For Data Submitted to FDA:
Manufacturing Data Are Trade Secrets

For over 30 years, FDA regulations have expressly provided that data regarding the innovator’s manufacturing methods or processes, whether submitted under a BLA or an NDA, constitute trade secrets and are protected from public disclosure. *See* 21 C.F.R. §§ 601.51(f), 314.430(g); *see also* 21 C.F.R. § 20.61(c) (“Data and information submitted or divulged to the [FDA] which fall within the definitions of a trade secret or commercial or financial information are not available for public disclosure.”). *See also Jerome Stevens Pharmaceuticals, Inc. v. FDA*, 402 F.3d 1249, 1254-56 (D.C. Cir. 2003) (FDA disclosure of manufacturing data in an NDA is actionable under the Federal Tort Claims Act).

Innovators’ safety and effectiveness data also are protected from disclosure during the approval process. Under the regulations governing NDAs, such information may become eligible for public disclosure after the product becomes eligible for generic competition, but disclosure is still prohibited upon a showing of “extraordinary circumstances.” *See id.* § 314.430(f). Under the BLA regulations, safety and effectiveness data are not “immediately available” to the public until the product has been approved, and even then will be protected from disclosure upon a showing of “extraordinary circumstances.” *Id.* § 601.52(e).

⁸ This interpretation was based in part on FDA’s conclusion that “the [FOIA] trade secrets exemption is at least as broad as, and is perhaps somewhat broader than, the confidentiality provisions of the other two statutes.” *See* 39 Fed. Reg. at 44612.

Division of Dockets Management

July 13, 2005

Page 6

2. FDA Has Had A Consistent Policy Against The Release Of Innovator Data Of Economic Value

As noted above, FDA's determination that BLA safety and effectiveness data did not require protection as trade secret or confidential commercial information was firmly based on the fact that such data, even if released to competitors, could never be used to support a competitor's approval and therefore had no economic value.

We are aware of only one situation – the request of Berlex Laboratories, Inc. for data contained in the BLA for the product Avonex (interferon beta-1a) submitted by Biogen, Inc. – in which a competitor has asked FDA to release the safety and effectiveness data submitted as part of an innovator's BLA. As illustrated by FDA's handling of this request, where there is any chance that release of innovator data, including safety and effectiveness data, could be used to a competitor's advantage, FDA's policy has been to limit the release of those data.

In the Avonex case, Berlex, a competitor of Biogen, sought release under FOIA of the safety and effectiveness data contained in Biogen's BLA. FDA considered this request under 21 C.F.R. § 601.52(e), which on its face would permit immediate disclosure of all safety and effectiveness data contained in the application unless "extraordinary circumstances" were shown. *See Letter From Mark Raza, Associate Chief Counsel, FDA to William C. Brashares, Counsel to Biogen, Inc. (Sept. 11, 1996) ("FDA Avonex Letter")*, at 1; 21 C.F.R. § 601.52(e).

Biogen, which had formerly shared manufacturing data with Dr. Rentschler Biotechnologie under a joint venture agreement, successfully argued to FDA that Rentschler's possession of those manufacturing data created an "extraordinary circumstance." The success of this argument turned on the competitive position of the companies involved. After ending its affiliation with Biogen, Rentschler had entered into affiliations with other competitors of Biogen, including Berlex. *See FDA Avonex Letter* at 1. Biogen argued that if Rentschler, Berlex, and/or their affiliates could combine the manufacturing data they already possessed with the clinical data from the Avonex BLA, the resulting compilation of data might be sufficient to obtain approval of a competing product, either in the U.S. or other countries. *See id.*; *see also Letter From William C. Brashares To Mark Raza (Sept. 18, 1996) (Biogen Letter On Avonex)*, at 2. Ultimately, FDA did allow some disclosure, but not of the entire safety and effectiveness section of the BLA. Instead, FDA agreed to disclose one pharmacokinetic study and two portions of Biogen's summary of safety data. *See FDA Avonex Letter* at 2. In addition, Biogen was invited to further limit these disclosures by demonstrating the extent to which "Berlex, Rentschler, or their affiliate could use [this] information to obtain approval of their own interferon-beta product in the United States or in specific foreign markets." *See id.*

FDA's broad interpretation of the "extraordinary circumstances" standard in this case reflects the agency's view that data contained in a BLA, even if technically not accorded the status of trade secret, or even of confidential commercial information, should not be released where it may be of use to competitors.

3. FDA Has Had A Consistent Policy Against The Approval of Follow-On Biologics

The legal and policy protections afforded innovator data, as described above, are integral to FDA's well-established policy against the approval of follow-on biologics.

In 1974, FDA recognized that unlike non-biologic drug products, "all biological products are required to undergo clinical testing in order to demonstrate safety, purity, potency, and effectiveness" prior to market approval, "regardless whether other versions of the same product are already marketed." *See* 39 Fed. Reg. at 44641.⁹ Given the inherent differences in manufacturing process between different manufacturers, each biologic "must be separately proved safe, pure, potent, and effective," and approval can "under no circumstances" be "granted . . . to a second manufacturer based upon published or otherwise publicly available data and information on another manufacturer's version of the same product." In other words, as the FDA stated in no uncertain terms, "there is no such thing as a 'me-too' biologic." *Id.*

FDA consistently has maintained and reiterated its policy against the approval of follow-on biologics. In June 1998, for example, Dr. David Finbloom of FDA's Center for Biologics Evaluation and Review ("CBER") stated that the agency's comparability guidelines (the criteria that must be met when biologics manufacturers make changes to their products) can only be used to compare pre- and post-change versions of *one* manufacturer's product. *See* Transcript, *Meeting of the FDA Advisory Committee for Pharmaceutical Science* (June 24, 1998) at 124-25. This is because, in FDA's view, comparability can only be established "within the same product based upon the same process with a history regarding the manufacturing operation of that particular product," as opposed to a comparison of one product with "another product with an unknown process." *Id.* at 125. Dr. Finbloom cited "the introduction to the FOIA [regulations] that there's no such thing as a 'me-too' biologic," stating that "[a]t CBER we are under regulations that say we have no generic drugs right now, and if we're going to have generic drugs, then something will have to be done to get us to that point." *Id.* Later the same year, then-FDA Commissioner Jane Henney stated that "[by] its terms, section 505(j) does not apply to biological drugs . . . FDA has no plans to allow submissions of abbreviated applications for biological products." *See* The Pink Sheet, *Henney FDA Will Be "Open, Timely and Responsive," Nominee Says* (August 31, 1998).

⁹ These statements, contained in the preamble to FDA's final regulations governing disclosure of information under the Freedom of Information Act, were made shortly after jurisdiction over the PHSA was transferred to FDA. *See* 39 Fed. Reg. 44602.

In recent remarks to the investment community, Dr. Steven Galson, Acting Director of FDA's Center for Drug Evaluation and Review ("CDER"), stated that in the review of biologics applications, "the information referenced [by FDA] must be in the public domain. FDA does not have the legal authority to reference information in an innovator company's BLA submission." See *The Pink Sheet, Transcript of Remarks of Dr. Steven Galson, FDA to Schwab Soundview Washington Research Group May 5, 2004* (May 10, 2004), at 1;¹⁰ see also Dickinson's FDA Review, *McClellan Outlines 'Generic' Biologics Proposal* (Mar. 2004) (reporting statement of outgoing FDA Commissioner Mark McClellan to the Generic Pharmaceuticals Association that "the agency still believes that the current law does not generally permit generic biologics").

In short, for more than 30 years the FDA has had: (i) explicit regulations preventing the public disclosure of trade secret information concerning a manufacturer's methods and processes; (ii) a restrictive practice with respect to the disclosure of any data from a biologic innovator's file, including safety and effectiveness data; and (iii) a policy of not approving or seeking to approve follow-on biologics.

III. Legal Principles

A. Summary of Takings Law

The Takings Clause provides: "[N]or shall private property be taken for public use, without just compensation." U.S. Const. amend. V. There are two basic categories of takings: *per se* takings and regulatory takings. The related doctrine of unconstitutional conditions applies when the government seeks to force a property holder to forfeit his right to receive just compensation in exchange for a discretionary benefit that has little or no relationship to the property taken.

1. Categories of Takings

a) *Per Se* Takings

A *per se* or "physical" taking occurs when the government permanently dispossesses a private individual or entity of property or requires the property holder to surrender an exclusive

¹⁰ Dr. Galson also stated that "[d]ue to scientific limitations on the concept of sameness [as set forth in FFDCa section 505(j) and related provisions on generic drugs], we cannot apply [those provisions] to protein molecules. This is because of the complexity of the protein molecule." See *The Pink Sheet, Transcript of Remarks of Dr. Steven Galson, FDA to Schwab Soundview Washington Research Group May 5, 2004* (May 10, 2004), at 3.

Division of Dockets Management

July 13, 2005

Page 9

right of possession.¹¹ See, e.g., *Kaiser Aetna v. United States*, 444 U.S. 164, 179-80 (1979); *Loretto v. Teleprompter Manhattan CATV Corp.*, 458 U.S. 419, 433 (1982). Thus, for example, the United States was required to compensate private marina owners for imposing a requirement that a marina on a navigable waterway be open to public use. *Kaiser Aetna*, 444 U.S. at 179-80. Similarly, the State of New York was required to compensate landlords when it required them to allow cable companies access to the landlords' apartment buildings to install cable television equipment, even though the "invasion" of the landlords' property rights was "minor." *Loretto*, 458 U.S. at 421, 435-37.¹²

b) Regulatory Takings

In contrast to a *per se* taking, a "regulatory taking" occurs when the government's action restricts the property holder's right to use, develop, or alienate the property in question, but does not directly dispossess the property owner or force the owner to share the property with others. In these circumstances, an "ad hoc, factual" test balancing the factors identified by the Court in *Penn Central Transportation Co. v. City of New York*, 438 U.S. 104, 124 (1978) determines whether just compensation is required. These factors are: (1) whether the government action interferes "with the reasonable investment-backed expectation" of the property owner; (2) the economic impact of the government action on the property holder; and (3) the character of the governmental action. *Id.*¹³

¹¹ A *per se* taking is sometimes referred to as a "physical taking," but the property involved may be tangible or intangible. See, e.g., *Nixon v. United States*, 978 F.2d 1269, 1284-85 (D.C. Cir. 1992) ("The Government argues that the *per se* takings doctrine applies only to the physical occupation of *real* property. This argument fails for want of authority or logic.")

¹² The Takings Clause applies to actions of the States through the Fourteenth Amendment. See, e.g., *Webb's Fabulous Pharmacies, Inc. v. Beckwith*, 449 U.S. 155, 159 (1980).

It has long been settled that the government may not take property from private party A solely for the purpose of transferring it to private party B, even if the government pays compensation to A. See *Calder v. Bull*, 3 Dall. 386, 388 (1798). If the FDA were to use or disclose an innovator's trade secrets to approve a follow-on biologic, the "most direct beneficiar[y]" would be a private party, namely the follow-on applicant. See *Monsanto*, 467 U.S. at 1014. For purposes of this analysis, I nevertheless assume that a taking of the innovator's trade secrets would satisfy the "public purpose" requirement of the Takings Clause. See *id.* at 1015; *Kelo v. City of New London*, No. 04-108, 2005 WL 1469529 (U.S. June 23, 2005) (discussing "public use" requirement) see also *id.* (concurring opinion of Justice Kennedy) (same).

¹³ The *Penn Central* balancing test embodies Justice Holmes's famous statement in *Pennsylvania Coal Co. v. Mahon*, that "[t]he general rule at least is that while property may be (continued...)

COVINGTON & BURLING

Division of Dockets Management

July 13, 2005

Page 10

The categories of regulatory and *per se* takings converge when the government action does not formally divest the owner of property, but instead leaves the owner with no viable use of the property in question. See *Lucas v. South Carolina Coastal Council*, 505 U.S. 1003, 1019 (1992); *Lingle v. Chevron U.S.A., Inc.*, 125 S.Ct. 2074, 2081 (2005). Thus, in *Lucas*, the Court found that a *per se* taking occurred when a State environmental law banning development on beachfront property effectively prohibited the property holder from making any use of his beachfront lots. See *id.* In so holding, the Court did not apply the *Penn Central* factors, instead determining that, upon a showing of complete deprivation of value, a taking existed that required just compensation, even though the government action did not formally expropriate the property or deny him the right of exclusive use.

c) Unconstitutional Conditions

Under the doctrine of unconstitutional conditions, “the government may not require a person to give up [his] constitutional right ... to receive just compensation when property is taken for a public use ... in exchange for a discretionary benefit conferred by the government where the benefit sought has little or no relationship to the property.” *Dolan v. City of Tigard*, 512 U.S. 374, 385 (1994). In *Dolan*, the Court held that a municipality could not condition approval of an owner’s application for a permit to double the size of her store on the owner’s dedication of all of her property that fell within a floodplain as a public “Greenway” and her provision of a public pedestrian/bicycle pathway. See *id.* at 387-88; see also *Nollan v. Calif. Coastal Comm’n*, 483 U.S. 825, 828 (1987) (city attempted to condition approval of permit to demolish bungalow and replace it with a three-bedroom house on the owner granting the city a lateral public easement across the lot). Under the unconstitutional conditions doctrine, the court must conduct two inquiries. First, it determines whether there is an “essential nexus” between the “legitimate state interest” the government purports to act under and the regulatory condition sought to be imposed on the property holder. See *Nollan*, 483 U.S. at 838 (purported state interest in providing “visual access” to the beach was not connected to condition that owner provide a lateral easement across his property). If the nexus exists, the court then determines whether the “degree of the exactions demanded” by the government is in “rough proportionality” with the property owner’s request for approval. *Dolan*, 512 U.S. at 388, 391. The conditions in *Dolan* failed this second prong of the analysis.

2. Property Subject to Takings Analysis

The Takings Clause, and the related unconstitutional conditions doctrine, apply to both tangible and intangible property. See *Monsanto v. Ruckelshaus*, 467 U.S. 986, 1003 (1984) (citing *Armstrong v. United States*, 364 U.S. 40, 44, 46, 80 (1960); *Louisville Joint Stock Land*

regulated to a certain extent, if regulation goes too far it will be recognized as a taking.” 260 U.S. 393, 415 (1922).

Bank v. Radford, 295 U.S. 555, 596-602 (1935); *Lynch v. United States*, 292 U.S. 571, 579 (1934)). The Court has not set out a comprehensive list of the types of intangible property protected by the Takings Clause, but it has expressly stated “[t]hat intangible property rights protected by state law are deserving of the protection of the Taking Clause.” *Monsanto*, 467 U.S. at 1003.

3. Trade Secrets and Other Intellectual Property

a) *Monsanto*

The leading decision applying Takings Clause jurisprudence to trade secrets is *Monsanto*. That case dealt with the Environmental Protection Agency (“EPA”)’s use of health, safety and environmental data that Monsanto had submitted to the EPA and the predecessor regulator, the Department of Agriculture, as part of the process required in order to register and receive approval to sell these products to the public. *See* 467 U.S. at 997-99. The Federal Insecticide, Fungicide, and Rodenticide Act (“FIFRA”), 7 U.S.C. §§ 136 *et seq.* governed these agencies’ use of this data. The Court considered three different regulatory frameworks under FIFRA:

- Prior to 1972, the FIFRA did not state whether the agency could disclose health and safety information; there was a prohibition on the disclosure of “any information relative to formulas of products.” *See Monsanto*, 467 U.S. at 991. The record contained conflicting evidence regarding the Department’s practices with respect to health and safety information. *Compare id.*, at 991 n.3 (EPA Administrator stated that “as a matter of practice, the Department of Agriculture did not disclose the health and safety information”) *with id.*, at 1010 n.14 (faulting district court’s finding that the Department did not disclose this information as a matter of practice, and noting that Congressional testimony indicated that “[s]uch information has, as a matter of practice ... been considered by the [agency] to support the registration of the same or a similar product by another registrant.”).
- From 1972 to 1978, the FIFRA contained a provision allowing a registrant to designate portions of its submitted material as “trade secrets or commercial or financial information,” in which case disclosure was prohibited. *See id.* at 992. In addition, these amendments permitted the EPA to consider data submitted by one applicant in reviewing the registration application of another, but only when the later applicant offered to compensate the original submitter. *See id.* at 992-93. The “trade secret or commercial or financial information,” however, could only be used in a follow-on application if the original submitter consented to such use. *See id.* at 993.
- After 1978, the framework changed again. FIFRA now provided for a 10-year period of exclusive use for data on new active pesticide ingredients, coupled with a 15-year period during which all other data could be cited and considered in support of a follow-on application, provided the follow-on applicant offered to compensate the initial submitter. *See id.* at 994. To aid in this process, the FIFRA provided for the initiation of binding arbitration

Division of Dockets Management
July 13, 2005
Page 12

between the original and follow-on applicant to determine the proper amount of compensation. *See id.* at 994-95.

Monsanto, a leading pesticide manufacturer, sought to enjoin enforcement of the FIFRA amendments on the ground that the use of its confidential safety and effectiveness data without its consent constituted a taking. The Court first held, as a general matter, that the Takings Clause protects trade secret property rights. *See id.* at 1001-03. In so holding, the Court observed that: (i) trade secrets, like other forms of property, are assignable, can form the res of a trust, and pass to the trustee in bankruptcy; (ii) the legislative history of FIFRA indicated a congressional acknowledgment of the “proprietary interest” applicants had in their data; and (iii) the Court had previously applied the Takings Clause to other forms of intangible interests. *See id.* at 1002-03.

The Court then applied the *Penn Central* factors to determine whether Monsanto had suffered a taking requiring just compensation. The Court found that it could resolve the issue solely on the basis of the “reasonable investment-backed expectations” factor, *id.* at 1005, and determined that Monsanto had demonstrated a valid takings claim for information submitted to the EPA between 1972 and 1978, but not for the other two time periods.

The post-1978 analysis was rather straightforward: FIFRA explicitly stated that such information would be made available after the 10-year period of exclusivity expired. *See id.* at 1006-07. Because the statute put Monsanto on notice that its data could eventually be shared with other pesticide manufacturers, Monsanto could “hardly argue that its reasonable investment-backed expectations are disturbed when EPA acts to use or disclose the data in a manner that was authorized by law *at the time of submission.*” *Id.* at 1007 (emphasis added).¹⁴

The Court then analyzed the pre-1972 regime and concluded that, during this time period, the FIFRA statute was silent regarding public disclosure of submitted information. *See id.* at 1008. The Court rejected Monsanto’s argument that this silence, coupled with the Trade Secrets Act, 18 U.S.C. § 1905, created the requisite reasonable, investment-backed expectation because “[i]n an industry that long has been the focus of great public concern and significant government regulation, the possibility was substantial that the Federal Government, *which had thus far taken no position on disclosure of ... data ...* would find disclosure to be in the public interest.” *Id.* at 1008-09 (emphasis added). The Court further noted that “there is some 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” during this time period. *Id.* at 1009.

¹⁴ The Court rejected Monsanto’s argument that the FIFRA imposed an unconstitutional condition on the right to the valuable government benefit of pesticide registration on the ground that FIFRA was “rationally related to a legitimate government interest,” a less demanding analysis than the “rough proportionality” test subsequently applied in *Dolan*.

Turning last to the 1972-1978 regime, the Court held that Monsanto could establish that takings occurred with respect to data submitted to EPA during this time period. *See id.* at 1011-13. Observing that FIFRA “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” that constituted a trade secret, the Court found that Monsanto had a reasonable, investment-backed expectation “with respect to its control over the use and dissemination of the data it had submitted.” *Id.* at 1011. The Court then rejected EPA’s argument that the regulatory framework preempted any intellectual property interest that Monsanto may have had in the information prior to submission, observing that EPA “by *ipse dixit* may not transform private property into public property without compensation.” *Id.* at 1012 (quoting *Webb’s Fabulous Pharmacies, Inc. v. Beckwith*, 449 U.S. 155, 164 (1980)).

b) Subsequent Lower Court Decisions

The Supreme Court has not revisited takings of intangible property since *Monsanto*, but several post-*Monsanto* lower court decisions have dealt with the issue.

In *Phillip Morris, Inc. v. Reilly*, 312 F.3d 24 (1st Cir. 2002) (en banc), the First Circuit held that a Massachusetts statute requiring tobacco companies to provide the ingredient lists of their tobacco products – which are trade secrets – as a condition for sale of those products violated the Takings Clause. The three judges who wrote opinions in the case all agreed that the State law would effect a taking if Massachusetts were to disclose the information to the public. *See id.* at 45-46; *id.* at 50-51 (Selya, J., concurring); *id.* at 52-53 (Lipez, J., dissenting).¹⁵ Writing for the court, Judge Torruella applied the *Penn Central* factors to determine that there was a taking; he also held that the law imposed an unconstitutional condition because the condition sought to be extracted (disclosure of trade secrets) was not in proportion to the offered government benefit – in effect, the right to continue selling one’s legal products. *See id.* at 46-47. Judge Selya agreed with the Takings Clause analysis, and also emphasized that, pursuant to *Monsanto*, the tobacco companies need only establish a reasonable, investment-backed expectation to make their case. *See id.* at 48-49 (Selya, J., concurring).

Judge Selya concluded that “*per se* takings analysis warrants very serious consideration in regard to the expropriation of trade secrets.” *Id.* at 51 (Selya, J., concurring). He observed that:

[T]he value of trade secrets, like the value of land, is inextricably tied to both the demand of others for access and the legal

¹⁵ Judge Lipez dissented on the ground that it was improper to invalidate the law on a facial challenge because it was not clear to him that Massachusetts would publicly disclose the information, or to what extent disclosure would take place.

Division of Dockets Management

July 13, 2005

Page 14

enforceability of the owner's right to exclude. In either case, if the right to exclude is diminished, the value decreases. And in either case, if the sovereign effectively deprives the owner of the right to exclude, the value is destroyed – and the Constitution requires just compensation.

Id. (Selya, J., concurring). Judge Selya also observed that the Court's analysis of trade secrets takings in *Monsanto* "mirror[ed] a *per se* takings analysis" because the Court there determined that *any* taking of a trade secret supported by a reasonable investment-backed expectation without just compensation would be unconstitutional. *Id.* at 51 n.26 (Selya, J., concurring); *see also id.* at 35 & n.8 (Toruella, J.) (observing that "[t]he decision in and reasoning behind *Lucas* certainly raise some interesting questions about" whether the Massachusetts statute constituted a *per se* taking of the tobacco companies' trade secrets). Although Judge Selya concurred in the decision to invalidate the Massachusetts law on the basis of a regulatory takings analysis, he indicated that *per se* treatment of trade secrets takings would be appropriate in future cases:

Limiting *per se* takings analysis to cases involving real property is a crude boundary with no compelling basis in the law. We should not be hesitant to take the next logical step when justice demands it.

Id. at 51 (Selya, J., concurring).

In *Lariscey v. United States*, the Federal Circuit held that a federal prisoner had a valid takings claim entitling him to just compensation for the forced disclosure of a trade secret. 949 F.2d 1137, 1143 (Fed. Cir. 1991), *reh'g granted*, 862 F.2d 1047 (Fed. Cir. 1992), *aff'd by an equally divided court*, 981 F.2d 1244 (Fed. Cir. 1992). While working on a Federal Prison Industries (UNICOR) project, the prisoner developed a jig and cutting device and process to cut Kevlar, a material used in helmets. *See id.* at 1139. Although the prisoner revealed this device to prison officials when asked to do so, the court found that he did not forgo his property right to his invention, and determined that he was entitled to just compensation for the taking that occurred when UNICOR reproduced the device design as its own. *See id.* at 1143-44. The court did not engage in a *Penn Central* analysis, apparently concluding that the forced disclosure of his trade secret was a *per se* taking. *See id.*

In *Tri-Bio Laboratories, Inc. v. United States*, 836 F.2d 135 (3d Cir. 1988), the Third Circuit upheld FDA's refusal to use a "pioneer" drug manufacturer's data in conjunction with a generic manufacturer's application for an animal drug. The generic manufacturer brought an Administrative Procedure Act ("APA") action after the FDA denied its application, which sought to utilize data submitted by the pioneer. *See id.* at 137. The court held that the FDA properly refused to use the original data because doing so would have constituted a taking of the pioneer's proprietary information. *See id.* at 141. The court observed that an FDA regulation providing that "any reference to information furnished by a person other than the applicant may not be

considered” in follow-on applications unless authorized in writing by the original applicant created the reasonable, investment-backed expectation necessary to support a takings claim, even though the expectation was based on an agency regulation, and not a statute. *See id.* at 141. The court also observed that “[w]e find nothing in the Act evidencing any intent to have the government compensate the pioneer registrant for the use of its data to review a ‘me-too’ application. Such a procedure would amount to a virtual government subsidy of the generic animal drug manufacturers.” *Id.*

B. Related Principles Governing Judicial Review of Agency Action

As *Tri-Bio Laboratories* implies, general principles guiding judicial review of agency action also come into play when the agency acts (or proposes to act) in a manner that may open the government to Takings Clause liability in the form of just compensation obligations. As the D.C. Circuit has held that, “[w]ithin the bounds of fair interpretation, statutes will be construed to defeat administrative orders that raise substantial constitutional questions.” *Bell Atlantic Tel. Cos. v. FCC*, 24 F.3d 1441, 1445 (D.C. Cir. 1994). Consequently, when an agency acts in a manner that may expose the government to Takings Clause liability, it is more likely that a court will hold that the agency has exceeded the authority delegated to it by Congress. *Id.* In addition, because the general issue in an agency action case is whether the agency is acting in accordance with its statutory grant of authority, agencies are not entitled to *Chevron* deference when they act in a manner that would “create a broad class of takings claims.” *Id.* *See generally* 5 U.S.C. § 706(2)(A) (federal courts shall “hold unlawful and set aside agency action” that is “arbitrary, capricious, or otherwise not in accordance with law”); *Jones v. United States*, 529 U.S. 848, 857 (2000); *Motion Picture Ass’n of Am. v. FCC*, 309 F.3d 796, 805 (D.C. Cir. 2002). Relatedly, “[c]ourts are generally deferential to longstanding policies or statutory interpretations of an agency, and they closely examine recent departures from such agency precedent.” *AFL-CIO v. Brock*, 835 F.2d 912, 917 (D.C. Cir. 1987) (citing *NLRB v. Bell Aerospace Co.*, 416 U.S. 267, 274-75 (1974)). An agency is subject to “hard look” judicial review when it reverses course on longstanding policies, procedures, and interpretations of statutory mandates.

IV. FDA Use Of Innovator Data To Approve A Follow-On Biologic Would Constitute A Taking

A. FDA Could Not Review The Follow-On Without Accessing The Innovator’s Manufacturing Data

Any attempt by FDA to approve a follow-on biologic inevitably would require a comparison of the innovator product and the follow-on. The goal of this comparison would be to establish that the follow-on product is the same as the innovator’s. As set forth in previous PhRMA submissions to FDA, under the current state of science and technology, few if any follow-on biologics could be determined to be the “same as” the innovator product. *See* Attachment B (Comments in Support of Citizen Petition Submitted By Genentech Inc. (Docket No. 2004P-0171)) to PhRMA Submission of November 12, 2004, FDA Docket No. 2004N-

Division of Dockets Management

July 13, 2005

Page 16

0355, at 10. If FDA reviewers were to undertake such a comparison, however, it could not be based solely on the innovator's safety and effectiveness data. Due to the close relationship between a biologic's manufacturing process and its clinical attributes, the safety and effectiveness data submitted with an innovator product cannot be meaningfully relied upon without reference to the innovator's manufacturing data.

This relationship is illustrated by the circumstances surrounding Berlex's request for release of safety and effectiveness data from the Avonex file, discussed above in Part II.B.3. In that case, the biologic innovator's safety and effectiveness data would have been useful to the competitor's evaluation of a follow-on *only* because the competitor *already* possessed the data concerning the manufacturing process and procedures due to disclosure of that information in the context of an earlier business venture. FDA accordingly limited the disclosure of the safety and effectiveness data because without these limitations, the release of safety and effectiveness data would have provided the competitor with a shortcut to BLA approval.

An analogous situation would exist if FDA undertook to evaluate a follow-on biologic: review of the follow-on product would require reference to the manufacturing data in the innovator's file, which is trade secret. As explained below, reference to these data would constitute a taking.

B. Use Of The Innovator's Manufacturing Data To Approve A Competitor Would Constitute A Taking

Under the principles developed in *Penn Central* and *Monsanto*, FDA's referencing of innovator data to approve follow-on biologics would be a taking. As noted above, FDA could not meaningfully evaluate a follow-on product without accessing the manufacturing data in the innovator's file. Such data, whether submitted under a BLA or an NDA, are trade secrets. See 21 C.F.R. §§ 601.51(f), 314.430(g). Trade secrets are subject to the full protection of the Takings Clause. See *Monsanto*, 467 U.S. 986, 1003.

All biologic innovators, regardless of whether they filed a BLA or an NDA, have a reasonable, investment-backed expectation that FDA will not disclose or use their trade secret data to support marketing approval of a competing product, for at least three reasons.

- *First*, FDA regulations explicitly protect innovators' trade secret data. See 21 C.F.R. 20.61(c); *id.* § 314.430(g)(1); *id.* § 601.51(f); *see also* 21 U.S.C. § 331(j) (proscribing FDA disclosure of trade secrets);
- *Second*, since its 1974 statement that "[t]here is no such thing as a 'me-too' biologic," 39 Fed. Reg. at 44641, FDA consistently has maintained a policy on biologics approvals that excludes follow-on products, recognizing that it does not have statutory authority to effect such approvals. Relatedly, Congress has not created any sort of abbreviated process for the approval of biologics under the PHS Act;

Division of Dockets Management

July 13, 2005

Page 17

- *Third*, FDA has maintained a consistent policy against the disclosure of any data in a biologic innovator's file when there is a possibility that that data will be used by competing companies to obtain approval for follow-ons.

These FDA regulations and policies clearly support innovators' reasonable, investment-backed expectation that trade secret data submitted to FDA would not be used in follow-on approvals. Biologic innovators have relied on these regulations and policies in submitting their data to FDA, and their reliance has been justified and reasonable. Accordingly, unlike the pesticide companies that submitted data to EPA under the post-1978 regime in *Monsanto*, biologic innovators whose marketing approvals are currently on file at FDA had a reasonable, investment-backed expectation of non-disclosure "at the time of submission." See *Monsanto* at 1007 (emphasis added).

Moreover, unlike the pre-1972 FIFRA regime analyzed in *Monsanto*, the FDA has taken a clear position *against* the disclosure of manufacturing methods and process data. *Id.* at 1008-09. There is no dispute here, as there was in *Monsanto*, over whether "as a matter of practice," FDA would consider individual companies' data in the review of subsequent registrations. See *id.* at 991 n.3; 1010 n.14. FDA has expressly stated on multiple occasions that it would *not* do so.¹⁶

These FDA policies constitute an "explicit assurance" to innovators that their trade secret data will not be used or disclosed for any purpose inconsistent with the innovator's original submission. *Monsanto*, 467 U.S. at 1011. By refusing to approve follow-on products – and by publicly declaring the agency's lack of authority to reference proprietary data in innovator files – FDA has "guaranteed" to biologic innovators "an extensive measure of confidentiality and exclusive use" that "form[s] the basis of a reasonable investment-backed expectation." *Id.*¹⁷ As has been recognized in the lower courts, reasonable investment-backed expectations can be

¹⁶ In response to questions received from the Senate Judiciary Committee following a hearing in June 2004, FDA suggested that review staff are permitted to review manufacturing specifications in one application before providing comments on another manufacturer's specifications. See *The Law Of Biologic Medicine, 2004: Hearing Before The Senate Comm. on the Judiciary*, 108th Cong., 2d Sess. at 65-66 (June 23, 2004). For the reasons explained in Part II of this submission, such review is expressly prohibited by law. The data contained in innovator marketing applications are subject to protection as trade secrets and confidential commercial information.

¹⁷ In contrast to the EPA under pre-1972 FIFRA, and as detailed in Part II.B.3 of this paper, FDA clearly and consistently has "taken a position" against the approval of "'me-too' biologics." 39 Fed. Reg. 44602, 44641.

COVINGTON & BURLING

Division of Dockets Management
July 13, 2005
Page 18

supported by an agency's interpretation of the law rather than by the explicit language of the governing statute. *See Tri-Bio Labs.*, 836 F.2d 135, 141.¹⁸

While the other *Penn Central* factors may not even be relevant given the Court's treatment of the investment-backed expectation factor as dispositive in *Monsanto*, it bears mention that any FDA reference to innovator applications to approve follow-ons would have a very significant detrimental economic impact upon the original innovator. The commercial value of a biologic innovator's manufacturing data resides in the fact that these data can be used by FDA *solely* to support marketing approval of the innovator's project.

Indeed, there is a strong argument that a follow-on approval process would amount to a *per se* taking, as the First Circuit observed in *Reilly*, and as the Federal Circuit assumed in *Lariscey*. As the Supreme Court noted in *Monsanto*, "With respect to a trade secret, the right to exclude others is central to the very definition of the property interest. Once the data that constitute a trade secret are disclosed to others, or others are allowed to use those data, the holder of the trade secret *has lost his property interest* in the data." *Id.* at 1011 (emphasis added). *See also Lucas*, 505 U.S. at 1015 (regulatory action that denies "all economically beneficial or productive use" of property is a *per se* taking that is "compensable without case-specific inquiry into the public interest advanced in support of the restraint"). As Judge Selya explained in his concurrence in *Reilly*, disclosure of a trade secret effectively destroys that form of property: a disclosed secret is a secret no longer. *See* 312 F.3d at 50-51 (Selya, J., concurring). Accordingly, a court analyzing FDA use of data to approve a follow-on biologic likely would "take the next logical step" and declare that disclosure (and hence, destruction) of the innovator's trade secret constitutes a *per se* taking. *Id.* at 51 (Selya, J., concurring).

Relatedly, any use of innovator data for future follow-on approval would pose serious issues under the unconstitutional conditions doctrine with respect to whether the government can justifiably compel disclosure of trade secrets as the price of doing business in a regulated

¹⁸ In his submission, Professor Yoo asserts that biologic innovators can entertain no reasonable investment-backed expectation that their data will be protected because the "relevant" statute – in his view, the FFDCA – is "silent" as to the use of innovator data to approve follow-on applications, and because FFDCA § 301(j) does not contain a "clear prohibition" on such use of innovator data. *See* Letter of John C. Yoo to FDA Docket No. 2004P-0171/CP & 2003P-0176/CP (October 21, 2004), at 8-10. Professor Yoo's argument fails to take account of the FDA policies and regulations described in this submission, which under the reasoning of *Tri-Bio* are fully sufficient to support reasonable investment-backed expectations. *See Tri-Bio Labs.*, 836 F.2d at 141. In particular, FDA regulations explicitly protect trade secret data submitted by innovators. *See* 21 C.F.R. §§ 601.51(f), 314.430(g). Professor Yoo's analysis also ignores the Court's discussion in *Monsanto* of the likely *lack* of any actual agency policy or practice of non-disclosure in the pre-1972 timeframe. *See Monsanto*, 467 U.S. at 1010 & n.14.

industry. This holds true with respect to both biologics manufacturing and process data *and* safety and effectiveness data, which, though meeting the definition of a trade secret under state law, are treated differently by the FDA disclosure regulations because of FDA's longstanding practice of *not* approving follow-on biologics.

In his submission to this docket, Professor Yoo contends that FDA use of innovator data to approve a follow-on biologic would not involve public disclosure of that information, but would instead constitute a permissible "intra-agency disclosure." *See* Letter of John C. Yoo to FDA Docket No. 2004P-0171/CP & 2003P-0176/CP (October 21, 2004), at 9-11 (*citing* FFDC § 301(j)). For purposes of a Takings Clause analysis, however, the economic harm caused by internal use of the secret to benefit a competitor is just as severe as publication of the data in the Federal Register. *See Monsanto*, 467 U.S. at 1012 (economic value of the property right "lies in the competitive advantage over others that [the originator] enjoys by virtue of its exclusive access to the data, and disclosure or use by others of the data would destroy that competitive edge"). Indeed, in *Monsanto*, the Supreme Court noted that Monsanto was given "explicit assurance that EPA was prohibited from disclosing publicly, *or considering in connection with the application of another*, any data submitted by an applicant" that constituted a trade secret, the Court found that Monsanto had a reasonable, investment-backed expectation "with respect to its control over the use and dissemination of the data it had submitted." *Id.* at 1011 (emphasis added).

C. *Use of the Innovator's Data Would Raise Additional Administrative Law Concerns*

When an agency's interpretation of a statute gives rise to a takings claim, that interpretation is not entitled to *Chevron* deference, and a court is more likely to conclude that the agency has exceeded the scope of its delegated authority. *See Bell Atlantic*, 24 F.3d at 1445 ("Chevron deference to agency action that creates a broad class of takings claims . . . would allow agencies to use statutory silence or ambiguity to expose the Treasury to liability both massive and unforeseen."). In addition, the decision to approve follow-on biologics would reverse FDA's 30-year policy against such approvals, a reversal that would be subject to close scrutiny under the Administrative Procedure Act as an abuse of discretion. *See Atchison, Topeka & Santa Fe Ry. v. Wichita Bd. of Trade*, 412 U.S. 800, 808 (1973).

* * * *

COVINGTON & BURLING

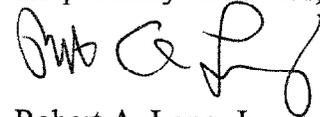
Division of Dockets Management

July 13, 2005

Page 20

In conclusion, the FDA's longstanding practice of protecting innovator data in biologics applications and its regulations on the subject are well-grounded. For the reasons discussed in this letter, an effort to approve follow-on biologics would result in an unconstitutional taking of property under the Fifth Amendment.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "R. A. Long, Jr.", written in a cursive style.

Robert A. Long, Jr.