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The Constitutional Protection of Trade Secrets and Patents under the Biologics Price Competition and Innovation Act of 2009

RICHARD A. EPSTEIN*

The Biologics Price Competition and Innovation Act of 2009 (“Biosimilars Act”)¹ is for the field of pharmaceutical products the single most important legislative development since passage of the Drug Price Competition and Patent Term Restoration Act of 1984 (“Hatch-Waxman Act”),² on which portions of the Biosimilars Act are clearly patterned. Congress revised section 351 of the Public Health Service Act (PHSA) to create a pathway for FDA approval of “biosimilar” biological products. Each biosimilar applicant is required to cite in its application a “reference product” that was approved on the basis of a full application containing testing data and manufacturing information, which is owned and was submitted by another company and much of which constitutes trade secret information subject to constitutional protection. Because the Biosimilars Act authorizes biosimilar applicants to cite these previously approved applications, the implementation of the new legislative scheme raises critical issues under the Fifth Amendment of the Constitution, pursuant to which private property—trade secrets included—may not be taken for public use, without “just compensation.” FDA must confront those issues as it implements the scheme set out in the Biosimilars Act. This article will discuss these issues, after providing a brief overview of the Biosimilars Act and a more detailed examination of the law of trade secrets.

INTRODUCTION

Under federal law, a biological product may not be introduced into interstate commerce without a biologics license granted under the PHSA. Prior to 2010, licenses were awarded only under section 351(a), which governs traditional full biologics license applications (BLAs) for “innovative” or “pioneer” products. BLAs filed under section 351(a) are required to show that the product in question is safe, pure and potent.³ These applications contain extensive analytical, preclinical and clinical data making this showing as well as elaborate discussions of the methods by which the product is manufactured. As one might expect, a BLA is extremely

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¹ Patient Protection and Affordable Care Act, Pub. L. No. 111-148, Title VII, Subtitle A, 124 Stat. 119, 804-821 (2010). See generally Krista Hessler Carver, Jeffrey Elikan & Erika Lietzan, *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 FOOD & DRUG L.J. 671 (2010) for an exhaustive description of the law and the relevant legislative and regulatory FDA history.

² Pub. L. No. 98-417, 98 Stat. 1585 (1984).

³ PHSA § 351(a)(2)(C)(i). In practice, the safe, pure, and potent standard works out to the same safe and effective standard that is used in dealing with non-biological drugs under the Federal Food, Drug, and Cosmetic Act (FDCA). See, e.g., FDA Guidance Concerning Demonstration of Comparability of Human Biological Products, Including Therapeutic Biotechnology-derived Products (April 1996) (referring to establishing that a biological product is “safe, pure, and potent (effective)” and referring to product “safety, purity, potency/effectiveness”).

expensive and time-consuming to prepare. Some estimates place the cost of developing a single innovative biologic at \$1.37 billion.⁴

The Biosimilars Act, passed in 2010, created section 351(k) to give FDA the authority to approve follow-on biologics that are deemed “biosimilar” to a reference product. This statute, like the Hatch-Waxman Act before it, is intended to balance twin goals that are necessarily in some tension. Its first goal is to preserve the incentive to bring innovative biological medicines to market. To do so, the Biosimilars Act offers pioneer biologics a 12-year period of exclusivity during which FDA approval of a biosimilar may not take effect. This period begins when the reference product is first licensed under the PHSA, i.e., upon approval of the original full length application.⁵ The exclusivity period offers the pioneer an opportunity to recoup at least part of its large initial investment in the approved molecule before facing any direct competition from a follow-on product. It also offers the owner of the pioneer biologic a term of protection that is roughly comparable in length to that received by the holders of patents on small molecules that are governed by the Hatch-Waxman Act.⁶ Congress also enacted section 351(l) of the PHSA, which contains an elaborate scheme to govern the commencement of patent litigation. In addition, Congress amended the Patent Act to create an artificial act of infringement enabling the pioneer firm to initiate premarket patent litigation against the biosimilar applicant. More specifically, the filing of a biosimilar application is now an artificial act of infringement with respect to certain patents identified by the reference product sponsor or biosimilar applicant during the patent information exchange process set forth in section 351(l) (if the biosimilar applicant intends to market the biosimilar before the relevant patents expire).⁷ These key features afford the innovator a clear path to injunctive relief against patent infringement prior to the release of the biosimilar onto the market.

The second goal of the Biosimilars Act is to facilitate the entry of new competition in the biological marketplace. To do so, the Biosimilars Act allows biosimilar companies to build their applications on the shoulders of pioneer full applications filed under section 351(a) of the PHSA. Thus once the 12-year exclusivity period expires, the new entrant may compete in the market so long as its product meets the “biosimilarity” requirements of section 351(k) of the PHSA. Further, the Bio-

⁴ See *Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the Subcomm. on Courts and Competition Policy of the H. Comm. on the Judiciary*, 111th Cong. 2 (2009) (statement of Rep. Henry C. Johnson, Jr., Chairman, Subcomm. on Courts and Competition Policy) (stating that some estimates place the cost of developing a new biologic at “as much as \$1.37 billion”); see also Henry Grabowski, *Follow-on biologics: data exclusivity and the balance between innovation and competition*, 7 NATURE REVIEWS DRUG DISCOVERY 479, 482 (2008) (calculating the capitalized research and development costs for a new biologic to be \$1.24 billion to \$1.33 billion).

⁵ PHSA § 351(k)(7). Under the “first licensure” provision of the statute, the 12-year exclusivity period is not available for supplements or any “subsequent application filed by the same sponsor or manufacturer” as an earlier application (or a “licensor, predecessor in interest, or other related entity”), if the subsequent application relates to: “(I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or (II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.” PHSA § 351(k)(7)(C). Most stakeholders assume that these subsequent applications will be protected under the umbrella of exclusivity that protects the first licensed product.

⁶ See, e.g., Henry G. Grabowski & Margaret Kyle, *Generic Competition and Market Exclusivity Periods in Pharmaceuticals*, 28 MANAGE. DECIS. ECON. 491, 496 (2007) (finding that the average market exclusivity period (i.e., the amount of time the brand name pharmaceutical is on the market before generic competition) for small molecule drugs that qualify as new molecular entities was 12 to 15 years during the time period between 1995 and 2005).

⁷ 35 U.S.C. § 271(e)(2)(C).

similaris Act does not set an impossible standard for market entry of the biosimilar. Rather than requiring the follow-on product to be exactly like its reference product—the standard that generic drugs are required to meet under the Hatch-Waxman Act⁸ but that many acknowledge is not possible for biologics⁹—the Biosimilars Act allows the new entrant to piggy-back on the BLA of a previously approved product by showing that its product is “highly similar” to the “reference product” and, further, that there are no “clinically meaningful differences” between the products. Accordingly, a biosimilar applicant need not undertake the monumental task of identifying from scratch a potential product candidate, developing that product and establishing *de novo* its safety, purity and potency. This shortcut thus allows the biosimilar to be approved on the basis of a smaller preclinical and clinical package than the pioneer submitted. Indeed, the statute gives FDA the discretion to waive analytical, preclinical and clinical data for the biosimilar altogether.

This statutory shortcut implicates both trade secret and takings law. By “trade secrets,” this means not only the manufacturing know-how described in the applications, but also the analytical, preclinical and clinical data generated at great expense and submitted to support the original pioneer BLA. Trade secret status is a function of state law, and under state law the protection of trade secrets lasts in perpetuity (so long as they are kept confidential by the owner). Under the Biosimilars Act, however, 12 years after approval of a pioneer product, a new entrant may rely on FDA’s finding that the pioneer product was safe, pure and potent. This finding was based on the trade secrets in the pioneer BLA. This reliance at year 12 constitutes a taking of private property, which in turn requires compensation. This compensation need not be supplied in cash, but may be supplied in-kind.

In the Biosimilars Act, in-kind compensation derives from a complex interplay of regulatory and patent provisions. This interplay is no accident, for Congressional negotiations involved both the innovator and generic industries. This scheme narrowly cabined the taking of pioneer trade secrets (through clear instruction about the basis for biosimilar approval as well as a robust exclusivity provision) *and* fashioned an in-kind quid pro quo for the “taking” (a meaningful opportunity to enforce relevant patents before biosimilar market entry). Failure to preserve the integrity of the approach (the narrowness of the taking and the precise quid pro quo) would raise serious questions about the constitutionality of the statute. Moreover, while this statutory quid pro quo scheme works going forward, it should not be applied with respect to trade secrets submitted to the agency before the Biosimilars Act was enacted. The Biosimilars Act cannot be applied retroactively to change the legal consequences associated with submitting these data, which was done under a different legal regime. A taking of these data would therefore be unconstitutional without just compensation.

⁸ I refer here to products that are the subject of applications under section 505(j) of the FDCA, i.e., traditional generic drugs subject to abbreviated new drug applications (ANDAs). For a discussion of section 505(b)(2) of the statute, also added as part of the Hatch-Waxman Act, see *infra* section I.D. For some highly idiosyncratic reasons, FDA has approved a handful of complex proteins under the FDCA rather than the PHSA and at least one “biosimilar” under section 505(b)(2)—i.e., Omnitrope—using a regulatory standard (whether the products are “highly similar”) that is very similar to the one that applies under the Biosimilars Act.

⁹ See, e.g., *Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 110th Cong. (May 2, 2007) (statement of Janet Woodcock, M.D. Deputy Commissioner, Chief Medical Officer, Food and Drug Administration) (“Because of the variability and complexity of protein molecules, current limitations of analytical methods, and the difficulties in manufacturing a consistent product, it is unlikely that, for most proteins, a manufacturer of a follow-on protein product could demonstrate that its product is identical to an already approved product.”).

I. THE PROTECTION OF TRADE SECRETS UNDER THE BIOSIMILARS ACT

A. *Some General Principles of Trade Secrets Law*

The initial question asks how the express provisions of the Biosimilars Act protect the trade secrets of biological innovators. To undertake this analysis, it is important to offer a brief account of the law of trade secrets, which in two key features are the polar opposites of patents. Patents are exclusive rights granted by the federal government, for a fixed period of time, pursuant to a scheme created by Congress and described by the federal Constitution.¹⁰ As part of the complex statutory “bargain” for his receipt of a patent, the inventor must publish to the world the “best mode” of its preparation.¹¹ Put otherwise, the grant of an exclusive patent right is so powerful that it is conditioned on forcing the patentee to release information that will help the next generation of inventors to circumvent the patent, thereby increasing the overall level of innovation. The implicit social judgment behind the best mode requirement is that over time this mutual and reciprocal disclosure of information speeds overall scientific progress. Just as the present inventor is able to build on the work of his predecessors, so must he allow his successor to build on his work. Nothing about the distinctive features of biologics, or their regulatory framework, requires any alteration of that general judgment.

Trade secrets involve the exact opposite configuration. Unlike patents, which are exclusively creatures of federal statute, the origin of trade secret protection lies exclusively in state common law. In one sense, trade secrets offer weaker protection than patents, because the holder of a trade secret cannot prevent its rival from independently acquiring, using and concealing precisely the same information that the former now holds as a trade secret. In another sense, the protection is stronger, because in principle state law offers trade secrets protection that lasts in perpetuity. Moreover, on this critical issue in the interpretation of this distinctive body of law, there is—as there must be—extraordinary uniformity. This condition must be satisfied, because a trade secret published in one place is with the click of a single button necessarily lost everywhere else in the world, including in states that would otherwise protect those trade secrets. Wholly apart from the particulars of any case, therefore, the expectations that these trade secrets create are necessarily powerful, uniform, and durable.

In light of this set of uniform practices, it is therefore not surprising that trade secrets receive constitutional protection against takings under the Fifth Amendment, as discussed in more detail in Section II. It is clear that no firm is entitled to obtain by stealth or other improper method the trade secrets of its rivals in order to speed its own products to market. It seems equally clear that it cannot accept trade secret information, either for free or for payment, that it knows has been stolen from another firm. The central inquiry therefore in the regulatory context asks whether the interjection of the government alters the balance between rival firms. Exactly how and when a trade secret possessed by one firm can be used in passing on the

¹⁰ See U.S. CONST. art. I, § 8, cl. 8 (“The Congress shall have Power . . . To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries; . . .”); 35 U.S.C. § 101 (authorizing the issuance of patents).

¹¹ See 35 U.S.C. § 112; see also *Glaxo, Inc. v. Novopharm LTD.*, 52 F.3d 1043, 1050 (Fed. Cir. 1995) (“[T]he sole purpose of the best mode requirement is to restrain inventors from applying for patents while at the same time concealing from the public preferred embodiments of their inventions which they have in fact conceived.” (internal citations omitted)).

application of a second firm raises hard questions of constitutional law, which shall be examined in due course.¹² For the moment it is sufficient to note that if FDA were to take the wrong approach to implementation of the Biosimilars Act, it could not only wreck the statutory scheme but also expose the U.S. government to constitutional challenges, including claims for compensation.¹³

B. *Trade Secrets in BLAs*

The confidential and proprietary information in a BLA includes both information about the manufacturing process and the results of extensive analytical, preclinical and clinical testing, all of which is viewed as “trade secret” under state common law and federal law. The Third Restatement of Unfair Competition, for example, defines a “trade secret” to mean “any information that can be used in the operation of a business or other enterprise and that is sufficiently valuable and secret to afford an actual or potential economic advantage over others.”¹⁴ An earlier definition of a trade secret was found in the Restatement (First) of Torts, which reads: “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 an opportunity to obtain an advantage over competitors who do not know or use it. It may be a formula for a chemical compound, a process of manufacturing, treating or preserving materials, a pattern for a machine or other device or a list of customers.”¹⁵ The earlier definition was slightly more limited than the current definition, but both clearly cover all of the trade secrets discussed in this article.¹⁶

Federal trade secret law also protects these data contained in a BLA. Under the Federal Trade Secrets Act, a federal employee is prohibited from disclosing “any information” that relates to “trade secrets, processes, operations, style of work, or apparatus” if the information was obtained in the course of his employment.¹⁷ This prohibition applies to disclosures by an agency, like FDA, in the course of its statutory duties.¹⁸ Trade secrets are also protected by FDA regulations. For example, trade secrets are exempt from FDA’s Freedom of Information Act (FOIA)

¹² See *infra* at section II.C.

¹³ See 28 U.S.C. § 1491 (giving the United States Court of Federal Claims jurisdiction over claims against the United States alleging a Constitutional violation).

¹⁴ RESTATEMENT (THIRD) OF UNFAIR COMPETITION § 39 (1995).

¹⁵ RESTATEMENT (FIRST) OF TORTS § 757 cmt. b (1939).

¹⁶ See, e.g., *Wyeth v. Natural Biologics, Inc.*, 395 F.3d 897, 899-900 (8th Cir. 2005) (confirming the trade secret status of manufacturing process data associated with Premarin, a conjugated estrogen product); *Jerome Stevens Pharm., Inc. v. FDA*, 402 F.3d 1249, 1251, 1256 (D.C. Cir. 2005) (reversing the district court’s dismissal of a drug company’s claims arising from FDA’s publication of “trade secret” information from the company’s NDA); *Webb v. Dep’t of Health & Human Servs.*, 696 F.2d 101, 102-03 (D.C. Cir. 1982) (“Every manufacturer of a new drug must obtain a separately approved NDA. Thus, a drug manufacturer which has submitted an NDA has a competitive interest in seeing that the information contained in its NDA is not prematurely released to the public. If a manufacturer’s competitor could obtain all the data in the manufacturer’s NDA, it could utilize them in its own NDA without incurring the time, labor, risk, and expense involved in developing them independently. Premature disclosure of NDA data is further discouraged by the existence of criminal sanctions for FDA officials who release trade secrets without the submitter’s consent.”); see also Letter from Mark Raza, Associate Chief Counsel, FDA to William C. Brashares, Esq. & Kate C. Beardsley, Esq., Counsel to Biogen, Inc., at 1 (Sept. 11, 1996) (stating that the “Trade Secrets Act, 18 U.S.C. 1905, prohibits FDA from publicly disclosing any trade secrets or confidential commercial information in the [BLA] file”).

¹⁷ 18 U.S.C. § 1905.

¹⁸ See, e.g., *Tri-Bio Labs., Inc. v. United States*, 836 F.2d 135, 141 n.7 (3d Cir. 1987) (stating that the Federal Trade Secrets Act prohibits FDA disclosure of “application data”).

disclosure provisions.¹⁹ FDA itself tracks the standard definition of a trade secret when it states that such 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.”²⁰ The agency takes a broad view of the meaning of a trade secret and has already rejected the argument that the Restatement (First) of Torts definition was too broad.²¹ FDA also exempts “[c]ommercial or financial information that is privileged or confidential,” meaning “valuable data or information which is used in one’s business and is of a type customarily held in strict confidence or regarded as privileged and not disclosed to any member of the public.”²² And in regulations specifically applicable to BLAs, FDA has reaffirmed that manufacturing data are trade secrets.²³

On this point it is instructive to trace the extent of FDA’s commitment to the protection of trade secrets in relationship to its own biologics approval processes. In 1974, FDA stated that “the safety and effectiveness information” in an approved BLA is “immediately available for public disclosure” absent a showing of “extraordinary circumstances.”²⁴ At that time, FDA took the position that release of this information could do no harm in light of the fact that each biologic had to be separately approved in an environment in which “me-too” or follow-on biologics did not exist. In that environment, the agency reasoned, the safety and effectiveness data had no economic value to competitors. As FDA wrote, “[s]uch data afford no competitive advantage because, unlike the situation with new drugs, no competitor can utilize it to gain approval for his product.”²⁵ Even with this regulation on the books for well over 30 years, I am aware of only one case in which a competitor successfully requested access to a company’s safety and effectiveness data. And in this one circumstance, which was factually quite unique, FDA sensed the risk of disclosure and thus broadly interpreted the “extraordinary circumstances” exception in a way that allowed it to limit the disclosure it was prepared to authorize.

The instructive precedent involved the request by Berlex Laboratories for data contained in Biogen’s approved BLA for Avonex (interferon beta-1a). Biogen had previously shared manufacturing data with Dr. Rentschler Biotechnologie pursuant to a joint venture agreement. Rentschler then entered into an affiliation arrangement with Berlex, a Biogen competitor. Biogen argued to FDA that Rentschler and Berlex should not be allowed to combine the manufacturing data they already possessed with the data contained in the Avonex BLA. The concern was that access to the broader data set would allow Rentschler and Berlex to free ride off Biogen in order to obtain approval for their competing product. FDA accepted this protest, noting that, if the information were released, “Berlex, Rentschler, or an affiliate could use data from the Avonex [BLA] to obtain approval of its own interferon-beta product in the United States or in foreign markets.”²⁶ Accordingly, FDA denied Berlex’s

¹⁹ 21 C.F.R. § 20.61(c).

²⁰ 21 C.F.R. § 20.61(a).

²¹ See 39 Fed. Reg. 44,602, 44,612-13 (Dec. 24, 1974) (rejecting an argument that the Restatement’s definition was inconsistent with promoting an “open society” and stating that “the Restatement definition of a trade secret should remain the basic guideline for application of this exemption from the Freedom of Information Act”).

²² 21 C.F.R. § 20.61(b), (c).

²³ 21 C.F.R. § 601.51(f).

²⁴ 21 C.F.R. § 601.51(e); 39 Fed. Reg. at 44,656.

²⁵ 39 Fed. Reg. at 44,641.

²⁶ Letter from Mark Raza, *supra* note 16 at 1.

initial release requests, and HHS thereafter upheld the denial. In the end, Berlex reformulated its request for a much more limited set of data that could not support the application for a competing product in the United States or abroad. FDA agreed to release this information, but only after allowing Biogen the opportunity to object specifically to any information that could be used to obtain approval of a competing product in either place.²⁷

In sum, until enactment of the Biosimilars Act in 2010, federal law did not authorize FDA to approve follow-on biologics applications, and the agency had followed a single clear principle with respect to trade secrets in pioneer BLAs: it had not relied on, or used, the trade secrets in one company's application—or even the fact that it had previously approved that application—to support approval of a competitor's application. Nor had FDA ever fully disclosed the trade secrets in an application to the public or a competitor. This intense concern with trade secret protection is, in fact, carried forward in the Biosimilars Act.

C. *Benefits of Trade Secret Protection*

One simple instinct that drives FDA's practice of protecting trade secrets is that health regulation should not distort the competitive balance between two firms that would otherwise exist in the absence of regulation. That position is widely accepted as a gold standard in the law of taxation, where it is generally understood that any selective differential tax on some, but not all, competitors could create an implicit subsidy for one party at the expense of another, thereby distorting the efficient decisions otherwise made by competitive firms.²⁸ Differential trade secret regulation poses the same risk. Thus every party should be—and prior to enactment of the Biosimilars Act was—entitled to create and preserve for itself whatever trade secrets it sees fit and to do so in perpetuity. The ability to create the trade secret does not exclude any rival party from making independent discovery of the information that is contained in someone else's trade secret or, indeed, from making a discovery of a new trade secret that is superior to a prior one.

Some have argued that innovators seeking to prevent FDA reliance on their trade secrets for the benefit of a competitor are merely trying to promote monopolies in the pharmaceutical market.²⁹ To see why this monopoly claim is erroneous, assume first we operate in a legal regime in which there is no FDA inspection of new biologics before they reach the marketplace. Under these circumstances the legal system can (as it presently does) allow for remedies in contract for breach of warranty, or in tort for the marketing of defective products. In this legal regime a whole raft of new competitors may enter instantaneously upon the expiration of any patent associated with the first product. Yet none can ever use a claim of health and safety to at any time gain access, directly or indirectly, to the trade secrets of the first entrant to the market. Any subsequent competitor can of course ask to license the trade secret technology from the initial competitor; it can seek the license of substitute trade secrets from third persons; it can develop its own portfolio of

²⁷ See *id.* at 2; see also Letter from William C. Brashares, Esq., Counsel to Biogen, Inc. to Mark Raza, Associate Chief Counsel, FDA (Sept. 18, 1996).

²⁸ See, e.g., *Arkansas Writers' Project, Inc. v. Ragland*, 481 U.S. 221, 233 (1987) (holding unconstitutional a differential tax scheme that exempted newspapers and religious, professional, trade, and sports journals, but not general interest magazines).

²⁹ See, e.g., Comments on behalf of Barr Laboratories, Inc., FDA Docket Nos. 2004P-0171, 2004P-0231, and 2003P-0176, at 1 (Nov. 12, 2004).

trade secrets. In some limited circumstances it can avail itself of reverse engineering; and, of course, it can take advantage of any products or processes that fall into the public domain after expiry of patent protection. In this scenario, therefore, the original entrant is entitled to keep its trade secrets in perpetuity under the ordinary rules that govern their use and protection under state law. Moreover, the original entrant remains free of the charge that it is seeking to perpetuate a monopoly or dominate the market.

The question then arises as to how this scenario should change once FDA is granted extensive statutory powers to inspect and license new pharmaceutical products, including biologics, for safety and efficacy. The answer is: not at all. FDA's power is granted for specific purposes, and its coercive power should be exercised only for the purposes for which it was granted. The power of FDA to review for safety and efficacy should be exercised only for that end. It should not be pressed into service as a roaming veto power over existing property rights, which government officials could use at will as the opening wedge to create a system of cross-subsidies between present and future market participants, upsetting the competitive balance within the marketplace. Hence it is proper for FDA to use the trade secrets submitted by an applicant to evaluate the safety of the applicant's products and manufacturing processes prior to sale. But if a competitor could not gain access to these trade secrets as of right in the absence of FDA, it should not be allowed access to the information as of right through the coercive intervention of FDA.

In evaluating the need to protect trade secrets, it is tempting to assume that the forced sharing of valuable information will create some net social benefit by allowing for the entry of a second useful product hard on the heels of the first. But the fallacy in that welfarist claim is that it assumes that the entry time for the original discoverer of the trade secret remains the same whether or not that company is allowed by the law to retain the exclusive use of its information. Once it is recognized that the creation and use of trade secret information is a two-staged process, that naïve one-dimensional position is no longer defensible. The effort to enhance the return for the second investor will necessarily reduce the return for the first investor, which in turn will delay or deter the introduction of innovative products. It must be constantly stressed that the difference between a market with *zero* products and a market with *one* product with a particular desirable attribute is far greater than the difference between a market with *one* product and a market with *two* products with that same attribute. The social gain of going from zero to one is far greater than the social gain of going from one to two. In other words, better there be a market that yields the holder of a trade secret a short-term monopoly than there be a market with no products at all in the relevant class. In more explicit terms, suppose that the initial product is delayed by one year because the holder of a trade secret fears the expropriation of its labor. During that one-year period, *no one* gets the benefit of that product. One year without a beneficial product counts as a far greater social loss than a wait, far down the road, of one more year for a second product in competition with the first. In light of this inexorable economic constraint, a forced sharing policy through FDA regulation would come at a very high social cost.

Protecting trade secrets, moreover, does not just benefit the parties who innovated them. Two other processes allow these gains to be spread throughout society. First, innovator use of trade secret information both lowers the cost and raises the benefit of the products produced with that innovation. These gains are captured at least in part by the general public in the form of a broader product menu at a

lower cost.³⁰ The public is perfectly able to internalize these gains even if it has no knowledge of the role that trade secrets have played in product development or price reduction. Either way, a company can increase its profits by lowering its price in order to attract additional sales units, over which it can then spread the fixed costs of production. The case is one where private and social incentives are in proper alignment. Second, any holder of a trade secret can use a combination of exclusive and nonexclusive licenses to allow the protected trade secret information to be shared by other parties under conditions of confidentiality. These conditions are now routinely enforced by courts, which well understand that all gains from trade with respect to trade secrets depend on shielding their content from third parties.³¹

In sum, then, FDA's longstanding and steady policy of neither disclosing, nor relying on (for the benefit of a third party), nor allowing third parties to rely on, the trade secrets in pioneer BLAs is fully defensible on fundamental social welfare grounds.

D. *The Biosimilars Act*

The trade secret status of the information presented in pioneer BLAs necessarily shapes the approval process for biosimilars. A biosimilar application must contain information demonstrating that the products are biosimilar, derived from (1) analytical studies demonstrating that the products are highly similar “notwithstanding minor differences in clinically inactive components,” (2) animal studies and (3) a clinical study or studies. Even so, FDA may waive submission of data in any of these categories, if the agency finds that the data are “unnecessary.”³² A biosimilar application will therefore likely contain substantially fewer data than the reference product application, and, indeed, under the terms of the statute, it could lack clinical data (or clinical efficacy data) altogether.

The biosimilar application must also contain “publicly-available information” regarding FDA’s “previous determination that the reference product is safe, pure and potent”³³ and may contain, at the applicant’s option, “additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.”³⁴ The limitation to *publicly available information* about the reference product—not confidential information in the innovator’s file or indeed any other file—is explicit.³⁵ Equally important, when FDA determines whether to approve a biosimilar application, it

³⁰ For the analogous situation with external patent gains, see William D. Nordhaus, Schumpeterian Profits in the American Economy: Theory and Measurement (Cowles Foundation Discussion Paper No. 1457 (April 2004)). Nordhaus concludes that “only a miniscule fraction of the social returns from technological advances over the 1948-2001 period was captured by producers, indicating that most of the benefits of technological change are passed on to consumers rather than captured by producers.” *Id.* at 1. The same logic applies to trade secrets. For further discussion, see ROBERT P. MERGES, PETER S. MENELL & MARK A. LEMLEY, *INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE* 10-13 (4th ed. 2006).

³¹ See, e.g., *Rockwell Graphic Sys., Inc. v. DEV Indus., Inc.*, 925 F.2d 174, 177 (7th Cir. 1991) (finding that a company that “disclosed its trade secrets to a limited number of outsiders for a particular purpose . . . did not forfeit trade secret protection. . . . On the contrary, such disclosure, which is often necessary to the efficient exploitation of a trade secret, imposes a duty of confidentiality on the part of the person to whom the disclosure is made.” (internal citations omitted)).

³² PHS § 351(k)(2)(A)(i)-(ii).

³³ PHS § 351(k)(2)(A)(iii)(I).

³⁴ PHS § 351(k)(2)(A)(iii)(II).

³⁵ This limitation contrasts with the approach taken in bills that were not enacted. For example, Representative Waxman introduced a bill that defined an “abbreviated biological product application” as “an abbreviated application for a license of a biological product that relies in part on *data or information in an application* for another biological product licensed under [section 351 of the PHS] or approved under section 505 of the [FDCA].” H.R. 1427, 111th Cong. § 2 (2009) (emphasis added).

may consider only “the information submitted in the application (or [a] supplement [to an application]).”³⁶ The question whether FDA is authorized to examine and consider the information in the reference product application, when reviewing the biosimilar application, should therefore be regarded as fully settled by the statute itself. FDA may not do so.

To be sure, the data in the biosimilar application support approval of the biosimilar precisely because they bridge the gap between the biosimilar and a product that FDA has previously approved on the basis of a full application. And, as discussed below, even indirect reliance on the data in the prior application constitutes a taking. But the distinction between approval on the basis of the agency’s prior *finding* that a reference product was safe and effective and approval on the basis of another company’s previously submitted *data* is critical from a trade secret perspective, and is, appropriately, a longstanding feature of FDA follow-on product approvals under section 505(b)(2) of the FDCA. Section 505(b)(2) was part of the Hatch-Waxman Act and, like the generic drug provision (and the Biosimilars Act), it permits use of a “reference” product. Unlike the generic drug provision, however, it does not require the proposed product to be the “same” as its reference product, and it permits the submission of clinical data. So in many respects, a 505(b)(2) application is analogous to a biosimilar application. In 1999, FDA explained that, in approving a 505(b)(2) application, it relies on its “previous finding of safety and/or effectiveness” for the reference drug.³⁷ Moreover, in litigation in 2004, the agency conceded that it may not actually look at the data in the reference product application when reviewing a 505(b)(2) application. The agency’s reasoning in that situation should apply equally to its review of biosimilar applications.

That case involved an application from Dr. Reddy’s Laboratories for approval of Amvaz (amlodipine maleate). Dr. Reddy’s sought to rely on Pfizer’s NDA for Norvasc (amlodipine besylate), a different salt of the same active moiety. Pfizer challenged FDA’s interpretation of section 505(b)(2) in general and its specific application to the Amvaz application in two citizen petitions.³⁸ Among other things, Pfizer argued that FDA could not use or rely on its nonpublic data to approve 505(b)(2) applications without violating federal statutes protecting trade secrets and confidential commercial information. In October 2003, FDA denied the petitions and approved the Dr. Reddy’s application. In its response to the citizen petitions, FDA emphasized that it relies on its public findings of safety and efficacy for approved drugs—not the nonpublic safety and effectiveness data for those drugs—to approve 505(b)(2) applications.³⁹ Pfizer then sued FDA to contest the approval.⁴⁰ While

³⁶ PHS § 351(k)(3).

³⁷ FDA, Draft Guidance for Industry: Applications Covered by Section 505(b)(2), at 2 (October 1999).

³⁸ Pfizer, Inc. & Pharmacia Corp., Citizen Petition, Docket No. FDA-2001-P-0369 (formerly 2001P-0323) (July 27, 2001); Pfizer Inc., Citizen Petition, Docket No. FDA-2002-P-0390 (formerly 2002P-0447) (Oct. 11, 2002).

³⁹ Letter from Janet Woodcock, M.D., Director, CDER, to Katherine M. Sanzo, Esq. and Lawrence S. Ganslaw, Esq., Morgan, Lewis & Bockius, LLP; Jeffrey B. Chasnow, Esq., Pfizer; Stephan E. Lawton, Esq. and Gillian R. Woollett, Ph.D., BIO; and William R. Rakoczy, Esq., Lord, Bissell & Brook LLP, Docket No. FDA-2003-P-0014 (formerly 2003P-0408), PDN 1, at 10 n. 14 (Oct. 14, 2003) (“FDA may rely on its earlier conclusions regarding safety and effectiveness to whatever extent the conclusions are appropriate for the drug under review in the 505(b)(2) application. Although reliance on an FDA finding of safety and effectiveness for an NDA is certainly indirect reliance on the data submitted in the original NDA, reliance on the conclusions supported by that data is not the same as manipulating those data to reach new conclusions not evident from the existing approval.”)

⁴⁰ Complaint, *Pfizer v. FDA*, No. 03-2346 (D.D.C. Nov. 13, 2003).

FDA was preparing the administrative record to submit to the court, the agency discovered that “a first line reviewer made reference to certain studies of Pfizer’s in the documentation of his review.”⁴¹ As a result, FDA stayed the Amvaz approval until the agency confirmed it was “based on data from appropriate sources.”⁴² FDA then moved to stay the court proceedings while it re-evaluated the basis for Amvaz’s approval.⁴³ Subsequently, Pfizer received a favorable ruling in related patent litigation that rendered the controversy over the Amvaz application moot.⁴⁴

Two years later, FDA further explained its approach when it approved a 505(b)(2) application for Omnitrope (recombinant somatropin) filed by Sandoz and rejected a series of citizen petitions that had been filed between 2001 and 2004.⁴⁵ Genentech’s petition, in particular, asked that FDA “refrain from taking steps that prejudice Genentech’s property rights in trade secret and confidential commercial data and information provided to the agency for the limited purpose of reviewing and approving Genentech’s products.”⁴⁶ The gist of the argument was that any “direct or indirect” use of that information was improper. FDA responded to the Genentech petition, as well as two other pending petitions that raised similar issues, in 2006. It focused on the specific question of what approval of an application under section 505(b)(2) entailed. According to the agency, its *finding* of safety and effectiveness for a drug is not confidential commercial or trade secret information, but sponsors are nonetheless “entitled to expect that information in the application will be protected” under FDA regulations when it is trade secret or confidential commercial information.⁴⁷ FDA also assured the petitioners that it did not rely on or reference any data other than Sandoz’s in approving the Omnitrope application. Therefore, it wrote, “FDA has not compromised the protections afforded under the law to [innovative] data and information.”⁴⁸

Based on the plain language of the Biosimilars Act, the agency’s statements in the Norvasc case, and the agency’s response to the 505(b)(2) citizen petitions, it is both indisputable and indispensable that the Biosimilars Act, read as a whole, flatly precludes FDA from reviewing and considering the trade secret information in an

⁴¹ Federal Defendants’ Motion for Stay of Proceedings at 3, *Pfizer v. FDA*, No. 03-2346 (D.D.C. Feb. 18, 2004).

⁴² FDA, Administrative Stay of Action Re: NDA 21-435 (Feb. 4, 2004).

⁴³ Federal Defendants’ Motion for Stay of Proceedings, *Pfizer v. FDA*, No. 03-2346 (D.D.C. Feb. 18, 2004).

⁴⁴ Unopposed Motion for Dismissal Without Prejudice, *Pfizer v. FDA*, No. 03-2346 (D.D.C. Sept. 30, 2005).

⁴⁵ Pfizer and Pharmacia asked that FDA make it clear that it could not rely on nonpublic proprietary information in an NDA to approve an application submitted under section 505(b)(2), and that it not rely on or otherwise use nonpublic proprietary information in an NDA to approve an application submitted under section 505(b)(2). Letter from Kathleen M. Sanzo and Lawrence S. Ganslaw, Morgan, Lewis & Bockius, LLP, to FDA, Docket No. FDA-2001-P-0369 (formerly 2001P-0323) (July 27, 2001). BIO asked, among other things, that FDA withdraw the draft guidance on applications under section 505(b)(2). BIO, Citizen Petition, Docket No. FDA-2003-P-0003 (formerly 2003P-0176) (Apr. 23, 2003). Genentech asked, among other things, that FDA refrain from approving a biotechnology-derived product characterized as “similar to” or “the same as” a Genentech product, where the application relied in whole or in part on trade secrets or confidential commercial information belonging to Genentech. Letter from Stephen G. Juelsgaard, Genentech, Inc. to FDA, Docket No. FDA-2004-P-0214 (formerly 2004P-0171) (Apr. 8, 2004).

⁴⁶ Letter from Stephen G. Juelsgaard, Genentech, Inc. to FDA, Docket No. FDA-2004-P-0214 (formerly 2004P-0171) (Apr. 8, 2004), at 2.

⁴⁷ Letter of Steven K. Galson, M.D., M.P.H., Director, CDER, to Kathleen M. Sanzo, Esq., Morgan, Lewis & Bockius LLP; Stephan E. Lawton, Esq., BIO; and Stephen G. Juelsgaard, Esq., Genentech, Docket Nos. FDA 2004P-0231, 2003P-0176, 2004P-0171, 2004N-0355 (May 30, 2006), at 38.

⁴⁸ *Id.*

incumbent's file for the benefit of its competitors.⁴⁹ That guarantee should be rock solid wholly apart from any constitutional guarantee of the protection of trade secrets unless compensation is received for their use by the government or a competitor.

Of course, any conclusion that FDA is prohibited from looking at the BLA data under the Biosimilars Act and agency regulations and practice does not end the inquiry. Even indirect reliance on these trade secrets by FDA when it approves a biosimilar has serious constitutional implications. FDA's act of relying on a prior approval of a BLA in order to license a follow-on competitor constitutes an unconstitutional taking if done without the provision of just compensation to the BLA holder. The public finding of safety, purity, and potency is not a trade secret itself, but this finding has value solely because its soundness is directly attributable to trade secrets belonging to the pioneer. And the finding—just like the underlying data were they not protected—gives biosimilar applicants a significant shortcut. It is therefore necessarily the case that FDA's reliance on the prior finding of safety, purity and potency in approving a biosimilar application appropriates the underlying trade secrets for the benefit of the biosimilar applicant. That partial loss of exclusive property rights in trade secrets thus triggers the application of the Takings Clause just as if the agency were accessing or releasing the data. The extent of the government taking may differ in the two cases, but that difference goes only to the question of how much compensation is required. It does not let the government sidestep the constitutional implications altogether.

II. ANALYSIS UNDER THE TAKINGS CLAUSE

A. *Basic Principles of Takings Law*

The prior section gives rise to the important and difficult question whether the Biosimilars Act provides sufficient constitutional protection for the trade secrets submitted by biological product innovators. In order to undertake this analysis, it is necessary to begin with a general overview of takings law, starting from the full text of the Takings Clause of the Fifth Amendment: “nor shall private property be taken for public use without just compensation.” As drafted, this provision applies to all forms of private property, whether tangible or intangible. In addition, the clause has always operated as a guarantee against actions of the federal government that take this property, even when the rights in question are created under state law, as is the case with trade secrets.⁵⁰

⁴⁹ There is, however, one situation in which FDA may—indeed must—take into account information from one application when reviewing a second application. In light of the fact that FDA may not approve a product that is unsafe (and must take steps to remove a product from the market that is found to be unsafe following its approval), it makes sense for the agency to take known safety concerns with a molecule into account when evaluating new applications for that, or a related, molecule—even when those safety concerns are found in proprietary data files. There is, after all, no competitive advantage for a second applicant who must devise his own response to a safety problem apparent from the innovator's file, in order to obtain approval of his own product. The correct social response uses that negative information to be sure that the new applicant attains the relevant safety standards. At the same time, however, the pioneer's solutions to the safety problem may not be used to aid the biosimilar applicant, unless they are either publicly available to FDA or licensed to the biosimilar applicant. If the pioneer redesigned its product to eliminate the concern, the biosimilar rival should not have access to that redesign effort, lest it give the late entrant a comparative advantage.

⁵⁰ See, e.g., *Ruckelshaus v. Monsanto*, 467 U.S. 986, 1001 (1984) (stating that “[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) (quoting *Board of Regents v. Roth*, 408 U.S. 564, 577 (1972)))).

In dealing with these issues, moreover, it is clear that the federal government cannot redefine the content of relevant property interests in order to avoid the reach of the Takings Clause. As the Supreme Court noted in *Webb's Fabulous Pharmacies*, “a State, by *ipse dixit*, may not transform private property into public property without compensation. . . . This is the very kind of thing that the Taking Clause of the Fifth Amendment was meant to prevent. That clause stands as a shield against the arbitrary use of governmental power.”⁵¹ The same restrictions surely apply to any effort of the federal government to alter the content of state law property rights. A simple decree that information may be used by competitors counts as an *ipse dixit*.

Matters get complicated because the conventional categories of takings law do not apply easily to the various forms of intellectual property, including trade secrets. The regnant legal distinction in takings law is between “physical” and “regulatory” takings. The first of these covers the *occupation* of land by the government or by private parties acting under its authorization. Physical takings include both cases where the government completely dispossesses the owner from the land (such as where state law requires a landlord to permit a cable company to physically occupy a portion of the building with television cables⁵²) and cases where it requires the owner to surrender his exclusive right of possession by sharing the property with some other party (such as where the federal government requires a marina owner to grant public access to the marina⁵³). Regulatory takings are those cases that leave an owner in exclusive possession of his property but *restrict* how the owner may use or dispose of the property (such as prohibiting a land owner from building structures on purchased plots of land⁵⁴).

The importance of this distinction lies in the level of scrutiny that the courts give to these two different forms of government action. The Supreme Court now imposes a virtual *per se* obligation upon the government to compensate a landowner deprived of exclusive possession of his property, even if he is required only to share that property with the public at large.⁵⁵ But for government actions that only restrict the owner’s right to use, develop or alienate the property in question, the Court—in *Penn Central Transportation Co. v. City of New York*—directed a more nuanced inquiry into: (1) whether the government action may be properly said to interfere with “the reasonable investment-backed expectation” of the owner; (2) the economic impact of the regulation on the owner; and (3) the character of the government action.⁵⁶ In *Penn Central*, the relevant government action was the

⁵¹ 449 U.S. at 164.

⁵² *Loretto v. TelePrompeter Manhattan CATV Corp.*, 458 U.S. 419 (1982).

⁵³ *Kaiser Aetna v. United States*, 444 U.S. 164 (1979).

⁵⁴ *Lucas v. South Carolina Coastal Comm'n*, 505 U.S. 1003 (1992).

⁵⁵ See *Loretto*, 458 U.S. at 426 (“We conclude that a permanent physical occupation authorized by government is a taking without regard to the public interests that it may serve. Our constitutional history confirms the rule, recent cases do not question it, and the purposes of the Takings Clause compel its retention.”); see also *id.* at 442-56 (Blackmun, J., dissenting) (characterizing the *Loretto* majority as having adopted a *per se* takings rule with respect to physical occupations); *Philip Morris v. Reilly*, 312 F.3d 24, 35 (1st Cir. 2002) (describing *Loretto* as “a case which announced a *per se* rule in a physical takings context.”).

⁵⁶ *Penn Central Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978). In *Loretto*, the Court sought to resolve the evident tension between that case and *Penn Central*, by holding that in thinking about the *Penn Central* factors it has “long considered a physical intrusion by government to be a property restriction of an unusually serious character for purposes of the Takings Clause. Our cases further establish that when the physical intrusion reaches the extreme form of a permanent physical occupation, a taking has occurred. In such a case, ‘the character of the government action’ not only is an important factor in resolving whether the action works a taking but also is determinative.” 458 U.S. at 426.

City of New York's refusal to permit a landowner to build an office building above a historic landmark. The Court's three-part inquiry for regulatory takings affords far more leeway to the government than the virtual *per se* rule for violations of the right of exclusive possession. Indeed, it is generally viewed as allowing regulatory takings to be judged by the low constitutional standard of rational basis review, according to which any respectable public reason for imposing the limitation will insulate the state from the duty to compensate the property owner, no matter how many weighty reasons may be found on the other side.

Which approach applies depends on how one characterizes the government action (i.e., on whether the action is viewed as an utter dispossession or merely as a restriction and regulation). So, for example, in *Penn Central*, the Supreme Court insisted that the parcel of land on which the Penn Central Terminal sat should be treated as a whole, such that the landowner who retained occupation of the ground for operation of a terminal could complain only of the loss of rights to develop in the airspace above the footprint under the regulatory takings framework. So long as the landowner can cover the costs of the operation of the terminal facility, the loss of development rights in the airspace above the land does not count under current law as a taking, given the public interest in preserving the openness of the neighborhood.

The *Penn Central* ruling, which forms the basis of takings analysis with respect to trade secrets, is fraught with ambiguity that has not been resolved in the 33 years since the decision came down. One serious difficulty is that, even within its original context of land use, the decision gives no guidance as to what should be done if the landowner does not have a facility currently in place that covers its cost. That could happen if the current structure was losing money on a plot of land where the development rights could be worth a small fortune. The Court's opinion also offers no insight into what would have been decided if the air rights had been sold off long before the preservation ordinance was adopted. In that situation, the owner of the air rights would suffer a complete loss of its state law property interest, as it would receive no compensation—simply because the party retaining possession of the structure on the land was able to operate his plant as before. The Supreme Court has yet to resolve these questions authoritatively. The only clear subsequent Supreme Court ruling is that a refusal to allow any development of raw land counts as a compensable taking.⁵⁷ What compensation is owing when some use is allowed is still a question for which there is still today no firm answer.

The line between physical and regulatory takings may be a fixed feature of current law, but neither the Supreme Court nor a raft of academic commentators has been able to demonstrate its intellectual coherence. The ordinary law of property works precisely because it offers full protection to all parties who hold divided interests. Full protection for divided interests makes it possible for people to increase the value of property by dividing it among different parties, if the total value of the divided interests is greater than the value of the land as a whole by an amount that exceeds the transaction costs needed to create these multiple interests. It is the failure of the public law to track this private law that leads to a deep intellectual incoherence that will remain unresolved so long as the difference between physical and regulatory takings is said to justify the application of different levels of review.

Much of the doctrinal confusion stems from Justice Brennan's casual use of the term "investment-backed expectations" as a key component of the *Penn Central*

⁵⁷ *Lucas*, 505 U.S. 1003.

analysis.⁵⁸ This test is widely disparaged as circular, on the ground that no one can form reasonable investment-backed expectations once the law is announced that no one is entitled to have any expectations at all.⁵⁹ If the circular test is accepted, the notion of private property comes to an end. Now that everyone has *notice* of the prospective legal rule (eviscerating property rights), no one is entitled to any legal protection for their property interests. As I will explain in section II.C.2, subsequent decisions have made it clear that the doctrine of unconstitutional conditions places important limitations on the judicial inquiry into “investment-backed expectations”—limitations that, in turn, affect how FDA may apply the Biosimilars Act.

B. *Application to Intellectual Property*

The facile substitution of “investment-backed expectations” for private property has also led to an immense confusion about the constitutional protection that should be afforded to trade secrets. The first question to ask is whether a decision to force the sharing of trade secrets with competitors should be treated as a physical taking or a regulatory taking.⁶⁰ In *one* sense this question seems to answer itself. There can, by definition, be no physical taking of any interest in intellectual property. But there must be, even under current law, at least some instances of *per se* takings in the domain of intellectual property rights. Thus suppose that the United States announced that a trade secret or patent owner could no longer practice his trade secret or patent, which was also made available to any and all comers at will. There is no question that this decision would count as a *per se* taking for which compensation was required because *all* the intellectual property rights vested under state law (for trade secrets) or federal law (for patents) would have been stripped away from the owner. If that double whammy (whereby others could use the intellectual property, when its former owner could not) did not count as a *per se* taking, it is not clear that any form of government action with respect to intellectual property would ever be subject to a *per se* rule. This extreme example establishes at least this result: it is possible to find cases of *per se* takings in the world of intellectual property. Thus, physical dispossession is not a strict prerequisite for the application of the *per se* compensation rule.

One can, in fact, draw relevant analogies between physical and intellectual property. In the case of physical property, the law uses a virtual *per se* rule even where the owner is not forced off his own property, so long as the owner is required to surrender *exclusive* possession of his own property by *sharing* its use with an outsider. In *Kaiser Aetna v. United States*, for example, the owner of a marina (Kaiser Aetna) was told that it could not connect to public waters unless it opened up its marina for the use of the public at large. The Court held that the United States could proceed only if it compensated the owner for the loss of the exclusive use of its marina.⁶¹ In *Loretto v. TelePrompster*, the Supreme Court required the state to pay compensation if it wanted to require that a cable box be placed on the roof of the apartment building owned by Loretto for the benefit of the cable company

⁵⁸ See 438 U.S. at 124, 127, 130; see also Frank I. Michelman, *Property, Utility, and Fairness: Comments on the Ethical Foundations of “Just Compensation” Law*, 80 HARV. L. REV. 1165, 1229-34 (1967).

⁵⁹ For further discussion, see Richard A. Epstein, *Lucas v. South Carolina Coastal Council: A Tangled Web of Expectations*, 45 STAN. L. REV. 1369 (1993).

⁶⁰ See Richard A. Epstein, *The Constitutional Protection of Trade Secrets under the Takings Clause*, 71 U. CHI. L. REV. 57 (2004), for a further development of this theme.

⁶¹ *Kaiser Aetna*, 444 U.S. 164.

and its customers.⁶² Both cases unquestionably satisfied the public use requirement, meaning that a taking could occur, provided the state supplied just compensation.⁶³ But compensation was required under the *per se* rule. Any government conversion of private to common property thus counts as a *per se* taking.

That same analysis applies to intellectual property. As with tangible property, there is—as a matter of first principles—no categorical distinction between restricting the owner’s use of his own trade secrets, on the one hand, and permitting the use of those trade secrets by others, on the other hand. The only material distinctions between these two types of government action should relate to the different level of compensation required for the losses sustained in the two settings. Current law, however, incorrectly rejects this unitary vision of takings law. Instead it starts from the fundamental premise that the distinction between physical and regulatory takings in land use cases must carry over to the constitutional protection of intellectual property, including trade secrets. On this occasion, I shall not attack the major premise of a two-tier system of protection for all forms of private property.⁶⁴ Instead the sole task is how best to apply to intellectual property (here, the trade secrets in pioneer BLAs) the current law of takings that accepts the distinction between physical and regulatory takings.

One possibility is to conclude that *per se* compensation rules should never be applied in any intellectual property context, on the ground that intellectual property is by its very nature not susceptible to physical occupation.⁶⁵ But that contrived view overrates the importance of physical possession in a world that defines private property as dealing with the exclusive rights of use. Although it is impossible to have exclusive physical possession of intellectual property, it is strictly necessary to have the right to exclude others from use of intellectual property. Indeed, the exclusive right to use is the unifying feature of patents, copyrights, trademarks and trade secret law.

In light of this fundamental attribute of intellectual property, the constitutional jurisprudence with respect to intellectual property distinguishes between the forced sharing of a trade secret with others, on the one hand, and the restriction on use of a trade secret by its owner, on the other hand. The former is subject to *per se* rules of *Kaiser Aetna* and *Loretto*, so that compensation necessarily is owing when the distinctive feature of exclusive use is lost. In the latter situation, where the state says that a trade secret may not be used in certain lines of business while allowing it in others, under current law the more forgiving test of *Penn Central* applies. One asks the court to balance the loss to the trade secret owner of unrestricted use with the strength of the government interest advanced to justify the restriction.

In my view, the action taken by FDA 12 years after approval of an innovative application—indirect reliance on the innovator’s trade secrets, for the benefit of the innovator’s competitor—constitutes a *per se*, albeit partial, taking for which compensation is required under *Loretto* and *Kaiser Aetna* because the innovator has lost the right to exclusive use of those trade secrets. As explained in the next section, however, even under the lower standard of regulatory takings law, a taking occurs and compensation is required (although *prospectively*, a generally applicable and negotiated statutory “bargain” may suffice in lieu of monetary compensation).

⁶² *Loretto*, 458 U.S. 419.

⁶³ The government may not take property from one private party solely for the benefit of a second private party, even if it pays compensation.

⁶⁴ See Epstein, *supra* note 60.

⁶⁵ See Epstein, *supra* note 60 and accompanying text.

C. *Analysis of the Biosimilars Act*

1. *Monsanto*

The lawfulness of the handling of trade secrets in the Biosimilars Act turns on a close examination of the Supreme Court's decision in *Ruckelshaus v. Monsanto Co.*⁶⁶ This case examined the lawfulness of the use and disclosure of trade secrets submitted in applications under three sequential iterations of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).⁶⁷

The original 1947 version of FIFRA was largely a labeling statute. Under it, the Department of Agriculture was prohibited from disclosing "any information relative to formulas of products."⁶⁸ In contrast, the act was "silent with respect to the disclosure of any of the health and safety data submitted with an application."⁶⁹ The government's practice was not to publicly disclose any health and safety information, although it is not clear whether the government adopted this position for constitutional or prudential reasons.⁷⁰

The implicit norm of nondisclosure prior to 1972 became the legal requirement under the 1972 FIFRA Amendments,⁷¹ which remained in effect until 1978. The 1972 Amendments transferred control of the program to the Environmental Protection Agency (EPA). With that transfer of control came a major expansion in government mission. No longer was FIFRA concerned solely with labeling. As the Supreme Court wrote, the amended "FIFRA regulated the use, as well as the sale and labeling, of pesticides; regulated pesticides produced and sold in both intrastate and interstate commerce; provided for review, cancellation, and suspension of registration; and gave EPA greater enforcement authority."⁷² Congress also added a new criterion for registration: that EPA determine that the pesticide will not cause "unreasonable adverse effects on the environment."⁷³ This broader power to collect information brought with it explicit statutory protection for "trade secrets or commercial or financial information."⁷⁴ Specifically, the statute expressly prohibited EPA from disclosing any "trade secrets or commercial or financial information" and from granting a registration to a second applicant on the basis of a first applicant's trade secret, unless compensation was paid.⁷⁵ Further, in litigation applicants were able to persuade the courts that the statutory "trade secret" provision applied to all information protected under section 757 of the Restatement of Torts.⁷⁶ This constellation of provisions meant that the 1972 scheme provided the holders of trade secrets with broad and strong protections.

The statutory framework changed again in 1978 with the addition of explicit use and disclosure provisions. Subject to some narrow exceptions for product formulas and manufacturing processes, the 1978 Act required disclosure of "health, safety, and environmental data" in pesticide registration applications to qualified requesters.⁷⁷

⁶⁶ 467 U.S. 986.

⁶⁷ *Id.* at 990-97.

⁶⁸ *Id.* at 991.

⁶⁹ *Id.*

⁷⁰ *Id.* 991 n.3.

⁷¹ *Id.* at 992.

⁷² *Id.* at 991-92.

⁷³ *Id.* at 992.

⁷⁴ *Id.*

⁷⁵ *Id.*

⁷⁶ *Id.* at 993; see also *Mobay Chem. Corp. v. Costle*, 447 F.Supp. 811, 824-26 (W.D. Mo. 1978); *Chevron Chem. Co. v. Costle*, 443 F.Supp. 1024, 1031-32 (N.D. Cal. 1978).

⁷⁷ *Monsanto*, 467 U.S. at 995-96.

For pesticides registered after September 30, 1978, the 1978 Act supplied a 10-year period of exclusive use for data supporting new active ingredients, following which those data could be used free of charge by other companies to support their own registrations.⁷⁸ All other data (i.e., non-active ingredient data) submitted after December 31, 1969 were entitled to a 15-year period during which they could be cited and considered in support of another application, provided compensation was paid to the original submitter.⁷⁹ After 15 years, the data could be used without compensation. Congress effectively asserted a police power justification for forcing the sharing of information to those who could use it most, competitors.

The task before the Supreme Court was, in part, to articulate the constitutional framework needed to evaluate these three sequential schemes. To answer this question, the Court started with the view that trade secret data are property and thus protected under the Takings Clause.⁸⁰ One might have thought that this determination would have ended the analysis, on the theory that any government-mandated sharing of a trade secret deprives its owner of the exclusive right to the information. But the Supreme Court eschewed any *per se* rule. Instead, it held that the level of constitutional protection afforded depended on the “investment-backed expectations” that the scheme extended to any individual firm at the time its data were filed. In other words, the *Monsanto* Court applied the lower regulatory takings standard of *Penn Central*.

The Court concluded that a firm’s investment-backed expectations were shaped exclusively by the legal framework in effect at the time the data were submitted to EPA. Most relevant to our consideration of the Biosimilars Act is the conclusion that Monsanto—as the holder of the trade secrets at issue—was entitled to full protection for the data that it submitted during the 1972 to 1978 period. The language of the Court could not be clearer:

Thus, with respect to trade secrets submitted under the statutory regime in force between the time of the adoption of the 1972 amendments and the adoption of the 1978 amendments, the Federal Government had explicitly guaranteed to Monsanto and other registration applicants an extensive measure of confidentiality and exclusive use. This explicit governmental guarantee formed the basis of a reasonable investment-backed expectation.⁸¹

With respect to data submitted to FDA by biological innovators prior to enactment of the Biosimilars Act, this portion of the *Monsanto* decision is squarely on point. As explained earlier,⁸² state and federal law and longstanding FDA practice conferred robust protection to the trade secrets in applications submitted under section 351(a) of the PHSA prior to the passage of the Biosimilars Act.⁸³ From the time FDA received authority to administer the biologics licensing scheme in 1972 to enactment of the Biosimilars Act in 2010, the agency maintained that it did not have legal authority or a scientific basis to approve follow-on or generic versions of

⁷⁸ *Id.* at 994.

⁷⁹ *Id.*

⁸⁰ *Id.* at 1003-04.

⁸¹ *Id.* at 1011.

⁸² See *supra* section I.B.

⁸³ See also *Tri-Bio Labs., Inc. v. United States*, 836 F.2d 135, 140-41 (3d Cir. 1987) (“Although in *Monsanto* the governmental guarantee against internal agency use was grounded on the statute, we are convinced that this agency regulation provided pioneer animal drug manufacturers with an equally reasonable investment-backed expectation that the FDA would refrain from nonconsensual use of research material.”)

biological products. For example, in 1974, the agency recognized that because each biologic must be demonstrated to be safe, pure and potent “a biologics license is under no circumstances granted by the Food and Drug Administration to a second manufacturer based upon published or otherwise publicly available data and information on another manufacturer’s version of the same product. . . . There is no such thing as a ‘me-too’ biologic.”⁸⁴ Throughout the 1990s and 2000s, agency officials repeatedly confirmed that FDA did not have the authority to approve follow-on versions of biologics. For example, in 1998, Commissioner of Food and Drugs nominee Jane Henney testified before Congress that the agency had “no plans to allow submissions of abbreviated applications for biological products.”⁸⁵

Prior to enactment of the Biosimilars Act, innovative applicants submitted their data under a scheme in which the data would not—and could not—be used to facilitate market entry by a follow-on competitor. These applicants had investment-backed expectations—based in statute, FDA regulations, and longstanding FDA practice—that their data would not be used or relied on by the agency, directly or indirectly, for the purpose of approving competitors. Taking these trade secrets for the benefit of a competitor thus requires just compensation in order to avoid a constitutional violation. Moreover, these pre-enactment applicants were not able to weigh the alternative statutory bargain (*quid pro quo*) of the Biosimilars Act when submitting their data, so this general deal may not be imposed by fiat retroactively. This means that for these BLAs, case-by-case assessment of just compensation under the Fifth Amendment is needed. In short, then, while I would apply the *per se* takings rule that requires just compensation regardless of any inquiry into investment-backed expectations, even under the lower standard of the *Penn Central* and *Monsanto* cases, all property interests in pre-enactment BLAs are entitled to full protection and may not be “taken” at year 12 without just compensation, which would need to be determined on a case-by-case basis.

In fact, however, FDA and the courts need not consider case-by-case compensation, a task that has proven notoriously difficult.⁸⁶ This is because of the well-established rule that statutes do not operate retroactively unless Congress expressly dictates that they should. In the leading case of *Landgraf v. USI Film Products*, the Court set forth its presumption against the retroactive application of any statute in the absence of “clear evidence of congressional intent” otherwise. Accordingly, it held that a portion of the Civil Rights Act of 1991 did not apply retroactively to claims arising before its enactment.⁸⁷ Retroactive application of legislation is “disfavored,” the Court explained, and “the presumption against retroactive legislation is deeply rooted in our jurisprudence,”⁸⁸ particularly with regard to property rights, a “matter[] in which predictability and stability [is] of prime importance.”⁸⁹ Indeed, “settled expectations should not be lightly disrupted.”⁹⁰ Private parties are routinely required to make extensive investments over time. Their planning is often upended if the rules that are put into place today are not the same ones that are applied tomorrow.

⁸⁴ 39 Fed. Reg. at 44,641.

⁸⁵ *Henney FDA Will Be “Open, Timely and Responsive,” Nominee Says*, The Pink Sheet (Aug. 31, 1998); 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”).

⁸⁶ See, e.g., Clynn S. Lunney, Jr., *Compensation for Takings: How Much Is Just?* 42 CATH. U. L. REV. 721 (1993).

⁸⁷ 511 U.S. 244 (1994).

⁸⁸ *Id.* at 265, 268.

⁸⁹ *Id.* at 271.

⁹⁰ *Id.* at 265.

Under current law, the first question in a retroactivity analysis asks whether the statute, if applied, would operate retroactively by “attach[ing] new legal consequences to events completed before its enactment.”⁹¹ In this case, applying the Biosimilars Act to the data in BLAs submitted before enactment (i.e., stripping away all of the firm pre-Act protections for these data) would certainly attach new legal consequences to events completed before enactment. The relevant event would be the submission of the data to FDA. The legal consequences are the partial, but still significant, loss of trade secrets rights for the benefit of a competitor at year 12. Before the Biosimilars Act, FDA did not have the authority to rely on its prior finding of safety, purity and potency to approve a follow-on biologic. Accordingly, the submission of data carried with it no potential adverse consequence to long-standing trade secret protection. These legal consequences would certainly change if the Biosimilars Act applied to these pre-enactment data.

The issue of retroactivity bears a close relationship to the Court’s use of reasonable investment-backed expectations in its *Penn Central* analysis. Thus in *Landgraf*, the Court explained that “familiar considerations of fair notice, reasonable reliance, and settled expectations offer sound guidance” in determining whether a statute would operate retroactively.⁹² As discussed above, given FDA law and longstanding agency practice, biologic innovators had settled expectations that their data would not be used to support the approval of a follow-on competitor. Accordingly, these innovators reasonably relied on this expectation when submitting their data to FDA.

Once it has been determined that application of a statute to a particular instance or group of events would entail applying the statute retroactively, the next question becomes whether Congress has “made clear its intent” that the statute so operate.⁹³ If it did not, a court may not apply the statute retroactively. The Court has previously looked to “clear, strong, and imperative language requiring retroactive application” and “language so clear and positive as to leave no room to doubt that such was the intention of the legislature.”⁹⁴ In the instant case, there is *no* evidence in the statutory language itself that Congress intended the Biosimilars Act to apply retroactively, let alone clear evidence. Wholly apart from any constitutional challenges to its retroactive application, therefore, it appears that the Biosimilars Act does not under *Landgraf* apply retroactively to *any* data submitted prior to its enactment.

2. Unconstitutional Conditions

As stated previously, I accept for the purposes of this article the application of the lower regulatory takings standard (i.e., the three-part test from *Penn Central*, which was later applied in *Monsanto*) to post-Biosimilars Act BLAs. But a portion of the *Monsanto* Court’s opinion suggests that Congress could prospectively “take” pioneer trade secrets, simply by announcing that henceforth trade secrets submitted to FDA in an application for approval of a biologic will be in some sense “taken”—without compensation—12 years after licensure. This approach is wrong as a matter of constitutional theory because it fails to take into consideration the doctrine of unconstitutional conditions. The application of this doctrine, moreover, is far from fanciful for it has become quite clear that both the Supreme Court and the Courts of Appeal have deep misgivings about this part of *Monsanto*.

⁹¹ *Id.* at 270.

⁹² *Id.*

⁹³ *Id.*

⁹⁴ *Id.* at 270, 272 (internal citations omitted).

The origin of this problem is the *Monsanto* Court's interpretation of the investment-backed expectations prong from *Penn Central* with regard to the pre-1972 and post-1978 trade secrets submitted to EPA (i.e., trade secrets that were not submitted under an explicit guarantee of confidentiality). With respect to those trade secrets, the Court found under an application of the *Penn Central* test that there was no investment-backed expectation of confidentiality. In the Court's view, the lack of this expectation meant the government could use the information as it wished, wholly without regard to any putative constitutional constraint. In other words, any party that submitted trade secrets with notice of the possible uses to which the EPA (or competitors) could put them no longer had any reasonable investment-backed expectation that the information would be kept confidential. Thus, the owner of a trade secret has only one way to keep the information private: keep its own product off the U.S. market—which necessarily deprives it of any economic return inside the United States.

Two passages in *Monsanto* make this point most forcibly. First, for the post-1978 period, Justice Blackmun wrote that “Monsanto could not have had a reasonable, investment-backed expectation that EPA would keep the data confidential beyond the limits prescribed in the amended statute itself.”⁹⁵ Specifically, “Monsanto was on notice of the manner in which EPA was authorized to use and disclose any data turned over to it by an applicant for registration.”⁹⁶ Thus, “[i]f, despite the data-consideration and data-disclosure provisions in the statute, Monsanto chose to submit the requisite data in order to receive a registration, it can 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 the submission.”⁹⁷ Second, for applications submitted before 1972, Justice Blackmun wrote, “the Trade Secrets Act provided no basis for a reasonable investment-backed expectation that data submitted to EPA would remain confidential.”⁹⁸ These quotations are, not surprisingly, heavily relied on in the academic literature that approves of this part of the *Monsanto* decision.⁹⁹

Justice Blackmun, however, makes a major conceptual mistake by insisting that the level of constitutional protection of trade secrets depends exclusively on the will of Congress. Moreover, in this regard, the distinction between the virtual *per se* rule of *Loretto* and *Kaiser Aetna* and the nuanced balancing test under *Penn Central* does not matter. In either case, the weakness of the *Monsanto* Court's reasoning regarding the pre-1972 and post-1978 doctrines turn on its failure to consider the law of unconstitutional conditions, which Justice Blackmun misconstrues when he writes:

Monsanto argues that the statute's requirement that a submitter give up its property interest in the data constitutes placing an unconstitutional condition on the right to a valuable Government benefit. But Monsanto has not challenged the ability of the Federal Government to regulate the marketing and use of pesticides. Nor could Monsanto successfully make such a challenge, for such restrictions are the burdens we all must bear in exchange for “the advantage of living and doing business in a civilized

⁹⁵ 467 U.S. at 1006.

⁹⁶ *Id.*

⁹⁷ *Id.* at 1006-07.

⁹⁸ *Id.* at 1009.

⁹⁹ See, e.g., John C. Yoo, *Takings Issues in the Approval of Generic Biologics*, 60 FOOD & DRUG L.J. 33, 38-39 (2005); see also Barr Comments, *supra* note 29, at 11-13.

community.” *Andrus v. Allard*, 444 U.S. 51, 67 (1979) . . . This is particularly true in an area, such as pesticide sale and use, that has long been the source of public concern and the subject of government regulation. That Monsanto is willing to bear this burden in exchange for the ability to market pesticides in this country is evidenced by the fact that it has continued to expand its research and development and to submit data to EPA despite the enactment of the 1978 amendments to FIFRA . . .¹⁰⁰

As written, the quoted passages make it appear that Congress may impose any condition on the exercise of any constitutional right.¹⁰¹ Certainly where Congress has explicitly granted trade secret protection, this mandate controls (as it did for data submitted to EPA between 1972 and 1978).¹⁰² But the converse does not help. It does not follow that once Congress removes its mantle of protection around trade secrets that its provision of “notice” means that a taking of trade secrets can never take place. As a general proposition, that has never been the law. To see why, return for a moment to *Kaiser Aetna*. Although that case was not cast explicitly as an unconstitutional conditions case, it surely was one. The case did not arise because the United States sought to commandeer the right to use Kaiser Aetna’s self-contained marina for public purposes. Rather, it arose because Kaiser Aetna requested that boats moored in its marina have access to the navigable waters of the United States, and the United States sought to condition this access from its arena on opening the marina to public access. Without the doctrine of unconstitutional conditions, the United States could sidestep the takings issue altogether. All it needed to do was respond to Kaiser Aetna as follows: “You own your marina, and we are the exclusive owners of the public waters. Hence we propose this bargain: if you allow the public to use your marina, we will allow your clients to use public waters. Take it or leave it. Otherwise your boats can stay safely moored at home.”

Note the staggering implications that follow if this bargaining is viewed as acceptable. Every plot of land in the United States needs unimpeded access to public highways and public waters. The entire Takings Clause could be nullified if the state were allowed to impose bargains like this, saying, “We will allow you to enter public roads only if you deed to us half your lands, agree not to build a single family home, or whatever.” The *Kaiser Aetna* decision thus clearly and correctly rejects the argument that individuals can be made to waive their constitutional right to exclusive possession in order to gain access to public waters. Of course the United States could restrict access to the public waters, if the private waters held out some risk of obstruction, pollution, or flooding; the ordinary concept of the police power would justify those restrictions. But simple *notice* from the government that the United States will claim as navigable the waters that anyone wishes to hook up with public waterways counts as a taking.¹⁰³

The key point here is that Monsanto did not operate within a competitive market where it could refuse to do business with the EPA, without any collateral consequences, if it did not wish to accept the imposed conditions. This is the way to think of biological product innovators. The state’s monopoly power made it impossible

¹⁰⁰ *Monsanto*, 467 U.S. at 1007.

¹⁰¹ I have written on this doctrine at length. See, e.g., Richard A. Epstein, *Foreword: Unconstitutional Conditions, State Power, and the Limits of Consent*, 102 HARV. L. REV. 4 (1988); RICHARD A. EPSTEIN, *BARGAINING WITH THE STATE* (1993).

¹⁰² *Monsanto*, 467 U.S. at 1011 (“This explicit governmental guarantee formed the basis of a reasonable investment-backed expectation.”).

¹⁰³ *Kaiser Aetna*, 444 U.S. at 172 n.7.

for Monsanto to walk away from the government unless it was prepared to give up its right to sell its product in the United States. Justice Blackmun was undaunted by this prospect, writing, “[b]ecause the market for Monsanto’s pesticide products is an international one, Monsanto could decide to forgo registration in the United States and sell a pesticide only in foreign markets. Presumably, it will do so in those situations where it deems the data to be protected from disclosure more valuable than the right to sell in the United States.”¹⁰⁴ But this response surely proves too much. Monsanto already enjoyed the right to sell its products in foreign markets. Of course, that right to sell outside the U.S. borders would prove nugatory if those countries adopted the same punitive strategy with respect to Monsanto as did the United States.

The notion that parties have validly consented to any conditions of which they have notice in advance would lead to the conclusion that the United States may by statute impose *any* condition that it wants on holders of trade secrets who seek to license them for use in the United States—provided that the government advertises those conditions prior to the trade secret owner’s decision to file for a license, even long after millions of dollars have been spent in the preparation of the new products for government review.¹⁰⁵ The passages quoted, if taken literally, could require that a trade secret protected under the 1972 Act be made public in order to gain approval of a new pesticide under the 1978 Act. Indeed, nothing in the twisted logic of *Monsanto* limits the rationale of the quoted passages to the sacrifice of trade secrets. Under the logic of the quoted passage, the EPA could, by statute, give notice that any person who wanted to receive a license to sell pesticides must waive all patent protections for its products, donate the company headquarters to the Red Cross, or provide the United States with a year’s free supply of chemicals! Moreover, so long as the cost of these conditions is less than the anticipated profit from the new good to be licensed, a rational party would comply with the conditions.

The doctrine of unconstitutional conditions thus ensures that actions that look rational from the point of view of the regulated individual being put to the hard government choice are not undertaken solely because they look rational to the individual. The doctrine subjects the state’s monopoly power to the same kind of constraints when the state bargains with private parties as when it commands them, by use of its regulatory authority, to act in certain ways.

It is therefore necessary to distinguish between those conditions that are acceptable in constitutional terms and those conditions that are not. One strong test of a sound set of conditions asks what happens if the identical conditions are imposed uniformly by all participants operating in other states. Thus it is surely correct to allow a state to impose a rule that requires as a condition for the use of its roads that individual drivers consent to state jurisdiction for accidents arising within its boundaries.¹⁰⁶ All states can impose that condition without disrupting the operation of a national highway system. But if all states were to insist that no one could drive on their roads unless he agreed to litigate all business and personal disputes

¹⁰⁴ *Monsanto*, 467 U.S. at 1007 n.11.

¹⁰⁵ *See id.* at 998 (“The District Court found that development of a potential commercial pesticide candidate typically requires the expenditure of \$ 5 million to \$ 15 million annually for several years. The development process may take between 14 and 22 years, and it is usually that long before a company can expect any return on its investment. For every manufacturing-use pesticide the average company finally markets, it will have screened and tested 20,000 others. Monsanto has a significantly better-than-average success rate; it successfully markets 1 out of every 10,000 chemicals tested.” (internal citations omitted)).

¹⁰⁶ *See, e.g., Hess v. Pawloski*, 274 U.S. 352 (1927).

within the state, the situation is otherwise. Now drivers could access the national highway system only if they were prepared to litigate all business transactions in each of the 50 states simultaneously. In these cases, it is never an answer that the driver may decline to enter a particular state if the condition imposed by that state proves too onerous, for it is wholly unacceptable to allow the unilateral actions of individual states to Balkanize a national market by forcing people to stay within the borders of their home states. The doctrine of unconstitutional conditions reflects the massive difference between those conditions that improve the overall operation of the legal system, on the one hand, and those conditions that wreak havoc upon its operation, on the other hand.

This doctrine, moreover, is not a radical departure from traditional law. Indeed it flows naturally from the rules that govern operation of both common carriers and public utilities, each of which can exert monopoly power within its market. These parties have never been permitted to set whatever terms and rates they choose, simply because customers have the option to go elsewhere.¹⁰⁷ The rule instead is that they must charge reasonable and nondiscriminatory rates. Both terms matter. The first condition (reasonable rates) was imposed so that the carriers and utilities could not extract monopoly profits from the exercise of their dominant position. The second condition (nondiscriminatory rates) was imposed to make sure that these carriers and utilities could not play favorites among the various individuals seeking their services.

The weaknesses in *Monsanto's* rickety intellectual structure are evident in the rocky reception that its reasoning has received in subsequent cases. Most notably, in *Nollan v. California Coastal Commission*, the Supreme Court explicitly invoked the unconstitutional conditions doctrine and brushed aside *Monsanto* while holding that the proposed state action constituted a taking for which compensation was required.¹⁰⁸ In *Nollan*, the question was whether California could require a beachfront landowner to sacrifice a lateral easement across the front of its property, in order to secure Coastal Commission approval to build a new and larger house on his beachfront lot. Under *Monsanto*, the landowner would have been helpless to resist the imposition of any condition that the Commission announced in advance. But the Court's decision treats the Commission's insistence of the sacrifice of the lateral easement as an "out-and-out" case of extortion, in the absence of any health and safety justification for requiring the easement.¹⁰⁹ Substitute competitor use of trade secrets for lateral easement, and *Monsanto* and *Nollan* read like carbon copies of each other. Justice Scalia, writing for the majority, tries to tiptoe around the distinction:

Justice Brennan also suggests that the Commission's public announcement of its intention to condition the rebuilding of houses on the transfer of easements of access caused the Nollans to have "no reasonable claim to any expectation of being able to exclude members of the public" from walking across their beach. He cites our opinion in *Ruckelshaus v. Monsanto*, 467 U.S. 986 (1984), as support for the peculiar proposition that a unilateral

¹⁰⁷ For a detailed explanation of the evolution of the common law rules, see RICHARD A. EPSTEIN, *PRINCIPLES FOR A FREE SOCIETY* ch. 10 (1998).

¹⁰⁸ 483 U.S. 825, 833 n.2 (1987). The tension between *Nollan* and *Monsanto* was taken up by the First Circuit in *Philip Morris v. Reilly*, 312 F.3d at 46-47, which is discussed later in this section.

¹⁰⁹ See *Nollan*, 483 U.S. at 837 ("In short, unless the permit condition serves the same governmental purpose as the development ban, the building restriction is not a valid regulation of land use but 'an out-and-out plan of extortion.'" (internal citation omitted)).

claim of entitlement by the government can alter property rights. In *Monsanto*, however, we found merely that the Takings Clause was not violated by giving effect to the Government's announcement that application for "the right to [the] valuable Government benefit," *id.* at 1007 (emphasis added), of obtaining registration of an insecticide would confer upon the Government a license to use and disclose the trade secrets contained in the application.¹¹⁰

This proposed distinction is mere artifice. Let the government license to market an insecticide (or a biological product) count as a benefit, then so too is the government permit to build a house. The difficulty in both cases is that the government does not have the power of a property owner when it imposes these conditions. It cannot therefore admit or exclude at will. Whether it deals with biologics or with land, it always exerts its sovereign power and must do so therefore in ways that do not subvert the proper functioning of takings doctrine. The requirement of just compensation operates as a powerful and consistent check against the ever-present risk of letting the government convert to public use property that is ultimately more valuable when it is allowed to remain in private hands. The bundling technique to which the Coastal Commission resorted in *Nollan* (i.e., tying the easement to permission to build a larger house) would have facilitated just that result, if it had not been neutralized by the Court's decision.

A simple numerical example helps make the point. Assume that the lateral easement is worth \$1,000 to the township and \$1,500 to the landowner. Under those circumstances it makes no sense for the state to condemn the easement, which costs more than it is worth. In a well-governed state, that condemnation will not occur, because taxpayers will not pay more for the easement than it is worth.¹¹¹ But if the bundling technique is allowed, the local government may insist that it will allow the owner of property to rebuild in a form that will increase his land value by \$10,000 only if the owner surrenders the lateral easement that he values at \$1,500. At this point a rational owner will gladly surrender the less valuable easement to get the more valuable building permit. But through this transaction, the government condemns land that should clearly (from a systemic perspective) be left in private hands. It is this misuse of government power to achieve an untoward end that provoked Justice Scalia's response that the government's conduct was "out-and-out-extortion." The faulty logic of *Monsanto* cannot survive the more precise understanding of unconstitutional conditions that derives from *Nollan*.

The unsoundness of this part of *Monsanto* is equally evident from the decision in *Philip Morris v. Reilly*.¹¹² In *Philip Morris*, the tobacco companies sought to enjoin the enforcement of Massachusetts' Disclosure Act,¹¹³ which required all tobacco companies, as a condition of the ability to sell tobacco products within the state, to disclose to the state, in the order of their concentration, the ingredients in their products other than tobacco and water. This would have required disclosure of non-tar, non-nicotine ingredients such as additives and flavorings. Once these additives and flavorings were disclosed to the state, the state would have in due course

¹¹⁰ *Id.* at 833 n.2 (internal citation omitted).

¹¹¹ I ignore all problems that arise within the tax system that could itself misallocate resources. These problems could arise, for example, in those situations where an unbalanced tax imposes costs on those individuals who do not benefit from the condemnation. But the proper response to that issue is to fix the tax system. It is not to introduce the second error into the system via the bundling technique.

¹¹² 312 F.3d 24.

¹¹³ Mass. Gen. Law. ch. 94, § 307B.

disclosed them to the public. These ingredient lists are, however, recognized as trade secrets.¹¹⁴ The state asserted a health justification for publishing the ingredient lists: that publication would allow the public to identify potential health hazards. But the risk to each company was that any disclosure even of a partial list would allow its competitors to more easily reverse engineer the cigarettes it marketed. In a First Circuit decision striking down this abuse of regulatory power, Judge Torruella relied explicitly on the doctrine of unconstitutional conditions, sweeping aside the second half of the *Monsanto* decision.

Philip Morris involved partial disclosure of trade secrets, on purported public health grounds, in a way that would clearly benefit the competitors of the trade secret owners. The Biosimilars Act involves use of trade secrets, similarly on asserted public health grounds and also benefiting the competitors of the trade secret owner. Before turning to the doctrine of unconstitutional conditions, Judge Torruella addressed whether the virtual *per se* rule or the balancing of *Penn Central* factors should control the analysis. He first noted that “the Supreme Court has never said that intellectual property cannot be the subject of physical takings,” and he “decline[d] to read such a broad statement into the failure of one case [*Monsanto*] to speak to that issue.”¹¹⁵ Although Judge Torruella ultimately applied the *Penn Central* factors to the Massachusetts law, he noted “that applying the *Penn Central* regulatory takings framework is not practically different from utilizing *per se* rules” because “these *per se* rules are simply shortcuts.”¹¹⁶ Judge Torruella also concluded that “whether I apply a regulatory takings analysis or a *per se* rule should not impact the ultimate decision. If the Disclosure Act’s provisions are so extraordinary as to make it properly subject to a *per se* rule, the considerations that led to adoption of that rule will also counsel me to find a taking under the *Penn Central* framework.”¹¹⁷ Judge Selya took an even stronger approach in his concurrence, noting that “*per se* takings analysis warrants very serious consideration in regard to the expropriation of trade secrets.”¹¹⁸ He saw “no principled reason to refrain from extending *per se* takings analysis to alleged takings of trade secrets.”¹¹⁹ Indeed Judge Lipez, in his dissent, did not contest the relevance of the *per se* test; he simply insisted that a facial challenge was premature.¹²⁰

After applying the first two *Penn Central* factors and finding that the companies had “at least some reasonable investment-backed expectation that their trade secrets will remain secret and the economic impact of revelation is likely to be great,” Judge Torruella then evaluated whether Massachusetts had advanced a “convincing public policy rationale to justify the taking itself.”¹²¹ It failed to meet that burden. There was a perfectly coherent way for the government to deal with potential health risks of product additives, without disclosing to the public valuable trade secret information. As Judge Torruella noted, “it is not at all clear that protecting the overall integrity of the tobacco companies’ ingredient lists will interfere with Massachusetts’ goal of promoting public health.”¹²² He then cited to the scheme in Texas where cigarette companies are required to disclose brand-specific ingredi-

¹¹⁴ *Philip Morris*, 312 F.3d at 31-33.

¹¹⁵ *Id.* at 35 n.6.

¹¹⁶ *Id.* at 35.

¹¹⁷ *Id.* at 36 (internal citation and quotation marks omitted).

¹¹⁸ *Id.* at 51.

¹¹⁹ *Id.*

¹²⁰ *Id.* at 52-55.

¹²¹ *Id.* at 45-46.

¹²² *Id.* at 44.

ent information to the state, but this information is then kept confidential, as well as the scheme in Minnesota where the state requires public disclosures only when specific ingredients are used in a cigarette.¹²³ These schemes would have furthered the public health goals advanced by Massachusetts without effecting a “tremendous private loss” of trade secrets.¹²⁴

Judge Torruella then addressed the doctrine of unconstitutional conditions, noting that the state’s law was “unlike some other challenged government actions” insofar as the tobacco companies could “opt out entirely, simply by not selling their products in Massachusetts.” Their claim, he wrote, “is really that Massachusetts has placed an unconstitutional condition on their right to sell their products in Massachusetts.” Put another way, if the state “simply required the tobacco companies to submit their ingredient lists for possible publication, it would be unconstitutional.”¹²⁵ Thus, the question was “whether Massachusetts can constitutionally condition the right to sell tobacco products in Massachusetts on submission to this scheme.”¹²⁶

Under the logic of *Monsanto*, so long as the state announces the requirement before the importation of cigarettes into the state (or by analogy, so long as Congress announces that BLAs submitted henceforth are subject to a taking at year 12), no tobacco company (biologics company) could claim to rely on an “investment-backed expectation” that its information would be kept secret. The *Philip Morris* court thus faced the unenviable challenge of reconciling two decisions, the more recent of which (*Nollan*) applied the unconstitutional conditions doctrine in such a situation and the other and earlier of which (*Monsanto*) ignored it.¹²⁷ While Judge Torruella suggested that allowing a manufacturer to sell its legal product in Massachusetts was more similar to building on one’s land (*Nollan*) than to the license received pursuant to the complex regulatory scheme at issue in *Monsanto*,¹²⁸ the decision in fact clearly repudiates—on the ground of strong constitutional theory—what might otherwise pass for binding precedent. It is impossible to reconcile *Philip Morris* with *Monsanto*’s observation that any producer can forfeit sales in the American

¹²³ *Id.* at 45; see also 21 C.F.R. § 171.1 (setting forth the requirements for a food additive petition and providing that product formulas, as well as ingredients and combinations of ingredients shown to be trade secrets, cannot generally be disclosed to the public).

¹²⁴ *Philip Morris*, 312 F.3d at 45.

¹²⁵ *Id.* at 46.

¹²⁶ *Id.*

¹²⁷ Judge Torruella also distinguished dicta in the much earlier decision of the Supreme Court in *Corn Products Refining Co. v. Eddy*, 249 U.S. 427 (1919). In this case, the Supreme Court upheld a Kansas statute requiring that a proprietary syrup mixture be labeled a “compound,” despite a challenge on equal protection and commerce clause grounds. In a very broadly worded opinion, Justice Pitney wrote that, first, “[i]t is too plain for argument that a manufacturer or vendor has no constitutional right to sell goods without giving to the purchaser fair information of what it is that is being sold,” and, second, “[t]he right of a manufacturer to maintain secrecy as to his compounds and processes must be held subject to the right of the State, in the exercise of its police power and in promotion of fair dealing, to require that the nature of the product be fairly set forth.” *Id.* at 431-32.

The simplest way to read this comment is that requiring disclosure to prevent consumer deception falls within even the narrowest conception of the police power and therefore counts as a justified disclosure and not an improper taking. But, as Judge Torruella noted in the *Philip Morris* decision, the case really involved only two mundane questions: whether the company’s proprietary syrup mixture was a “compound” or a “single substance” and where it was manufactured. *Philip Morris*, 312 F.3d at 40 n.12. Further, in fact, under federal law, the “fair information” to be provided has meant far less than all ingredients in all foods. Indeed, typically one may note “spices, flavorings, and colorings” without specifying each. *Id.* at 40; see FDCA § 403(i)(2). Note too that *Corn Products* did not address the serious complications that arise when competitors are the parties best positioned to take advantage of the disclosed information.

¹²⁸ *Philip Morris*, 312 F.3d at 47.

market if it does not like the conditions imposed by the EPA. That is why Massachusetts could not defend its disclosure on the ground that Philip Morris was free to sell its cigarettes in Connecticut or Italy. Moreover, Judge Torruella's treatment of *Monsanto* repudiates the view that notice of future state action in and of itself insulates the government from the duty to compensate.

There is, then, no reason to read *Philip Morris* as anything other than a *de facto* rejection of the flawed *Monsanto* position. Indeed, the weakness of *Monsanto*'s extreme use of the notice doctrine is also evident in Supreme Court cases subsequent to *Monsanto*. In *Dolan v. City of Tigard*, for example, the Supreme Court applied the doctrine of unconstitutional conditions to limit the exactions that the state could impose on a landowner who sought to expand her small business.¹²⁹ *Monsanto* was not discussed. The key feature of the decision was that the conditions imposed had to show an "essential nexus" to the end in view and involve means that were "roughly proportional" to achieve that end. The Court acknowledged that it was reasonable to require that a landowner provide some increased drainage when she wished to pave over a larger fraction of her own land, but the Court demanded some explanation as to why that open space had to be handed over to the public when the same end could be achieved while the land remained in the possession of its owner. Likewise, the Court held that the city might well have exceeded its rights when demanding, as a condition for the permit, that the landowner supply a bike path over her land for public use. The city was required to show that the path was needed to service increased traffic generated by the business.

The entire opinion took place against a backdrop that the state could not simply announce in advance that these conditions could be imposed as a matter of right. *Dolan* thus imposes a principled limitation on the kinds of conditions that could be attached to the repaving of the parking lot. And it was wholly beside the point that the value to the landowner of paving the parking area would exceed her loss from the imposition of either or both these conditions. The purpose of the unconstitutional conditions doctrine is to prevent the state from bundling additional conditions on its approval of a project in ways that are likely to produce net social losses. The challenge for the courts is to allow regulations that control wrongful behavior while disallowing those that force one person to surrender his property, whether tangible or intangible, for the benefit of another.

Another subsequent Supreme Court decision casts serious doubt on the suggestion from *Monsanto* that notice is a cure-all. In *Palazzolo v. Rhode Island*, the plaintiff challenged as a taking certain restrictions imposed by the state, even though he had acquired the property after the state had put the restrictions in place.¹³⁰ More specifically, before Palazzolo became the sole owner of several waterfront plots of land, Rhode Island enacted legislation creating an agency to protect the state's coastal properties, which repeatedly denied Palazzolo's efforts to develop the land. The agency stated that his plans failed to meet the relevant standard, which required the planned development to serve "a compelling public purpose which provides benefits to the public as a whole as opposed to individual or private interests."¹³¹ Rhode Island appealed to the *Penn Central* idea of reasonable-investment backed expectations to urge "a single, sweeping rule: A purchaser or a successive title holder like petitioner is deemed to have notice of an earlier-enacted

¹²⁹ 512 U.S. 374 (1994).

¹³⁰ 533 U.S. 606 (2001).

¹³¹ *Id.* at 615.

restriction and is barred from claiming that it effects a taking.”¹³² The basic point was that “after all, they purchased or took title with notice of the limitation.”¹³³ The Supreme Court flatly rejected the state’s insistence that notice was a cure-all, which necessarily casts doubt on *Monsanto*’s suggestion that notice that a scheme will be put in place relieves the state of any obligation of compensation.

To bring the discussion back to the issue of FDA regulation of biologics: the government cannot put the biological applicant to the choice of sacrificing its property in order to gain access to the marketplace. The state as a regulator may not offer parties “take it or leave it” propositions, any more than may the private common carrier. Each party must justify the decision it makes by showing that it uses proper means to achieve legitimate ends. Congress, working through FDA, faces the doctrine of unconstitutional conditions, if it says that it will allow a biologic to be sold on the market today only if the applicant surrenders its control over use of its trade secrets at some time in the future, say after the expiration of the 12-year exclusivity period. Standing alone, that condition is unacceptable. To be sure, it is possible that in some cases, the value of some of these trade secrets will have diminished over time. But no such reduction would excuse the government from the obligation to pay compensation for the taking at year 12.

D. *Just Compensation and Maintaining the Quid Pro Quo*

In principle, it is always possible for the government to pave the way for new entrants by offering the innovator just compensation for the trade secrets that the government wishes to take to advance the position of a new entrant. The theory here is that enabling that new competitor lowers price toward marginal cost in a way that advances static efficiency, which in the short run should increase the number of consumers that could benefit from the product (and its biosimilars). In other words, state use of trade secrets might be justified in the view of some for the same reason that it has been proposed with respect to patents: condemnation lets the underlying good be sold at a price that is closer to marginal cost.¹³⁴ To be sure, the social effort to share trade secrets with all subsequent takers counts as a public use, for which it is permissible to exercise the takings power.¹³⁵ The real difficulty comes with calculating just compensation in ways that do not prevent increased use, without upsetting the incentives to invest that the current rules create. In working with this issue, it is possible to attempt this valuation by looking at either *costs* incurred by the holder of trade secrets or the *benefits* obtained from the use of the trade secret by the new entrant. The overall scheme is fraught with difficulty no matter which approach is taken.¹³⁶

On the cost side, the first difficulty is this. Why use cost figures at all in calculating the compensation owed to a trade secret holder when his trade secret is used to

¹³² *Id.* at 626.

¹³³ *Id.*

¹³⁴ For this discussion, see Michael Kremer, *Patent Buyouts: A Mechanism for Encouraging Innovation*, 113 Q.J. ECON. 1137, 1137 (1998) (“[P]atent buyouts could potentially eliminate the monopoly price distortions and incentives for rent-stealing duplicative research created by patents, while increasing incentives for original research.”).

¹³⁵ See *Hawaii Housing Auth. v. Midkiff*, 467 U.S. 229 (1984) (broadly defining public use). But even narrower definitions could well allow this sharing to take place, so I will not explore this question further here.

¹³⁶ For discussion, see RICHARD A. EPSTEIN, *OVERDOSE: HOW EXCESSIVE GOVERNMENT REGULATION STIFLES PHARMACEUTICAL INNOVATION* 82-96 (2006).

evaluate the application of a potential competitor? In the usual case where property is taken for public use, its value—not its cost—is the appropriate measure of compensation. In those cases, where property depreciates in value, the cost figure is too high. In the more common case, however, the value of the property will exceed its cost, such that all cost-based measures of compensation fall short, especially for risky ventures that generate a high rate of return. The compensation shortfall is even greater if the cost-based calculations do not include a fair share of the joint costs that are allocable to the generation of any particular trade secret. Yet even revealing these costs could have the further difficulty of disclosing to outsiders valuable information that relates to the use of the firm's other trade secrets, giving out valuable trade secret information about the firm's research plans.

On the value side, the use of a trade secret by a rival does not mean that the embedded information is of no value on the original holder of the trade secret. It is not as though the information that is supplied is no longer available to the party who created the trade secret in the first place. Quite the contrary, both parties can use the trade secret. Indeed, depending on how much use the new entrant is permitted to make, the restrictions on that use, and the remaining use the incumbent may make, the reduction in value could be quite large. Still, the offset should be a good deal smaller if that trade secret information helps propel the biosimilar onto the market where it now may be sold in opposition to the pioneer biologic. The holder of a trade secret, moreover, should theoretically be indifferent to whether it receives its return over time or in a lump sum, so long as the two figures have the same discounted present value, but determining present value is no easy task. In addition, government regulators are likely to lowball their estimates of value by treating the present value of a trade secret as being closely correlated to its cost. In practice, the government will seek to condemn only trade secrets for those products that have proved their worth in the marketplace over time. For this select group of products, that value is likely to be many multiples of costs, especially for products that have surmounted the high risk of failure during the development phase.

Stated otherwise, the embedded profits in the initial holding of the trade secrets should not be lost by a lowball government estimate of the level of compensation required. In all these novel settings, moreover, a sound valuation process has to overcome the nontrivial challenge of finding reliable and impartial experts to do the valuation needed in both arbitration and litigation. These institutional and procedural difficulties are easily underestimated by economists who are often inattentive to the frictions that can overwhelm the valuation process. But these administrative difficulties have to count as a strike against any proposal that starts from the premise that the payment of just compensation offers an effective route for the forced sharing of information with new market entrants.

Owing to these massive calculation difficulties, it is not easy to introduce any just compensation scheme that preserves the proper competitive balance between the first and subsequent entrants. All questions of legal rules are choices between second-best alternatives. At this point, it seems clear that any effort to work out compensation measures on a case-by-case basis will be very costly. The question then remains whether in any sense the larger scheme of the Biosimilars Act may obviate the need for case-by-case compensation determinations going forward. In other words, can the overall structure of the Biosimilars Act serve as in-kind just compensation for innovators? The holders of biological product trade secrets necessarily lose some protected property rights when their competitors may rely on FDA's prior finding

of safety, purity, and potency at the end of 12 years. The best way to understand the Biosimilars Act as a whole is to treat the special protections it provides to innovators (in the form of a narrowly conceived taking at year 12 and an opportunity to litigate patent infringement claims prior to biosimilar market entry that would not have existed absent this law) as the “quid pro quo” for removing at year 12 the innovator’s otherwise permanent right to prevent competitors from benefitting from the government’s use of those trade secrets. These quid pro quos applied prospectively eliminate the need for case-by-case just compensation decisions.

It is of course not possible to create a legislative bargain that provides perfect parity to the parties or to put a precise value on the two elements of the exchange. But there is little reason to think that in this instance the relative values bear little or no relationship to each other. The future use of the product is worth a good deal in present value terms. In a world in which no precise valuation is possible, the best approach is to assume that the relevant interest groups each thought that they obtained certain important benefits under the legislative bargain. This assumption is particularly warranted in the case of the Biosimilars Act, which was the subject of extensive four-year negotiations between the innovator and generic industry (both of which are sophisticated and well-informed).¹³⁷ Although it is doubtful that either side is completely satisfied with the enacted statute, the resulting bargain should in this context be sufficient to put to rest the constitutional doubts that would attend the artificial truncation of trade secrets through the legislative process. The situation here, moreover, is far from unprecedented in light of other schemes that resorted to these larger legislative bargains to establish a broad institutional framework.

One of the most instructive of these schemes was the workers’ compensation scheme upheld in *New York Central Railroad v. White*.¹³⁸ In that decision, the Court upheld—in the face of a due process claim grounded in the taking of the employer’s private property—the validity of New York’s 1913 worker’s compensation law, which had ushered in a major change to the common law rules for employer liability. On the one hand, the employer was no longer able to raise the defenses of its own due care, or of the assumption of risk or contributory negligence of its workers. On the other hand, workers could no longer recover the full amount of damages that successful claimants could recover at common law. There was no specific demonstration that this scheme would necessarily work well in all cases, but there was sufficient evidence from the offsetting considerations that the statute had a tendency to improve the position of both parties, and through that action, overall social welfare. For example, the Court noted that “[i]f the employee is no longer able to recover as much as before in case of being injured through the employer’s negligence, he is entitled to moderate compensation in all cases of injury, and has a certain and speedy remedy without the difficulty and expense of establishing negligence or proving the amount of the damages.”¹³⁹ Indeed, “[i]nstead of assuming the entire consequences of all ordinary risks of the occupation, he assumes the consequences, in excess of the scheduled compensation, of risks ordinary and extraordinary.”¹⁴⁰ At the same time, although “the employer is left without defense respecting the question of fault,” he is “assured that the recovery is limited, and that it goes directly to the relief of the designated beneficiary.”¹⁴¹ The Court presumed

¹³⁷ For a detailed legislative history, see Carver, Lietzan, & Elikan, *supra* note 1.

¹³⁸ 243 U.S. 188 (1917).

¹³⁹ *Id.* at 201.

¹⁴⁰ *Id.*

¹⁴¹ *Id.*

that just as “the employee’s assumption of ordinary risks at common law presumably was taken into account in fixing the rate of wages, so the fixed responsibility of the employer, and the modified assumption of risk by the employee under the new system, presumably will be reflected in the wage scale.”¹⁴² In short, the scheme was “intended as a just settlement of a difficult problem, affecting one of the most important of social relations, and it is to be *judged in its entirety*.”¹⁴³

To be sure, the workers’ compensation precedent is not exactly on all fours with the current case because the parties to the workers’ compensation bargain do have, as the Court noted, the ability to adjust the rates of wages to offset any imbalance of benefits that the workmen’s compensation law might make. But that point has not proved decisive. The instructive precedent in this regard comes from the automobile no-fault statutes, which truncated the tort remedy traditionally available to injured parties at common law, in exchange for which they received a potentially smaller, but prompt and certain, financial remedy from their own insurers. In *Pinnick v. Cleary*,¹⁴⁴ for example, the Massachusetts Supreme Judicial Court upheld the constitutionality of the state’s automobile no-fault statute¹⁴⁵ after finding that the quid pro quo it offered met not only a low rational basis review standard, but also the “stricter test” derived from the workers’ compensation case of *New York Central Railroad v. White*, which asked “whether the statute provides an adequate and reasonable substitute for preexisting rights.”¹⁴⁶ In applying this test, the Massachusetts court acknowledged the difference between the workman’s compensation statute and the no-fault statute: “we cannot view it from the point of view of plaintiffs and defendants, for these are not preexisting categories as are the employers and employees affected by a workmen’s compensation act.”¹⁴⁷ In other words, the court applied this test even though it is manifestly impossible for all Massachusetts drivers to make any adjustments with other drivers over the proper level of compensation to offset any imbalances from the no-fault statute.

The key point here is that with these complex schemes, rough averages are what matters—not precise equivalence. To impose a more exacting test means that sensible general schemes will be aborted on the grounds that they leave someone worse off at some time. To take that view when it is unclear who will suffer means that the state sacrifices the potential for enormous social gains on the altar of excessive concerns for some particular party who might be left off under the larger statutory scheme. In light of the combined operation of the precedents for workers’ compensation and the automobile no-fault statutes, it is not necessary in this context to ask the extent to which innovator and follow-on biologics can make licensing arrangements between them. So long as the overall thrust of the Biosimilars Act is positive, the statutory scheme should survive constitutional scrutiny so long as all its key parts are observed.

Rightly construed, therefore, the Biosimilars Act should be regarded as constitutional *prospectively* so long as the complex statutory bargain *in its entirety* is preserved. Three aspects of the scheme are essential to preserving the bargain, beginning with the complex patent litigation provisions, which offer the greatest counterweight to the taking of trade secrets under the Biosimilars Act.

¹⁴² *Id.* at 201-02 (emphasis added).

¹⁴³ *Id.* at 202.

¹⁴⁴ 271 N.E. 2d 592 (Mass. 1971).

¹⁴⁵ St. 1970, c. 670.

¹⁴⁶ *Pinnick*, 271 N.E. 2d at 602 (citing *New York Central R.R. v. White*, 243 U.S. at 201).

¹⁴⁷ *Id.* at 606.

1. *Maintaining the Integrity of the Litigation Provisions*

The Biosimilars Act, through changes to the Patent Act *and* a new section 351(l) of the PHSa, permits the pioneer who owns (or licenses) patents that may be infringed by the biosimilar product to litigate possible infringement prior to the biosimilar's market entry. This brings certainty to the biosimilar applicants (indeed, a risk-free opportunity to determine whether they may market their products), but it also allows the innovator to avoid multi-year patent litigation proceedings while an infringing biosimilar product is eroding its market share.

The elaborate procedures that govern this interaction begin with a clear statutory duty imposed on the biosimilar applicant. The statute states that in this initial stage, the biosimilar applicant "shall" provide to the reference product sponsor "[n]ot later than 20 days after the Secretary notifies the [biosimilar] applicant that the application has been accepted for review," "confidential access" to two sorts of information.¹⁴⁸ The first consists of the biosimilar application itself.¹⁴⁹ The second is "such other information that describes the process or processes used to manufacture the biological product" described in the application.¹⁵⁰ There is at this stage no need to mention any patents that may be implicated by the applicant's manufacturing process or eventual sale of the product. The use of the word "shall" carries with it the unmistakable implication that the follow-on applicant is under a strict duty to supply this information.¹⁵¹ In addition, and in contrast, the applicant "may" in its own discretion also supply whatever additional information the reference product sponsor requests.¹⁵²

This information supplied to the reference product sponsor will of necessity contain information that helps to identify not only the relevant reference product sponsor patents but also possible trade secrets that the biosimilar applicant uses for its own products. Recognizing this reality, the Biosimilars Act works to protect the intellectual property of the biosimilar applicant to the same degree that it protects the rights of the pioneer. It puts in place a mechanism whereby the individuals to whom this information is transferred comprise one in-house and "one or more" outside counsel who do not engage "formally or informally" in any patent prosecution relevant or related to the product in question.¹⁵³ In addition, the information is not automatically disclosed to the patent owner if that person is different from the reference product sponsor. Instead, the information "may" be disclosed to the patent owner, if (1) the patent is exclusively licensed to the reference product sponsor, (2) the patent owner has retained a right to assert the patent or participate in litigation concerning the patent and (3) the patent owner agrees to be subject to the confidentiality provisions of the Biosimilars Act.¹⁵⁴ The information also may be transferred to scientific consultants and "other" outside counsel (presumably those who *do* engage in patent prosecution), with "the prior written consent of the [biosimilar] applicant, which shall not be unreasonably withheld."¹⁵⁵

¹⁴⁸ PHSa § 351(l)(2).

¹⁴⁹ PHSa § 351(l)(2)(A).

¹⁵⁰ PHSa § 351(l)(2)(A).

¹⁵¹ The word "shall" appears in multiple contexts with respect to such vital topics as notification at least 180 days before commercial launch of the biosimilar and cooperation in discovery matters if the pioneer seeks a preliminary injunction. PHSa § 351(l)(8)(A), (C).

¹⁵² PHSa § 351(l)(2)(B).

¹⁵³ PHSa § 351(l)(1)(B)(ii)(I) & (II).

¹⁵⁴ PHSa § 351(l)(1)(B)(iii).

¹⁵⁵ PHSa § 351(l)(1)(C).

In the next stage of the process, the reference product sponsor is under a duty to generate, within 60 days, a list of patents for which it “believes a claim of patent infringement could reasonably be asserted” against the biosimilar applicant.¹⁵⁶ Of course it would not be possible for the reference product sponsor to compile any such list without the information supplied by the new applicant. This list of patents is not limited to patents claiming the product or a method of using the product and thus reaches process patents, unlike the Hatch-Waxman Act’s litigation provisions, which exclude process patents.¹⁵⁷

Once this is done, the action switches back to the biosimilar applicant who may, but need not, supply a list of additional patents that it believes could be the basis of a reasonable claim against it.¹⁵⁸ Whether or not it adds patents to the list, the biosimilar applicant must provide a “detailed statement” explaining why any patent listed (by either company) is “invalid, unenforceable or will not be infringed.”¹⁵⁹ In the alternative, the biosimilar applicant may signal a truce with respect to any particular patent by providing a statement to the reference product sponsor that it “does not intend to begin commercial marketing of the biological product before the date that such patent expires.”¹⁶⁰ This statement is not filed with FDA; it is sent only to the reference product sponsor.

The submission of the biosimilar application is an artificial act of infringement with respect to any patent identified by either party in this list exchange process, creating federal court jurisdiction for resolution of the patent litigation that follows.¹⁶¹ Without this important amendment to the patent code, the premarket patent litigation scheme could not be implemented.

Once the biosimilar applicant has sent its statement regarding patent validity, enforcement and infringement, section 351(l) provides a roadmap for litigation of the resulting patent issues.¹⁶² In brief, the parties identify a set of patents to be litigated immediately,¹⁶³ leaving the rest for litigation shortly before biosimilar market entry.¹⁶⁴ If the innovator prevails before the end of the 12-year exclusivity period on any patent in the first wave of litigation, the statute requires the court to enjoin infringement until the patent expires.¹⁶⁵ Where the statutory injunction provision does not apply, the pioneer will presumably seek an injunction and if the biosimilar has been approved and marketed, damages. The governing case will be the recent decision in *eBay v. MercExchange*. Even under the four-part

¹⁵⁶ PHS § 351(l)(3)(A).

¹⁵⁷ Compare PHS § 351(l)(3)(A) (referring to “a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted”) with FDCA § 505(j)(2)(A)(vii) (Hatch-Waxman) (requiring a generic applicant to file a certification with respect to “each patent which claims the listed drug . . . or which claims a use for such listed drug for which the applicant is seeking approval . . .”).

¹⁵⁸ PHS § 351(l)(3)(B)(i).

¹⁵⁹ PHS § 351(l)(3)(B)(ii)(I).

¹⁶⁰ PHS § 351(l)(3)(B)(ii)(II).

¹⁶¹ 35 U.S.C. § 271(e)(2)(C).

¹⁶² See PHS § 351(l)(3)(C), (4), (5), and (6) (providing that (1) the reference product sponsor must explain its opinion regarding the potential infringement, (2) the parties must negotiate in good faith to determine which listed patents will be the subject of litigation, (3) the parties must then exchange lists regarding patents that should be addressed in the initial stage of litigation, and (4) the reference product sponsor has 30 days within which to bring suit on the patents on the lists).

¹⁶³ PHS § 351(l)(2)-(6).

¹⁶⁴ PHS § 351(l)(8).

¹⁶⁵ 35 U.S.C. § 271(e)(4)(D).

test for injunctive relief laid out in *eBay*,¹⁶⁶ such relief should remain available to ensure the orderly transition from a market of patent-protected innovative biological products to a market with freely available biosimilars.¹⁶⁷ Nevertheless, the availability of the statutory injunction is particularly critical given the uncertain application of the traditional injunction test laid out in *eBay*.

This statutory sequence makes good sense. Even if the biosimilar applicant were to make a good faith determination that it would not be infringing, the possibility remains that the reference product sponsor would disagree with it about the scope and validity of the relevant patents. Sharing the information in confidence thus gives the reference product sponsor an opportunity to voice its view about any potential conflicts, at a point early enough in the process that the remainder of the dispute can be resolved in an orderly fashion under the well-articulated statutory procedures.

At this point, it should be clear that a meaningful exchange of information is critical to both sides if they are to be able to litigate patent infringement issues before biosimilar market entry. Thus, for the Biosimilars Act to work—for the bargain, the quid pro quo, to remain intact—it is imperative that neither side be allowed to unilaterally subvert this process at any stage. It would be indefensible, for example, for a reference product sponsor to deliberately refuse to comply with the obligations that the Biosimilars Act imposes on it. The reference product sponsor could not, for example, use or disclose the biosimilar applicant's proprietary information in some unauthorized fashion. The whole point of the system is to induce rapid and reliable exchange of relevant information in order to reduce the various risks on both sides of the transaction. For that reason, therefore, the biosimilar applicant similarly should not be allowed to skip the first step of the patent scheme—that of providing its application and complete manufacturing process information to the pioneer.

The interactive and mandatory nature of the patent protection provisions is not required solely as a matter of statutory construction. If the patent exchange process is not initiated as required by the statute, the Biosimilars Act will be subject to constitutional challenge on the ground that a pioneer would not get the statutory quid pro quo (the opportunity to effectively litigate relevant patents) but yet would still be subject to a significant taking of its trade secrets at the end of the 12-year exclusivity period. The two parts of the statute (i.e., those provisions allowing the biosimilar applicant to rely on FDA's prior finding of safety, purity and potency for the reference product and those provisions allowing the pioneer to enforce its patents prior to biosimilar market entry) are dependent on each other. Both are essential pieces of an elaborate statutory bargain. This quid pro quo is at the heart of the constitutional analysis, for the superior patent remedies are part of the offset

¹⁶⁶ A plaintiff must demonstrate: (1) that it has suffered an irreparable injury; (2) that remedies available at law, such as monetary damages, are inadequate to compensate for that injury; (3) that, considering the balance of hardships between the plaintiff and defendant, a remedy in equity is warranted; and (4) that the public interest would not be disserved by a permanent injunction. 547 U.S. 388, 391 (2006). For an update on injunctions after this decision, see Federal Trade Commission, *The Evolving IP Marketplace, Aligning Patent Notice and Remedies with Competition* ch. 8 (March 2011).

¹⁶⁷ It is an open question how much change the *eBay* formulation has exerted in general, but the more careful studies indicate that courts applying the formulation have taken into account the subject matter area of the various patents. See Lily Lim & Sarah E. Craven, *Symposium Review: Injunctions Enjoined; Remedies Restructured*, 25 SANTA CLARA COMPUTER & HIGH TECH. L.J. 787, 798 (2009) (stating that post-*eBay* courts consider, among other things, whether the parties compete in the same marketplace and whether the patent covers a component of limited importance to the overall device).

for the significant loss of trade secrets. The two halves of the Biosimilars Act either stand together or fall together.

Yet in spite of the fact that the patent provisions play a key role in preserving the balance of the Biosimilars Act, some commentators have suggested that the first step in the process is optional to the follow-on applicant.¹⁶⁸ In their view, a biosimilar sponsor might decide not to provide a copy of the application and manufacturing information, either reasoning that the information is too valuable to share or otherwise sidestepping the pre-approval litigation process and statutory injunction. The penalty for nondisclosure, they claim, is vulnerability to a suit for declaratory judgment.¹⁶⁹

Proponents of this view offer two grounds for suggesting that biosimilar applicants may press forward with their applications without making the disclosures under section 351(l). The first is that the Biosimilars Act, unlike the Hatch-Waxman Act, does not explicitly state that FDA may not approve a biosimilar application if the applicant fails to comply with the statutory patent procedures.¹⁷⁰ The second suggests that there is some significance to the misalignment between the patents that must be identified under the patent exchange provision (section 351(l)(2)) and the patents covered by the special remedial provision (section 351(l)(9)(C)).¹⁷¹ As noted, the patent information exchange process reaches any patent that might reasonably be asserted by the reference product sponsor. The remedial provision states that if the biosimilar applicant fails to provide the application and information to the reference product sponsor, “the reference product sponsor, but not the subsection (k) applicant, may bring an action . . . for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product.”¹⁷² This provision does not reach process patents. How exactly this misalignment compels the conclusion that the application disclosure

¹⁶⁸ For example, in its comments to the FDA biosimilar docket, Momenta argued that FDA should not become involved in the patent exchange process. It reasoned that “[t]he filing of an application is a confidential matter, just as the filing of a BLA is a confidential matter. *It is up to the applicant to determine whether and when to disclose such a filing.* It is far from certain that there will be patents that relate to every or any application when filed, and even if there are, such patents may reasonably be expected to expire before FDA approval, or be determined by the applicant, at its own risk, to be non infringing, unenforceable, or invalid.” See Momenta Pharmaceuticals, Inc., Comment, Docket No. FDA-2010-N-0477-0029 (Dec. 22, 2010), at 13 (emphasis added).

¹⁶⁹ *Biosimilars ‘Patent Dance’ Could Be Interpreted as Volitional, Not Mandatory*, FDA WEEK (Mar. 11, 2011). See PHSA § 351(l)(9)(C) (“If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, United States Code, for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product.”). This cramped reading of the statutory consequences may not itself stand up to scrutiny. For example, section 351(f) of the PHSA makes it a federal crime to violate any provision of section 351, which would include the obligations of section 351(l) (e.g., “[n]ot later than 20 days after the Secretary notifies the [biosimilar] applicant that the application has been accepted for review, the [biosimilar] applicant . . . shall provide to the reference product sponsor a copy of the application . . .” (emphasis added)).

¹⁷⁰ See James N. Czaban, Karin A. Hessler & Matthew J. Dowd, *Panacea or Poison Pill? Making Sense of the New Biosimilars Law*, BNA PHARMACEUTICAL LAW & INDUSTRY (May 28, 2010), at 8 (citing FDCA § 505(j)(4)(J), which states that FDA must approve an application unless it finds that the application does not meet a requirement of section 505(j)(2)(A), which includes the obligation to include patent certifications).

¹⁷¹ See *id.*

¹⁷² PHSA § 351(l)(9)(C). Congress also created an artificial act of infringement in this case. See 35 U.S.C. § 271(e)(2)(C)(ii) (providing that, if the biosimilar applicant failed to provide its application and manufacturing information to the reference product sponsor, it is an act of infringement to file a biosimilar application “for a patent that could be identified pursuant” to the reference product sponsor’s initial patent list).

requirement is optional is not, however, explained. But at least one commentator has suggested that the apparent narrowness of the declaratory judgment provision might make the supposed non-disclosure “option” appealing; a biosimilar company might think this penalty “is not too bad,” because the suit does not extend to the manufacturing patents.¹⁷³

These arguments for reading the first step in section 351(l) as optional for the follow-on applicant are deeply flawed. First, the simple fact that FDA is not directed to disapprove an application that fails to include proof of compliance with section 351(l)(2) does not mean that it lacks a statutory duty to ensure compliance with section 351(l) or that the biosimilar applicant can ignore its own mandatory statutory duties.

Second, this argument is much like the misguided doctrine of efficient breach that has from time to time been proposed as an appropriate way of looking at contractual obligations. The doctrine of efficient breach essentially holds that the option to breach should be given to any promisor, because expectation damages put the plaintiff back in the position he would have occupied if the contract had been performed.¹⁷⁴ The proposition is provocative and misguided in this context, for reasons that are beyond the scope of this article,¹⁷⁵ but it is also irrelevant in

¹⁷³ *Biosimilars ‘Patent Dance’ Could Be Interpreted as Volitional, Not Mandatory*, FDA WEEK (Mar. 11, 2011).

¹⁷⁴ See OLIVER WENDELL HOLMES, *THE COMMON LAW* 301 (1881) (“The only universal consequence of a legally binding promise is, that the law makes the promisor pay damages if the promised event does not come to pass. In every case it leaves him free from interference until the time for fulfilment [sic] has gone by, and therefore free to break his contract if he chooses.”). For the origins of the term, see Charles J. Goetz and Robert E. Scott, *Liquidated Damages, Penalties and the Just Compensation Principle: Some Notes on an Enforcement Model and a Theory of Efficient Breach*, 77 COLUM. L. REV. 554 (1977). For criticism, see Daniel Friedmann, *The Efficient Breach Fallacy*, 18 J. LEGAL STUD. 1 (1989). For a judicial defense, see *Lake River Corp. v. Carborundum Co.*, 769 F.2d 1284 (7th Cir. 1985).

¹⁷⁵ For example, the most common cases in which the doctrine of efficient breach is invoked are simple contracts for sale where goods promised to one party are sold out from under him to a third person at a higher price. The implicit argument is that if the defaulting seller can pay the original buyer a sum equal to his expectation losses, the breach results in a social improvement. Specifically, upon receipt of the expectation damages the original buyer is no worse off than he would have been had the contract been performed, and both the original seller and the new buyer are better off. Because some people are better off and none is worse off, the transaction meets the tests for economic efficiency. The law should encourage parties to breach, the argument goes, so long as the expectation measure of damage is in force.

The argument cannot stand up to criticism. If these breaches made sense, there would be no reason to require a doctrine of efficient breach. At the time of contract formation, parties by voluntary agreement could stipulate that a seller always had the opportunity to breach so long as it was prepared to give the buyer his expectation. It is not credible to think that a device that no one wants should ever be regarded as efficient for the parties. Moreover, the doctrine of efficient breach does not represent an accurate statement of the law. To be sure, at common law damages are the only possible remedy. But in a variety of situations the law orders specific performance or enjoins a party from engaging in certain practices when specific performance is not possible. Contracts for the sale of land are thus enforceable by specific performance at the instance of the buyer and seller. Contracts for distinctive personal services may not be specifically enforced, but a defendant can be enjoined from rendering service to others even if fully willing to pay damages.

This widespread availability of specific performance and injunctive relief is widely understood to create a stability of expectations that increase the confidence that people have in their trading partners. The usual examples of expectation damages all have a neat mathematical ring that makes it appear that the numbers in question are actually known to the parties in question. But if the inability to receive a delivery of goods slows down the construction of a building or forces a general contractor to renegotiate subcontracts with other parties, those numbers are hard to calculate, especially if these damages are dismissed as speculative. It is for good reason that voluntary agreements forgo these difficult measures of damages. Expectation damages may well be required when breach takes place for reasons beyond the control of the party, at least if the parties do not have a liquidated damage clause. But it is one thing to take a stab at expectation damages when misfortune occurs. It is quite another to encourage deliberate breach when performance is possible.

the case of a statutory scheme that involves adverse parties who are not in a contractual relationship.¹⁷⁶

Third, the statutory provision regarding declaratory judgment actions does not change the overall situation. This section of the Biosimilars Act authorizes declaratory judgment actions with respect to only patents claiming the product and its use; it does not apply to the process patents that would be identified by one party or the other if the statutory information exchange process were followed. This misalignment, rather than suggesting disclosure is optional, supports the opposite conclusion. It makes no sense in terms of the overall structure of the statute to fail to offer reliable remedial relief with respect to a key form of patent protection. In addition, it is important not to over read the supposed limitation in the declaratory judgment provision. Congress included a different artificial act of infringement where the biosimilar applicant fails to provide its application, and this provision reaches *any* patent “that could be identified” pursuant to the information exchange process in section 351(l)(3).¹⁷⁷ That, most certainly, is not limited to process patents, and the scheme must be read as a comprehensive whole. In any case, the declaratory judgment provision is best read to serve the purpose for which it was drafted, which is to function as a *restriction* on biosimilar applicants. That purpose is to prevent any biosimilar applicant from making an end-run around the basic statutory scheme. More specifically, a biosimilar applicant is not allowed to submit its application to FDA, to withhold from the innovator any of its application and manufacturing information, to file a declaratory judgment action in a favorable forum, and only at that late stage in the process be obligated to disclose its relevant product information during discovery. So understood, the primary function of this provision is to prevent forum shopping. It is not to facilitate avoidance of the mandatory patent litigation process.

In principle, therefore, there is no reason why the pioneer may not enforce any and all patents once some act of infringement has been identified. The harder question is how it would know to do so. If the biosimilar applicant keeps the filing of its application confidential, the pioneer may not know to bring an action until the biosimilar is actually marketed, at which point it will face market erosion from a potentially infringing product.

Most importantly, as a matter of general constitutional law, statutes should normally be construed and implemented to avoid direct constitutional challenges.¹⁷⁸ It is the innovator’s meaningful opportunity to litigate potentially infringed patents prior to biosimilar market entry that makes the taking of its trade secrets

¹⁷⁶ Moreover, there is no reason to think that parties would prefer this doctrine from the *ex ante* perspective. If they did, they could have contracted to allow for these actions in advance. Instead, typically exactly the opposite course of action is followed; the common law remedy for damage is supplemented by actions for specific performance in the case of property and injunctive relief (against working for a competitor, for example) when specific performance is not possible. See, e.g., *Lumley v. Wagner*, 64 Eng. Rep. 1209, 1223 (Ch. 1852) (allowing injunction against singing for a rival opera company); *Lumley v. Gye*, 118 Eng. Rep. 749 (Q.B. 1853) (allowing action for tortious interference of contract). This routine availability of specific performance and injunctive relief is widely understood to create a stability of expectations that increase the confidence that people have in both their property interests and their trading partners. It is this strong preference for specific relief that should inform the interpretation of the Biosimilars Act.

¹⁷⁷ 35 U.S.C. § 271(e)(2)(C)(ii).

¹⁷⁸ See *Ashwander v. Tennessee Valley Auth.*, 297 U.S. 288, 348 (1936) (“When the validity of an act of the Congress is drawn in question, and even if a serious doubt of constitutionality is raised, it is a cardinal principle that this Court will first ascertain whether a construction of the statute is fairly possible by which the question may be avoided.” (internal citation omitted)).

at the twelfth year even arguably consistent with the Takings Clause. Take away the innovator's ability to make informed decisions about which patents to litigate during the exclusivity term, and the taking at year 12 becomes uncompensated. To avoid a major constitutional problem, therefore, the statement in section 351(l) (2) that the biosimilar applicant "shall" provide its application must be interpreted just as it is written—that is, mandatory.

Now that the mandatory nature of the first step in the patent process is clear, the question then becomes how to ensure that biosimilar companies are actually complying with the statutory mandates. What is most needed is a guarantee that review of the biosimilar application will not go forward if the biosimilar applicant has consciously sought to subvert the statutory process. A simple administrative remedy would be more efficient than, and vastly preferable to, the cost and confusion that would result if biosimilar applicants felt free to disregard this fully articulated statutory scheme. As noted, if the biosimilar applicant acted in open defiance of the section 351(l) process, the reference product sponsor would face the unappetizing task of finding the right remedy while operating from a weak knowledge base. If it even knew about the application in the first instance, it could of course try to identify the relevant patents for purposes of premarket patent litigation. It could also try to enjoin the agency from approving the biosimilar application, on the grounds that a condition essential to the overall statutory plan has not been satisfied. If faced with defenses like sovereign immunity, the reference product sponsor might seek to bring a similar action against the applicant, for example asking for an order that the information be provided or the biosimilar application withdrawn, or seeking to enjoin its marketing of the product following approval of the application (for failure to comply with the scheme, that is, i.e., a separate argument from the patent infringement argument). How these complex maneuvers would succeed is impossible to predict in the abstract. All that can be known is that they are sure to result in cost and confusion that will be borne in equal parts by all players within the system.

The solution, therefore, is for FDA to prevent this supposed "option" from being exercised. It must take steps to ensure that pioneers have a meaningful opportunity to identify and litigate relevant patents prior to biosimilar market entry. In order to implement this position, FDA need not take any role with respect to identifying relevant patents or adjudicating patent disputes, which it would surely refuse to do.¹⁷⁹ Instead, FDA need only ensure that the biosimilar applicant has agreed to use the process that the Biosimilars Act sets out for its use. FDA should, as a number of people have argued, refuse to process the biosimilar application of any company that has failed to comply with the unequivocally mandatory instruction to share its application with the reference product sponsor.¹⁸⁰ Such a policy would help to avoid any constitutional problems down the road as the scheme is implemented.

¹⁷⁹ For example, when the agency promulgated its regulations regarding patent certification notices under the Hatch-Waxman Act, it announced that "[d]isputes involving the sufficiency of the notice must be resolved by the applicant, patent owner, and holder of the approved application rather than by action on the part of FDA" because "the agency does not have the expertise or the desire to become involved in issues concerning patent law and sufficiency of notice." 59 Fed. Reg. 50,338, 50,350 (Oct. 3, 1994).

¹⁸⁰ See, e.g., Abbott Laboratories, Comment, Docket No. FDA-2010-N-0477-0041.1 (Dec. 28, 2010); Pharmaceutical Research and Manufacturers of America (PhRMA), Comment, Docket No. FDA-2010-N-0477-0036.1 (Dec. 27, 2010); The Biotechnology Industry Organization (BIO), Comment, Docket No. FDA-2010-N-0477-0035.1 (Dec. 27, 2010); Johnson & Johnson, Comment, Docket No. FDA-2010-N-0477-0037.1 (Dec. 27, 2010).

FDA should, and could, implement such a policy by stating that it will refuse to file a biosimilar application without a certification that the applicant will comply with 351(l). This policy would be a statement of agency procedure. As such, it would not be subject to notice and comment rulemaking.¹⁸¹ Indeed the agency often implements procedural policies relating to the filing of applications without rulemaking. For example, for non-biological drugs, the agency promulgated a specific regulation setting forth the circumstances under which it will refuse to file an NDA.¹⁸² For biologics, however, FDA set forth the rules in a Standard Operating Procedure and Policy.¹⁸³ Of course, it is clear that the agency could, if it wanted, proceed through regulations.¹⁸⁴

2. Institutional Safeguards

In the Biosimilars Act, Congress enacted a very specific deal. On the one hand, the biosimilar applicant is allowed limited indirect use of the trade secrets of the innovator, after 12 years—through reliance, by FDA, on the public fact of its prior decision that the trade secrets in the innovator's application demonstrated that the reference product was safe, pure, and potent. On the other hand, the innovator gets the benefit of an artificial act of infringement, a statutory injunction provision, and an opportunity to seek an ordinary injunction prior to biosimilar market entry. To preserve the integrity of this deal, and therefore the constitutionality of the entire scheme, FDA must take steps to ensure that the scope of the "taking" does not exceed the terms that were agreed to in fashioning the Biosimilars Act.¹⁸⁵

As part of this overall commitment, FDA must guard against the risk of *partial indirect* disclosures of trade secrets to biosimilar applicants. This would include explicit or implicit (even inadvertent) release of trade secret information to a subsequent applicant, thereby allowing it to reduce its costs of production and manufacture. Accordingly, FDA reviewers should not give hints to any new competitive applicant of problems that it might face in dealing with the preparation of the product. Trade secret preservation requires that any information supplied by one competitor not be used to expedite the evaluation of a product or a process submitted by a later competitor. There is simply no functional difference between transferring the fruits of digested information to the second applicant and transferring the undigested information itself. No leakage of information between competitors would ever take place without the intervention of FDA. The agency should not allow its premarket consultation and review functions to weaken or blur the property right protections that would otherwise be clear and firm in the absence of its regulation.

¹⁸¹ See 5 U.S.C. § 553(b) (providing that the Administrative Procedure Act's notice and comment rulemaking requirements do not apply to "general statements of policy, or rules of agency organization, procedure, or practice").

¹⁸² See 21 C.F.R. § 314.101(d).

¹⁸³ See SOPP 8404: Refusal to File Procedures for Biologic License Applications Version #3 (Aug. 27, 2007).

¹⁸⁴ See PHSA § 351(a)(2)(A) (directing FDA to "establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses").

¹⁸⁵ Some marginal adjustments to the statute that affect the initial balance have to be expected on a matter this complex. But by the same token, systematic skewing of the statutory system by a succession of one-sided changes cannot be allowed to take place in any form. For example, it would undermine the compromise—and therefore raise a serious takings problem—for FDA to take steps to truncate the 12-year exclusivity period (for example, by narrowing the category of products to which it applies).

The greatest challenge in this area lies not in the articulation of the applicable substantive principles, but in organizing the institutional arrangements that will make good on the Biosimilars Act's promised protection of trade secrets. In this regard, and particularly in view of the Norvasc experience discussed earlier,¹⁸⁶ it is dangerous to rely on instructions to FDA staff that they not use the information that they learn from one application when evaluating another application or consulting with a potential sponsor regarding a development program. The psychological abilities of the ablest public official are not robust enough to prevent inadvertent slippage along the way. Rather than rely exclusively on instructions of this sort, the more sensible strategy would be for FDA to require different individuals for the different applications and different development programs. The statute states only that a biosimilar application must be reviewed "by the *division* within the Food and Drug Administration that is responsible for the review and approval of the application under which the reference product is licensed."¹⁸⁷ It lies within FDA's discretion to require different reviewers within that division. Further, FDA staff working with biosimilar applicants must be instructed not to communicate with others who have worked on the reference biologic or another biosimilar application. Indeed, unless these, and other sensible safeguards are put into place, there could be an abuse of discretion¹⁸⁸ by virtue of impermissible (indeed, unconstitutional) cross pollination among applications.

3. *Skinny BLAs*

The final piece of the statutory quid pro quo is the clear differentiation between two very different pathways to market. To recap, the essence of the statutory quid pro quo has two parts. First, after 12 years a biosimilar applicant may file essentially a short-form BLA, relying on the agency's earlier conclusion that the pioneer product was safe, pure and potent. In exchange, however, this biosimilar applicant must comply with various notice and disclosure provisions designed to allow the two companies to litigate patent issues before the biosimilar reaches the market.¹⁸⁹ To be sure, any new entrant can avoid these notice and disclosure requirements for the abbreviated application, as well as the 12-year exclusivity period, by filing its own full application under section 351(a) of the PHSA, just as if the innovator company had never entered the market. If it takes that route, however, the competitor may no longer rely on the finding of FDA—based on the pioneer's analytical, preclinical, and clinical data—that the pioneer's product was safe, pure and potent. Instead, it must develop all the relevant information needed for a successful application through its own efforts.

In effect, thus, there are now two pathways for any new biological product entrant: the full application under section 351(a) and the abbreviated application under section 351(k). One major task of FDA and if necessary the courts, in interpreting and administering the Biosimilars Act, is to make sure that the advantages that are given new entrants with respect to 351(k) (biosimilar) applications are not allowed to bleed over into the section 351(a) process. The danger is that FDA will accept an application under section 351(a), i.e., as a full and traditional BLA, even though it is

¹⁸⁶ See *supra* section I.D.

¹⁸⁷ PHSA § 351(k)(5)(B) (emphasis added).

¹⁸⁸ See 5 U.S.C. § 706 (requiring a court to set aside any agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law").

¹⁸⁹ PHSA § 351(l).

actually the same as a biosimilar application, with the same amount and type of data as a biosimilar application, or is otherwise abbreviated in comparison to a full 351(a) application. Some commentators call these applications “skinny BLAs” because although they may contain some clinical data, they still rely in some way (even if neither the applicant nor the agency admits this) on FDA’s finding that a prior biologic was safe, pure and potent. Approval of this skinny BLA would allow the applicant to reach the market immediately, with a product that was effectively launched on the back of the trade secrets of the pioneer. The deviation from the standard procedure thus removes the quid pro quo that the pioneer receives for the loss of its trade secrets rights, and thus raises the identical constitutional issues considered earlier.

Regardless of whether the agency takes the stand that section 351(k) is not available, the overall risk—the key risk—is that the agency will say that it has adequate “discretion” under section 351(a) to accept applications that for all intents and purposes look like biosimilar applications or otherwise seek a “shortcut” to the market by relying on a prior agency finding. This risk is not wholly academic. A number of companies have expressed interest in submitting applications under section 351(a) for products that are effectively biosimilars. Further, shortly before the Biosimilars Act was passed, Teva filed an application under section 351(a) for a granulocyte colony-stimulating factor product, Neutroval, that it openly asserts is a biosimilar version of Amgen’s Neupogen.¹⁹⁰ In addition, FDA recently suggested that although it prefers companies to submit biosimilar applications under 351(k), it does not have the authority to require them to do so.¹⁹¹ This is incorrect, as the statute clearly contemplates “biosimilar” products proceeding under section 351(k) and the agency lacks any statutory authority to rely on prior findings when reviewing an application filed under section 351(a). The discussion in the prior sections should make it clear why it *also* presents a grave issue under the Takings Clause. If the agency cannot expressly rely on its prior finding that the pioneer product was safe, pure and potent until 12 years after pioneer approval (and with all of the other portions of the biosimilars scheme respected), it surely cannot do so *immediately* after pioneer approval, solely because the application in question was filed under 351(a). If the agency accepts an application that is largely comparative in nature (e.g., makes a showing that the molecules are highly similar and contains extensive comparative preclinical testing, used to justify a smaller clinical program), it counts as an abuse of discretion to *claim* that this 351(a) application does not ask the agency to rely in some fashion on what it knows about the pioneer product, largely (if not exclusively) from examination of the pioneer’s trade secrets. To issue that approval, does an end run around the statutory bargain, which counts as a taking. To avoid that charge, biosimilar applications or otherwise similarly abbreviated or “skinny” applications must not be approved under 351(a).

Once the question of principle has been answered, some vexing questions of implementation need to be briefly addressed. For the statutory scheme to work, some mechanism is needed to be sure that various biologic applications are slotted in the right category. The primary responsibility for discharging this task falls with FDA. The matter is so critical that the pioneer sponsor must have some means to raise the issue of categorization if FDA does not proceed correctly, either before

¹⁹⁰ See Press Release, Teva, Teva Announces The Submission Of A Biologics License Application (BLA) For XM02 For The Treatment Of Chemotherapy-Induced Neutropenia (Dec. 1, 2009). In September 2010, Teva received a complete response letter from FDA requesting additional information about the product. Press Release, Teva, Teva Provides Update on Status of Neutroval™ (G-CSF) Biologics License Application Submitted to the U.S. Food and Drug Administration (Sept. 30, 2010).

¹⁹¹ FDA Says It Prefers, But Can’t Mandate, Firms Utilize Biosimilars Pathway, FDA WEEK (Dec. 17, 2010).

the agency or, if need be, in court. But the primary responsibility must fall to FDA, because whether and when the pioneer will have enough information to know to make the argument is unclear. It is one thing to know that a BLA has been filed. While FDA treats the filing of an application under section 351(a) as confidential unless and until it is “publicly disclosed or acknowledged,”¹⁹² in practice companies routinely disclose these submissions, for example in securities filings. It is another thing to know enough about the content of that BLA to conclude that it should have been filed under section 351(k). For example, although aspects of the development programs themselves are public because most clinical trials are now posted on the National Institutes of Health website for all the world to see,¹⁹³ the key information proving that the application is really a biosimilar application may be analytical and preclinical (and non-public).¹⁹⁴ And while 351(a) applications that seem to correspond to previously approved biosimilar applications in Europe could be logically inferred to be false (skinny) BLAs in the United States,¹⁹⁵ sequential filings (first Europe, then the United States) may be a thing of the past, now that the U.S. law is in place. To the extent they survive, they can inform the proper slotting of biosimilar applications in the United States.

It is clearly possible to improve on the current unstable regime through which innovators petition FDA to prevent approval of a follow-on drug under the FDCA. In the Hatch-Waxman setting, typically innovators receive notice of the filing of a 505(j) application (in which case they *know* that the application lacks clinical data) or notice of the filing of a 505(b)(2) application (in which case they *know* that the application was more robust, but they know little else), but they do not know the contents of the application. They are left to file citizen petitions while the applications are pending, relying on speculative arguments about the contents of those applications. FDA typically responds to these petitions at the time it approves the generic product, which leaves the innovator little time to rush to the courthouse for a temporary restraining order even after the product launches. Hatch-Waxman thus offers a highly imperfect enforcement mechanism. Owing to the constitutional infirmities of an unbalanced legal regime, FDA must be careful not to place excessive reliance on *Chevron* to shut off challenges to skinny BLAs. To the contrary, the safe and prudent course is for FDA to put in place rules or policies that clearly differentiate between biosimilar applications and full applications—and it should commit publicly to preserving that distinction in its administration of the Biosimilars Act.

CONCLUSION

It would be foolish to defend the Biosimilars Act on the ground that it offers a perfect reconciliation of the various interests. No statute that seeks to deal with such a complex subject matter can claim to achieve that high level of perfection. But in these circumstances it is imperative not to make some unattainable vision of the future the enemy of the sensible and workable system that is now in place. Rather

¹⁹² See 21 C.F.R. § 601.51(b).

¹⁹³ PHS § 402(i).

¹⁹⁴ This is the case because many clinical trials for presumably innovative biologics are comparative in nature given the ethical implications of using a placebo.

¹⁹⁵ As mentioned above, Teva has a pending application under section 351(a) for a product that it claims is a “biosimilar” version of Neupogen. See *supra* note 190. In September 2008, Teva received approval for this product in the European Union. In this case, the approval documents in Europe may shed some light on the likely contents of the U.S. application, but for the pioneer much of this is guesswork. See EMA Assessment Report for Tevagrastim, EMEA/503293/2008 (Sept. 29, 2008), *available at* http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/000827/WC500036667.pdf.

the key point is to make sure that the main contours of the Biosimilars Act do not get lost in the policies, guidance and regulations that FDA will develop under the statute, in the approval decisions it will render, and in the judicial decisions that will be required to interpret its key provisions.

As an initial matter, the deal that is embodied in the Biosimilars Act does not apply to pre-enactment BLAs. That conclusion follows from the strong investment-backed expectations of pre-enactment applicants in the legal system in place when those applications were submitted. At the time that they submitted their data, these applicants had no ability to weigh the statutory bargain (*quid pro quo*) of the Biosimilars Act, which was not yet in place. For these pre-enactment BLAs, case-by-case assessment of just compensation would be needed in order to avoid an unconstitutional taking. But because Congress failed to include any indication that the Biosimilars Act applies retroactively as a statutory matter, courts and FDA need not concern themselves with these case-by-case calculations.

Prospectively, however, the relevant players should keep their eyes on the essential features of the *quid pro quo* between innovative biological manufacturers submitting data to the agency post-Biosimilars Act and their follow-on competitors. In view of these features, three principles emerge.

First, the integrity and distinctiveness of the two separate pathways must be observed. Any new entrant is entitled to follow the same path as the original entrant by going through the same substantive evidentiary hurdles as the pioneer to obtain approval for its product. One who wishes to piggyback on the pioneer's research may save substantial resources, but it must file its application under section 351(k). This comes with restrictions on entry to market (the 12-year window before approval of its product may be effective) and the provisions designed to permit premarket litigation of the patent issues. FDA must take steps to ensure that new entrants cannot file short-cut applications that avoid these restrictions on entry to market.

Second, new entrants must not free ride on the trade secrets of incumbents. The Biosimilars Act contains explicit guarantees that the pioneer will have its trade secrets fully protected throughout the process of examining the new entrant's application. But there is a clear danger that new entrants will benefit from pioneer trade secrets if FDA fails to adopt internal procedures that govern the assignment of review officers and the steps they must take to maintain confidences.

Finally, FDA must ensure that biosimilar applicants comply with the elaborate information sharing arrangements that form the foundation of the premarket patent litigation process created in the Biosimilars Act.

The entire legislative bargain falls to pieces—and the constitutionality of the statute is thus strongly called into question—unless each piece is read in accordance with the statute's overall intention. There are, of course, many additional points that will arise in the interpretation of the Biosimilars Act. The best mode of its interpretation will lie in an even-handed effort to be faithful to the structural commitments of a statute that in many ways is a model of the sophisticated interaction between private stakeholders and public administrative officials.