

TAKING BIOLOGICS FOR GRANTED? TAKINGS, TRADE SECRETS, AND OFF-PATENT BIOLOGICAL PRODUCTS

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ABSTRACT

Biologics are complex medicines which are often genetically engineered, and which are sure to play an important role in curing some of humankind's worst diseases. Not surprisingly, generic companies want a part of the biologic market. The FDA believes that it has the authority to approve off-patent versions of biologics that were originally regulated under the Food, Drug & Cosmetic Act, but in order to effectively do so the FDA would have to rely on findings based on data produced by the brand name companies. This iBrief examines whether the FDA's reliance on previous findings would give rise to a valid claim under the Takings Clause of the U.S. Constitution. In the end, it concludes that the FDA's proposed action likely would not constitute a taking.

INTRODUCTION

¶1 Many of the most promising advances in medicine belong to a class of compounds called biologics. Biologics are complex, large molecules that are often created by recombinant DNA technology.² One prominent example of a biologic is Amgen's Epogen®, a genetically engineered form of erythropoietin which combats anemia by stimulating the production of red blood cells.³ Sales of Epogen® during the second quarter of 2004 topped \$633 million.⁴ Indeed, the total market for biologics in 2003 has been estimated at \$30 billion and is projected to reach \$60 billion by 2010.⁵

¶2 The research and development costs associated with biologics are high because biologics are structurally complex and difficult to

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² *The Law of Biologic Medicine: Hearing Before the Subcomm. on the Judiciary, 108th Cong. 1* (2004) [hereinafter *Hearing*] (statement of Sen. Orrin Hatch, Chairman, Subcomm. on the Judiciary).

³ PHYSICIANS DESK REFERENCE 581 (2004) (Epogen® prescribing information).

⁴ *Biotech Firm Reports Adjusted Earnings Increased 27%*, DRUG WEEK, Aug. 27, 2004, at 264.

⁵ See *Hearing*, *supra* note 2, at 1 (statement of Sen. Orrin Hatch).

manufacture.⁶ One industry leader, Genentech, estimated that it has invested \$6.4 billion in research over the last 28 years.⁷ Amgen, in one year alone, spent \$1.7 billion on research.⁸ These high costs are then passed on to consumers, who often foot bills for biologic treatments ranging anywhere from \$10,000 to \$25,000 a year.⁹ In some rare cases, costs can exceed \$170,000 per year.¹⁰

¶3 However, consumers may see reduced costs for biologic treatments once many of the key biologic patents expire. Indeed, many of these key patents are approaching expiry.¹¹ In the past, one important way that Congress has successfully lowered prices for consumers is through encouraging generic competition.¹² The Drug Price Competition and Patent Term Restoration Act of 1984,¹³ which is generally known as the Hatch-Waxman Act, amended the Food, Drug and Cosmetic Act (FDCA).¹⁴ The Hatch-Waxman Act encouraged market entry of generic drugs by establishing an abbreviated pathway for generic approval. By most accounts, the Hatch-Waxman Act has been successful at walking the fine line between encouraging generic competition and respecting the intellectual property rights of brand-name innovators.¹⁵

⁶ *Id.* at 5 (statement of Sen. Patrick Leahy, member, Subcomm. on the Judiciary).

⁷ *Citizens Petition Regarding Standard of "Similarity" or "Sameness" of Biotechnology-Derived Products*, 3 (2004p-0171, Apr. 8, 2004) [hereinafter *Citizen's Petition*] available at <http://www.fda.gov/ohrms/dockets/dailys/04/apr04/040904/04p-0171-cp00001-01.pdf> (last visited Feb. 20, 2005).

⁸ See *Hearing, supra* note 2, at 80 (statement of David Beier, Senior Vice President, Global Government Affairs, Amgen, Inc.).

⁹ *Id.* at 117 (statement of Carole Ben Maimon, President and Chief Operating Officer, Barr Research, Inc.).

¹⁰ *Id.*

¹¹ Christine Hines, *Clock is Ticking on Several Lucrative Drug Patents; Generic Drug Makers Want Their Shot at a \$10 Billion Market*, 26 NAT'L L.J., No. 45 (2004), at 11.

¹² CONG. BUDGET OFF., HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 13 (1998) (estimating that consumers saved somewhere between 8 and 10 billion dollars through buying generic pharmaceuticals in 1994 alone).

¹³ Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355 (2000); 35 U.S.C. §§ 156, 271, 282 (2000)).

¹⁴ 21 U.S.C. § 355 (2000).

¹⁵ FED. TRADE COMMISSION, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY (2002) (noting loopholes but generally affirming success), *but see* Sarah Eurek, *Hatch-Waxman Reform and Accelerated Market Entry of Generic Drugs: Is Faster Necessarily Better?*, 2003 DUKE L. & TECH.

¶4 The approval of generic, or off-patent,¹⁶ biologic treatments is more complicated because most biologics are not approved under the FDCA, but rather under the Public Health Services Act (PHSA),¹⁷ which does not contain any provision regarding generic approval.¹⁸ Without this sort of provision in the PHSA, a manufacturer of an off-patent biologic is required to submit to the Federal Drug Administration (FDA) independent clinical studies that support the manufacturer's assertion that the product is safe and effective.¹⁹ Requiring the manufacturer to provide its own complement of studies may be warranted in some situations, but in other cases the data may be identical to the data originally supplied by the innovating company.²⁰ This submission of duplicative data by the off-patent company is inefficient and delays the price-lowering benefits of competition.

¶5 Aside from statutorily shortening the approval process, several scenarios have been formulated to speed off-patent biological products to market. One scenario envisions that the FDA could interpret a provision for generic approval into the existing PHSA.²¹ Another possible scenario sees the FDA reclassifying biologics as drugs and applying the Hatch-Waxman Act.²² A third scenario is that the FDA could apply the Hatch-Waxman Act, only to the small set of biologics that were originally approved under the FDCA.²³

REV. 18 (2003) (for an account of how Hatch-Waxman was recently amended in response to loopholes).

¹⁶ "Generic" and "off-patent" refer to the same proposition with regard to biologics, but usage has been a contentious matter since both terms have similar yet unique connotations. At root is the empirical question of whether generic biologics truly exist, since biologics are dependent so heavily on the manufacturing process. Brand name firms contend that the term generic is inapplicable and prefer the broader, more catch-all, off-patent. Generic firms contend the opposite. This remains an open question and this paper attempts to remain impartial. See *Hearing, supra* note 2 (response to follow-up questions by William B. Shultz, representing the Generic Pharmaceuticals Association).

¹⁷ 42 U.S.C. § 262 (2000).

¹⁸ Christine Hines, *Pressure Rises for FDA, Congress in Latest Drug Duel; Generic, Brand-name Drug Makers Face Off Over the Future of Biologics*, LEGAL TIMES, Jul. 12, 2004, at 1.

¹⁹ See *id.*

²⁰ See *Hearing, supra* note 2, at 2-3 (statement of Sen. Orrin Hatch).

²¹ See DONALD O. BEERS, *GENERIC AND INNOVATOR DRUGS: A GUIDE TO FDA APPROVAL REQUIREMENTS* §13.03 (Supp. 2003).

²² See *Hearing, supra* note 2, at 119 (prepared statement of Carole Ben-Maimon, Barr Laboratories).

²³ See Melissa R. Leuenberger-Fisher, *The Road to Follow On Biologics: Are We There Yet?*, 23 BIOTECHNOLOGY L. REP. 389, 390 (2004).

¶6 While the FDA has refused to apply the Hatch-Waxman Act to biologics that were originally approved under the PHSA,²⁴ the FDA believes that it has the authority to approve off-patent biologics originally regulated under the FDCA.²⁵ However, under this scenario, by approving the off-patent biologic the FDA would need to rely on the previous finding of safety and effectiveness associated with the brand name biologic. According to brand name firms, this action is a use of trade secret data, and that such use by the FDA would violate the Takings Clause of the Constitution.²⁶

¶7 This iBrief analyzes the takings argument. In doing so it examines the United States Supreme Court's takings case law, and puts particular focus on *Ruckelshaus v. Monsanto*.²⁷ In *Monsanto*, the Court examined how the Takings Clause of the United States Constitution applies to trade secrets and government regulation; its analysis turned on whether a company had "reasonable investment-backed expectation."²⁸ In the end, this iBrief concludes that it would be difficult for brand name firms to prove that they had "reasonable investment-backed expectations" in their safety and effectiveness data, such that the FDA could not rely on these earlier findings in order to approve off-patent equivalents of biologics which were originally approved under the FDCA.²⁹

I. THE REGULATION OF DRUGS AND BIOLOGICS

¶8 The regulatory framework for approving and monitoring medicines is complicated and rarely intuitive. Thus, it is valuable to provide a short orientation to the regulatory process. The FDCA requires that new drugs undergo close scrutiny for safety and effectiveness before they can reach the

²⁴ 21 C.F.R. § 314.101(e)(1).

²⁵ See *Hearing*, *supra* note 2, at 134 (prepared statement of Dr. David Crawford, Acting Commissioner, Food and Drug Administration).

²⁶ See *Citizen's Petition*, *supra* note 7, at 1; U.S. CONST. amend. V.

²⁷ 467 U.S. 986 (1984).

²⁸ *Id.* at 1005.

²⁹ It is important to be candid about what this iBrief does *not* purport to argue: whether data used to support biologics passed under the PHSA can be relied on by the FDA to approve off-patent biologics under the Hatch-Waxman provisions of the FDCA. Indeed, brand name biologics might have a strong case for a takings claim in light of the lack of any generic provision in the PHSA coupled with multiple assurances by the FDA against this sort of treatment. Lastly, a word of caution, even though it might not be a taking to evaluate a select number of biologics already regulated under the FDCA, it still may be unwise to do so. New legislation may be the better course for several reasons, including the development of a clear legislative record and an unambiguous and simplified process for generic approval.

market.³⁰ Drugs are defined under the FDCA in part, as “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals” and also as “articles (other than food) intended to affect the structure or any function of the body of man or other animals.”³¹ Drugs are evaluated and approved by the Center for Drug Evaluation and Research at the FDA.³²

¶9 Biologics, on the other hand, are regulated under the PHSA and are evaluated by the Center for Biologics Evaluation and Research (CBER).³³ It has been noted, however, that the FDCA’s definition of a drug is so broad that it actually encompasses most biologics.³⁴ Indeed, some biologics like insulin and human growth hormone are already regulated by the FDA under the FDCA. However, these delegations to the FDA are merely the result of historical practice and are not supported by any scientific rationale.³⁵

¶10 The idea of relying on the safety and efficacy of first generation drugs to shorten the approval process of generic drugs did not begin with Hatch-Waxman.³⁶ For example, applicants were allowed to rely on a finding of effectiveness for pre-1962 drugs under the Drug Efficacy Study Implementation program (DESI).³⁷ However, the Hatch-Waxman Act provided a more elaborate system of generic approval.³⁸ First, under §505(j), an applicant is permitted to file an Abbreviated New Drug Application (ANDA).³⁹ Under this section, generic manufacturers are not required to duplicate the safety and effectiveness studies performed by the brand name innovator if several statutory requirements are satisfied.⁴⁰ One of the most important requirements is a showing of bioequivalence between the generic and brand name product.⁴¹ However, unlike chemically-

³⁰ See JAMES T. O’REILLY, FOOD AND DRUG ADMINISTRATION §13.4 (2004).

³¹ 21 U.S.C. §321(g)(1) (2000); See also Jay M. Zitter, *What is “Drug” Within §201(g)(1) of the Food, Drug, and Cosmetic Act (21 U.S.C.A. 321(g)(1))*, 127 A.L.R. FED. 141 (for a detailed examination of the contours of the definition of “drugs”).

³² FDA, Intercenter Agreement Between the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research, III(A)(6) (Oct. 31, 1991) [hereinafter *Intercenter Agreement*].

³³ See *id.*

³⁴ Edward L. Korwek, *Human Biological Drug Regulation: Past, Present, and Beyond the Year 2000*, 50 FOOD & DRUG L. J. 123, 126 (50th Anniversary Special Issue, 1993).

³⁵ See Leuenberger-Fisher, *supra* note 23, at 391.

³⁶ *Id.* at 389.

³⁷ *Id.*

³⁸ See *id.* at 389-90.

³⁹ 21 U.S.C. § 355(j).

⁴⁰ *Id.*

⁴¹ *Id.*

synthesized drugs, where a showing of bioequivalence is relatively straightforward, proving bioequivalence between biologics is fraught with difficulty.⁴² Due to the unique physical properties of biologics, additional clinical studies may be necessary to prove bioequivalence. Therefore, using §505(j) of the FDCA, which requires strict bioequivalence, may not be appropriate to approve off-patent biologics.⁴³

¶11 Section 505(b)(2) of the Hatch-Waxman Act⁴⁴ holds more promise for off-patent biologics, since it provides a more flexible approach to accommodating similar but not identical compounds.⁴⁵ Again, since brand name and off-patent biologics are unlikely to be completely bioequivalent, off-patents cannot benefit from 505(j).⁴⁶ Yet, to the extent there *is* bioequivalence under §505(j), the off-patent biologic applicant can rely on a previous finding of safety and effectiveness under §505(b)(2).⁴⁷ Where no bioequivalence exists, the off-patent applicant must supply data that independently supports safety and effectiveness.⁴⁸ The FDA cannot fill gaps by delving into the proprietary data of the first generation drug.⁴⁹ The FDA contends that there is a legally significant difference between relying on the finding of safety and effectiveness as occurs when bioequivalence is proven under §505(j), versus relying on the underlying data itself.⁵⁰

II. TRADE SECRETS AND THE TAKING CLAUSE

¶12 To answer whether the FDA's reliance on a finding of safety and effectiveness constitutes a taking with regard to off-patent biologics, it is necessary to review the Supreme Court's treatment of the Takings Clause. The Takings Clause, found in the Fifth Amendment of the United States Constitution, protects property interests of private parties against uncompensated government interference.⁵¹ A takings claim must be grounded in some legal property right, such as a right to trade secret

⁴² Lincoln Tsang & Donald Beers, *Follow-on Biological Products: The Regulatory Minefield*, GLOBAL COUNSEL LIFE SCIENCES HANDBOOK 109 (2004).

⁴³ *Id.* But see *Hearing*, *supra* note 2, at 119 (written statement of Carole Ben Maimon, Barr Laboratories; arguing for approval of generic biologics under §355(j)).

⁴⁴ 21 U.S.C. §355(b)(2).

⁴⁵ See Leuenberger-Fisher, *supra* note 23, at 394-95. See also Tsang & Beers, *supra* note 42, at 110.

⁴⁶ Tsang & Beers, *supra* note 42, at 109.

⁴⁷ FOOD AND DRUG ADMINISTRATION, APPLICATIONS COVERED BY SECTION 505(B)(2) (DRAFT GUIDANCE) 2-3 (1999) [*hereinafter* DRAFT GUIDANCE].

⁴⁸ See Leuenberger-Fisher, *supra* note 23, at 394-95.

⁴⁹ See *Hearing*, *supra* note 2, at 65 (Questions to Dr. David Crawford).

⁵⁰ *Id.*

⁵¹ U.S. CONST. amend. V (“[N]or shall private property be taken for public use, without just compensation.”).

protection, based on either a state or federal statute.⁵² Many state laws follow the Restatement of Torts or the Uniform Trade Secrets Act in defining property interests.⁵³ Indeed, the FDA has relied on the Restatement for its definition of trade secret.⁵⁴ “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.”⁵⁵ Courts have also construed the definition of trade secret more narrowly, depending on the legislative context.⁵⁶

¶13 It is conceivable that the Takings Clause does not recognize trade secrets as a property right.⁵⁷ One argument against trade secrets as a property right is that the right to exclude in trade secrets is narrower than for other types of property: a trade secret holder cannot prevent competitors from using the once-secret if it was independently discovered.⁵⁸ However, the Court has, in at least one instance, determined that trade secrets are a property right subject to the Takings Clause. In *Ruckelshaus v. Monsanto*,⁵⁹ the statute in question was the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).⁶⁰ FIFRA was passed in 1947 as a labeling and licensing statute for pesticides, but was expanded in 1972 pursuant to fears about the safety of pesticides and the possible harm that they posed to the environment.⁶¹ Among other changes, the 1972 legislation authorized the Environmental Protection Agency (EPA) to rely on trade secrets or other

⁵² Ira S. Matsil, Comment, *Government Seizures of Trade Secrets: What Protection Does the Takings Clause Provide?*, 48 SMU L. REV. 687, 698 (1995). See also *Ruckelshaus v. Monsanto*, 467 U.S. 986, at 1001 (1984) (“[P]roperty interests . . . are not created by the Constitution. Rather, they are created and their dimensions are defined by existing rules or understandings that stem from an independent source such as state law.” (quoting *Webb's Fabulous Pharmacies, Inc. v. Beckwith*, 449 U.S. 155, 161 (1980))).

⁵³ See Matsil, *supra* note 52, at 698.

⁵⁴ Richard Fortunato, Note, *FDA Disclosure of Safety and Efficacy Data: The Scope of Section 301(j)*, 52 FORDHAM L. REV. 1280, 1289 (1984).

⁵⁵ 21 C.F.R. § 20.61(a) (2004).

⁵⁶ See *Public Citizen Health Research Group v. Food and Drug Admin.*, 704 F.2d 1280, 1288 (D.C. Cir. 1983).

⁵⁷ See Richard Epstein, *The Constitutional Protection of Trade Secrets Under the Takings Clause*, 71 U. CHI. L. REV. 57, 59 (2004) (presenting, but ultimately rejecting, an argument that trade secrets are not property).

⁵⁸ *Id.* See also *Ruckelshaus*, 467 U.S. at 1011.

⁵⁹ 467 U.S. 986 (1984).

⁶⁰ 61 Stat. 163, as amended, 7 U.S.C. §§ 136 *et seq.* (2000).

⁶¹ *Monsanto*, 467 U.S. at 991-92.

confidential information to approve similar chemical compounds if the beneficiary agreed to compensate the original innovator.⁶²

¶14 The 1972 amendments spurred litigation about the extent of trade secrets and other confidential information, and FIFRA was amended yet again in 1978.⁶³ The 1978 amendments provided that the EPA could not rely on innovator data for ten years after the date of submission.⁶⁴ However, after the ten years had passed, the EPA could rely on that data without permission.⁶⁵ Further, compensation for use of this data was required only for 15 years after the date of submission.⁶⁶

¶15 The Court in *Monsanto* held that the safety and effectiveness data submitted by Monsanto to the EPA was a property interest cognizable by the Takings Clause insofar as the information was protected by the laws of Missouri as a trade secret.⁶⁷ As the Court explained, trade secrets derive their economic value from the competitive edge which they provide.⁶⁸ Once they are disclosed, or used to evaluate other applications, their economic value is extinguished or diminished, and the holder might have a claim under the Takings Clause.⁶⁹ Applying the Court's reasoning, it will be assumed for the purposes of this iBrief that brand name safety and effectiveness data are trade secrets and subject to a takings analysis.

¶16 However, the question does not end there. For regulatory takings, the government action also needs to be evaluated in light of the ad hoc factors formulated in *Penn Central Transportation Co. v. City of New York*.⁷⁰ The *Penn Central* Court set forth several factors relevant to whether a taking has occurred: the character of the government action, the economic impact of the action, and whether the government action has vitiated reasonable investment-backed expectations.⁷¹

¶17 While not dispositive,⁷² the reasonable investment-backed expectations inquiry is often the central focus of a regulatory takings analysis.⁷³ Reasonable investment-backed expectations played a prominent

⁶² *Id.* at 992-93.

⁶³ *Id.* at 993-94.

⁶⁴ *Id.* at 1006.

⁶⁵ *Id.*

⁶⁶ *Id.*

⁶⁷ *Id.* at 1003-04.

⁶⁸ *Id.* at 1012.

⁶⁹ *Id.*

⁷⁰ 438 U.S. 104 (1978).

⁷¹ *Id.* at 124.

⁷² See *Palazzolo v. Rhode Island*, 533 U.S. 606, 635-36 (2001) (O'Connor, J., concurring) (reasonable investment-backed expectations should not be relied on exclusively).

⁷³ *E.g.*, *Monsanto*, 467 U.S. at 1005.

role in *Monsanto*, a situation strikingly similar to the present debate. In both situations, the government was concerned with ensuring public safety in the face of potentially dangerous but valuable compounds. Brushing aside the first two *Penn Central* factors, the *Monsanto* Court focused its analysis on whether the agency action disrupted Monsanto's reasonable investment-backed expectations. The Court reasoned that whether or not expectations were disrupted depended on the statutory scheme.⁷⁴ The Court held that the existence of a statute puts an innovator constructively on notice of the limits of an agency's authority with regard to the handling of confidential information.⁷⁵ The Court placed emphasis on the voluntary submission of data: "[A]s long as Monsanto is aware of the conditions under which the data are submitted, and the conditions are rationally related to a legitimate Government interest, a voluntary submission of data by an applicant in exchange for the economic advantages of a registration can hardly be called a taking."⁷⁶ Thus, a taking does not occur when there is a voluntary exchange of information for a valuable government benefit and the government provides notice that it has a license to use or disclose the submitted information.⁷⁷

¶18 This is a double-edged sword, however, since legislation affording protection to certain forms of information will require compensation if agency action violates the letter of the law.⁷⁸ The Court held that with regard to data submitted after the 1978 amendments, Monsanto could not have a reasonable investment-backed expectation that its data would not be treated as inviolate, since the statute explicitly stated that the data would not receive such treatment.⁷⁹ Similarly, before 1972, the statute was silent about the agency's obligations and provided no "express promise" to an innovator.⁸⁰ However, under the 1972 amendments, applicants were given the opportunity for compensation by labeling data as confidential.⁸¹ Therefore, with regard to the time period after 1972 but before 1978, the Court did find that Monsanto could have reasonable investment-backed expectations of nonuse and nondisclosure.⁸²

⁷⁴ See *id.* at 1005-07.

⁷⁵ *Id.* at 1007.

⁷⁶ *Id.*

⁷⁷ *Nollan v. California Coastal Comm'n*, 483 U.S. 825, 833 n.2 (1987) (discussing *Monsanto*, 467 U.S. at 1007).

⁷⁸ *Monsanto*, 467 U.S. at 1010-11.

⁷⁹ *Id.* at 1006.

⁸⁰ *Id.* at 1008.

⁸¹ *Id.* at 1011.

⁸² *Id.* at 1010-11.

III. DO BRAND NAME BIOLOGIC MAKERS HAVE “REASONABLE INVESTMENT-BACKED EXPECTATIONS”?

¶19 Within even the broader “muddle”⁸³ of takings case law, the reasonable investment-backed expectations test has been characterized as “at best useless and at worst mischievous.”⁸⁴ Indeed, numerous attempts have been made to clarify the concept and give it analytical teeth.⁸⁵ For better or worse, however, the reasonable investment-backed expectation notion of *Penn Central* is still used frequently by the Court.⁸⁶

¶20 Attempts to determine whether there are reasonable investment-backed expectations in a given situation can proceed in one of two fashions.⁸⁷ A bottom-up analysis begins with investor expectations and then evaluates reasonableness. Indeed, expectations can be evaluated by risk analysis,⁸⁸ or under a competing view, through evaluating the web of social and historical understandings about property rights.⁸⁹ Both assays are too complicated to complete meaningfully in this iBrief. By contrast, a top-down analysis begins with the statutes that shape expectations and evaluates whether or not they provide notice. While in theory, top-down and bottom-up approaches should yield the same result, the situation at hand admits more easily to a top-down analysis, since it is more feasible to analyze the notice-giving effect of statutes.⁹⁰

¶21 Legislative schemes that shape expectations and provide notice can come in three varieties.⁹¹ Legislation can prohibit use or disclosure, provide for use or disclosure, or remain silent on the issue.⁹² If legislation prohibits the use or disclosure of the trade secret, the holder has a strong case for a taking if the government acts contrary to the statute.⁹³ At the other end of

⁸³ Thomas F. Cotter, *Do Federal Uses of Intellectual Property Implicate the Fifth Amendment?*, 50 FLA. L. REV. 529, 529 n. 1 (1998).

⁸⁴ See Epstein, *supra* note 57, at 65.

⁸⁵ See generally David R. Mandelker, *Investment-Backed Expectations in Taking Law*, 27 URB. LAW. 215 (1995) (providing a survey of different approaches in analyzing the reasonable investment-backed expectations test).

⁸⁶ See generally David R. Mandelker, *The Notice Rule in Investment-Backed Expectations*, in TAKING SIDES ON TAKINGS ISSUES: PUBLIC AND PRIVATE PERSPECTIVES 21 (Thomas E. Roberts, ed. 2002).

⁸⁷ See Mandelker, *supra* note 85, at 227.

⁸⁸ *Id.* at 227-30 (describing Louis Kaplow, *An Economic Analysis of Legal Transitions*, 99 HARV. L. REV. 509, 524 (1986)).

⁸⁹ *Id.* at 230-32 (describing Richard H. Pildes, *Conceptions of Value in Legal Thought*, 90 MICH. L. REV. 1520, 1552 (1992)).

⁹⁰ *Id.* at 227-31.

⁹¹ See Matsil, *supra* note 52, at 707.

⁹² *Id.*

⁹³ *Id.*

the spectrum, if legislation affirmatively provides for the disclosure or use of trade secret information, the trade secret holder is put on notice, and consequently has no claim under the Takings Clause.⁹⁴ Finally, if legislation is silent about the use or disclosure of trade secrets, then it may be appropriate to look to the circumstances at the time the trade secret was submitted, including regulations.⁹⁵

A. Is there notice for the use of trade secret information for biologics approved under the FDCA?

¶22 Does the FDCA provide explicit notice that the FDA will not rely on earlier findings of safety and efficacy in approving later applications for biologics originally approved under the FDCA? If the FDCA provides such notice, then any action against the statute will constitute a taking. Critics of off-patent biologics have asserted that the FDCA expressly provides for the protection of data under section 301(j).⁹⁶ Section 301(j) prohibits, in relevant part,

the using by any person to his own advantage, or revealing, other than to [certain government officials and the courts, relevant], any information acquired under the authority of [a number of FDCA sections, including §505] concerning any method or process which as a trade secret is entitled to protection.⁹⁷

The FDA also requires those who accept a commission with the Department of Health and Human Services to affirm that they will not, “use this information to further [their] private interests or the interests of any other person.”⁹⁸ It is conceivable that the FDA’s reliance on brand name data would fall under the ambit of §301(j) if that section is given a broad interpretation. The argument is that §301(j) prohibits the FDA from approving an off-patent biologic application because relying on its earlier finding of safety and effectiveness is a use of data prohibited by the statute.⁹⁹ While the FDA may not be using the information “for its own advantage” it could be contended that they are furthering the interests of another person; namely, the applicant for the off-patent biologic.

⁹⁴ *Id.* at 707-08.

⁹⁵ *Id.* at 710-14.

⁹⁶ See *Citizens Petition*, *supra* note 7, at 12.

⁹⁷ 21 U.S.C. § 331(j) (2000).

⁹⁸ Food and Drug Administration, Regulatory Procedure Manual, Ch. 3, Commissioning State and Local Officials, *Acceptance of Commission*, page 30 (2004).

⁹⁹ See *Citizens Petition*, *supra* note 7, at 12-13.

¶23 Thus, it becomes critical to examine what “uses” are contemplated by §301(j). Unfortunately, attention to the “use” prong of §301(j) has been scant at best;¹⁰⁰ most of the scrutiny has focused on the second prong which prohibits disclosure.¹⁰¹ Most often, §301(j) is seen as a stopgap to agency discretion for disclosure pursuant to Freedom of Information Act¹⁰² requests.¹⁰³ The exemptions of the Freedom of Information Act remove trade secrets from mandatory disclosure but still allow discretionary disclosure as authorized by law.¹⁰⁴ Yet even this discretion is foreclosed because under §301(j) trade secrets are prohibited from disclosure and therefore not authorized by law.¹⁰⁵

¶24 This discussion about biologics brings to the surface a disturbing contention: that even Hatch-Waxman’s generic *drug* approval process affects an unconstitutional taking.¹⁰⁶ Reading §301(j) broadly to include the approval of follow-on applications as “a use to its own advantage” would extend beyond FDCA-approved biologics, like insulin and human growth hormone, to all drugs. The shortened approval process in either circumstance could be characterized as the FDA using pioneer data for the advantage of another. In this way, such a broad reading could frustrate the aims of both §505(b)(2) and §505(j). Indeed, no suit has been filed by a drug manufacturer asserting that the Hatch-Waxman Act violates the Takings Clause.¹⁰⁷

¶25 It seems most reasonable to construe §301(j) narrowly to encompass a smaller subset of cases, such as the situation where an agency employee, privy to confidential information, uses this information to advance the interests of her brother-in-law, an aspiring investor. It is a canon of statutory construction that “[a] statute should be construed so that effect is given to all its provisions, so that no part will be inoperative or superfluous, void or insignificant, and so that one section will not destroy

¹⁰⁰ S. Rep. 73-493 (1934) (only commenting that this section is a safeguard to manufacturers).

¹⁰¹ See, e.g., Fortunato, *supra* note 54.

¹⁰² 5 U.S.C. § 552 (2000).

¹⁰³ See Fortunato, *supra* note 54, at 1282.

¹⁰⁴ *Id.*

¹⁰⁵ *Id.*

¹⁰⁶ See DONALD O. BEERS, *GENERIC AND INNOVATOR DRUGS: A GUIDE TO FDA APPROVAL REQUIREMENTS* 6-1 (1999) (arguing that the Hatch-Waxman Act might be a taking, but no mention of §331(j)).

¹⁰⁷ *Id.* at 6-1. There might be two reasons for this. First, brand name companies may not believe that their data is actually being used. Second, they might believe that there is use, but because of the exclusivity and patent term extension benefits, they may believe that compensation already exists. Regardless, as a matter of construction, Section 301(j) would be at odds with §§505(b)(2) and (j) either way.

another unless the provision is the result of obvious mistake or error.”¹⁰⁸ On the other hand, a narrow reading preserves the substance of both terms.¹⁰⁹ Thus, with regard to §301(j), by construing use and “to his own advantage” narrowly, the substance of §301(j), §505(b) and §505(j) can be preserved.¹¹⁰ Therefore, while there is ample room for argument, it seems safe to say that the FDCA does not provide an explicit promise that a finding of safety and effectiveness for one FDCA-approved biologics application cannot be used as a basis for the approval of a follow-on application.¹¹¹

B. Does the FDCA affirmatively enable FDA action?

¶26 Since there is no explicit guarantee in the FDCA that the FDA cannot rely on previous findings, the next question is whether the FDCA affirmatively enables FDA action. Sections 505(j) and, in theory, 505(b)(2) of the FDCA could be cited to support this view. Both of these sections enable, to different degrees, the FDA to rely on earlier findings to approve generics with the limitation that the original application be approved under the §505 pathway of the FDCA.¹¹² Section 505(j) allows a generic drug manufacturer to take advantage of an Abbreviated New Drug Application (ANDA) if, among other statutory requirements, the generic drug is bioequivalent to the brand name drug.¹¹³ In an ANDA application, the generic applicant is not required to submit studies demonstrating safety and effectiveness.¹¹⁴ Section 505(b)(2) is similar to the ANDA pathway, however, it allows for greater flexibility.¹¹⁵ A generic applicant is allowed to rely on a finding of safety and effectiveness to the extent that the two

¹⁰⁸ Anderson v. Health & Human Servs., 907 F.2d 936, 944 (10th Cir. 1990) (quoting J. SUTHERLAND, STATUTES AND STATUTORY CONSTRUCTION § 46.06 at 104 (C. Sands 4th ed. rev. 1984)).

¹⁰⁹ See *id.*

¹¹⁰ Similar reasoning was used by the court in Public Citizen Health Research Group v. FDA, 704 F.2d 1280, 1288-89 (D.C. Cir. 1983). The canon was used to construe the meaning of trade secrets narrowly in the context of the Freedom of Information Act. A broad construction would engulf the substance of “commercial information”, which was also protected in the statute.

¹¹¹ See also Letter from John C. Yoo, Professor of Law, representing the Generic Pharmaceutical Association, to Sen. Orrin Hatch 9-10 (Oct. 21, 2004) (also arguing that 301(j) does not create reasonable investment-backed expectations).

¹¹² See 21 C.F.R. § 314.101(e)(1) (2004).

¹¹³ 21 U.S.C. § 355(j).

¹¹⁴ *Id.*

¹¹⁵ See Leuenberger-Fisher, *supra* note 23, at 394-95; see also Tsang & Beers, *supra* note 42, at 110.

compounds are bioequivalent; to the extent that they are not, the generic applicant must submit data demonstrating safety and effectiveness.¹¹⁶

¶27 By their language, Sections 505(j) and (b)(2) apply to *all* drugs.¹¹⁷ In this way, these provisions would apply to insulin and human growth hormone, since even though they would be considered biologics under a rough definition, they were approved under the FDCA, and are referred to as drugs.¹¹⁸ Indeed, there is nothing within Section 505(j) or (b)(2) that indicates that those sections only apply to drugs which admit to a straightforward classification.¹¹⁹ Thus, it seems that the existence of both statutes should put brand name manufacturers on notice that the FDA will rely on previous findings for certain biologics classified as drugs.

C. Is there another basis for investment-backed expectations?

¶28 Even if the appropriate legislation is silent or unclear, regulations can still shape reasonable investment-backed expectations.¹²⁰ In *TriBio Laboratories, Inc. v. United States*,¹²¹ the United States Court of Appeals for the Third Circuit held that a government regulation created reasonable expectations when it required that data from a first generation application could not be used to support a follow-on application unless the original submitter had consented.¹²² In *TriBio*, a pharmaceutical manufacturer attempted to obtain approval for a veterinary pharmaceutical called Gentaject, which was used for inoculating one day -old chicks against harmful bacteria.¹²³ Reasonable investment-backed expectations were created in light of a regulation relating to New Animal Drug Applications.¹²⁴ That regulation stated that, “any reference to information furnished by a person other than the applicant may not be considered unless its use is authorized in a written statement signed by the person who submitted it.”¹²⁵ A similar provision applies to New Drug Applications under the Hatch-Waxman Act, providing that an applicant can only reference data in a previous application when it obtains a right to reference that data from the submitter.¹²⁶

¹¹⁶ 21 U.S.C. §355(b)(2); *see also* Leuenberger-Fisher, *supra* note 23, at 394-95.

¹¹⁷ 21 U.S.C. §355(j), (b)(2).

¹¹⁸ *See Intercenter Agreement*, *supra* note 32, at III(A)(6).

¹¹⁹ 21 U.S.C. §355(j), (b)(2).

¹²⁰ *Tri-Bio Labs., Inc. v. United States*, 836 F.2d 135, 140-41 (3d Cir. 1987).

¹²¹ 836 F.2d 135 (3d Cir. 1987).

¹²² *Id.* at 140-41.

¹²³ *Id.* at 136.

¹²⁴ *Id.* at 140-41.

¹²⁵ 21 C.F.R. § 514(a) (1987).

¹²⁶ 21 C.F.R. § 314.50(g)(3) (2004).

¶29 However, this provision does not create reasonable expectations regarding the non-use of a finding of safety and effectiveness. The approval-shortening measures put in place by the Hatch-Waxman Act specifically provide for situations where the new applicant does not have a right to reference the data in the brand name application. In other words, even though an applicant does not have a right of reference, 505(b)(2) still provides a framework for the FDA to rely on previous findings of safety and effectiveness. No comparable statute existed for animal drugs in *Tri-Bio*.¹²⁷ Section 505(b)(2) provides that when there is no right to reference, an applicant can obtain approval, but only if further statutory requirements are met.¹²⁸ Under §505(b)(2), as described above, the FDA is authorized to rely on previous findings of safety and effectiveness, without actually delving into the data of the first application.¹²⁹ On the one hand, investors would have reasonable investment-backed expectations that the FDA would not allow an off-patent applicant to rely on an innovator's application to "fill gaps" in the off-patent application. On the other hand, investors would not have reasonable expectations, grounded in regulation, that the FDA would not rely on a finding of safety and effectiveness when the applicant did not have a right to reference, in light of §505(b)(2).

CONCLUSION

¶30 The high prices of biologic therapies make it imperative that generic or off-patent products be marketed as options for consumers after patent and exclusivity protections for manufacturers have expired. Brand name companies argue that the FDA cannot make off-patent biologics available without using proprietary data protected by the Takings Clause of the U.S. Constitution. A Takings analysis here hinges on whether the property holders had reasonable investment-backed expectations concerning the confidentiality of their information for biologics classified as drugs under the FDCA. This iBrief argues that § 301(j) of the FDCA did not create expectations of confidentiality. Furthermore, sections 505(j) and (b)(2) actively created expectations that the FDA would rely on previous findings of safety and effectiveness. Lastly, the FDA has not promulgated any regulations that create reasonable expectations about confidentiality. Consequently, it is unlikely that the approval of off-patent biologics originally approved under the FDCA would be a taking. For this subset of biologics, brand name manufacturers had notice, under the Hatch-Waxman amendments, that the FDA would consider follow-on products in light of previous safety and effectiveness findings.¹³⁰

¹²⁷ *Tri-Bio*, 836 F.2d at 139.

¹²⁸ See DRAFT GUIDANCE, *supra* note 47, at 2.

¹²⁹ See *Hearing*, *supra* note 2, at 65 (questions to Dr. David Crawford).

¹³⁰ See *supra*, note 29.