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ELECTRONIC AND HAND DELIVERY

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

Re: Docket No. 2004P-0171/CP

We submit this letter in response to comments filed by Barr Laboratories, Inc. (Barr) (Comment No. 5) and Professor John C. Yoo on behalf of the Generic Pharmaceutical Association (Comment No. 4) to the above-referenced docket opened by Genentech, Inc. See Genentech Citizen Petition filed to this docket on April 8, 2004 (Genentech Petition). In our petition, we demonstrate that current scientific and legal principles make it extremely difficult – if not impossible – for the Food and Drug Administration (FDA) to approve a generic biotechnology-derived product based on the "similarity" of that product to a Genentech product. Specifically, we demonstrate that to approve such a product would necessarily require that the FDA rely on the trade secret data and information about the manufacturing processes used to create innovator products or the confidential commercial safety and effectiveness information about the resulting product, all of which were submitted to FDA under a promise of confidentiality and for a limited purpose – the review and approval of one particular product

In its comments, Barr raises several issues including scientific considerations surrounding approval of "generic biologics" or "follow-on protein products"; whereas Yoo considers Fifth Amendment issues presented by the FDA's consideration of trade secret and confidential commercial data and information in connection with generic biologics. As explained below, the Barr and Yoo comments are deeply flawed in several key respects. First, the comments mischaracterize the regulatory scheme governing the review and approval of biologics, including the significance of the Hatch-Waxman amendments in 1984. Second, the comments misconstrue the Supreme Court's decision in Ruckelshaus v. Monsanto, 467 U.S. 986 (1984). Third, the comments erroneously dismiss the fundamental Fifth Amendment takings problems that would arise if the FDA were to approve generic biologics or "follow-on" protein products on the basis of the trade secret and confidential commercial data and information submitted by the innovators of such products.

It is critical to note at the outset that neither Yoo nor Barr seriously challenge the proposition that manufacturing data and information is entitled to trade secret protection.[1] Barr contends that safety and effectiveness data is only potentially protected as trade secret but does not contest the "confidential commercial" nature of that information. (Barr Comments at 10-11.) Professor Yoo, on the other hand, makes a critical error throughout his analysis when he treats trade secret manufacturing data as if it has no greater protection than confidential commercial information like safety and effectiveness data. In fact, trade secret manufacturing data is never used in support of another manufacturer's application—not even when generic drug applications are reviewed under the Hatch-Waxman amendments to the Food, Drug, and Cosmetic Act (FDCA). The statutory generic drug approval process only permits an applicant to rely upon earlier conclusions the FDA reached after considering particular confidential commercial information, i.e., safety and effectiveness data submitted by an innovator. It does not permit the FDA to rely on trade secret manufacturing data. Allowing an applicant seeking approval of a generic biologic to rely upon trade secret manufacturing data would be a new and unprecedented step that neither Yoo nor Barr directly addresses.

Executive Summary

The FDA's reliance on trade secret or confidential commercial data and information submitted by an innovator in approving the application of a generic biologic would give rise to a classic regulatory taking. In Ruckelshaus v. Monsanto, the Supreme Court held that the EPA's consideration of health, safety, and environmental data submitted by the applicant for the registration of a pesticide under federal law would constitute a taking with respect to data submitted during the period that the government had expressly promised that it would remain confidential. Under the reasoning of Monsanto, the FDA's public disclosure or consideration of both trade secret or confidential commercial data and information submitted by a biologics innovator in evaluating a generic biologic would effect a taking as well.

For decades, the FDA has assured innovators that trade secret manufacturing and confidential commercial safety and effectiveness data and information submitted in connection with a biologics application submitted under section 351 of the PHSA would be closely guarded. Statutory provisions protect the confidentiality of such information, which Congress has ratified through its own actions, including in the Hatch-Waxman amendments. Specifically, Hatch-Waxman carved out a special regime for the approval

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[1] Barr does baldly state that "Genentech made no showing" that its manufacturing information qualifies as a trade secret. Barr Comments at 10, see also id. at 7 n.5. This is simply untrue. Confidential manufacturing processes are clearly considered trade secrets under state law. See Genentech Pet. at 9-12. Moreover, trade secret data and information contained in both biologic license applications (BLAs) and new drug applications (NDAs), including chemistry, manufacturing and controls (CMC) information, remains protected from use and disclosure by FDA. 21 U.S.C. § 331(j); 21 C.F.R. § 20.61; 21 C.F.R. § 601.51(f).

of generic drugs under the FDCA, but reaffirmed the rule of confidentiality with respect to data submitted in connection with biologics, especially those licensed under the Public Health Service Act. In reliance on that longstanding regulatory scheme, innovators such as Genentech have invested the hundreds of millions of dollars in research and development necessary to bring new biologics to market, and the public has benefited immensely from the creation of new and life-altering products.

These governmental actions have created a reasonable investment-backed expectation that trade secret and confidential commercial data and information will be kept confidential. Any change to this regulatory framework must be both carefully considered and implemented only after a credible, transparent, and rigorous scientific dialogue with all relevant stakeholders. Absent such steps, the Fifth Amendment prohibits the FDA from considering the trade secret and confidential commercial data submitted by an innovator in connection with an application to market a generic biologic without providing the innovator with just compensation for that taking.

The Barr And Yoo Comments Are Premised On A Mistaken Characterization Of The Existing Regulatory Scheme

Both the Barr and Yoo comments are premised on an incomplete construction of the regulatory scheme governing biologics. Indeed, Yoo's entire constitutional analysis is premised on the assumption that "a proposal for approving generic biologics would be modeled to some degree on the approval of generic pharmaceutical products under Hatch-Waxman." Yoo Letter at 1 (emphasis added). There is no reason for the FDA to adopt that hypothetical premise. Rather, the longstanding regulatory scheme with respect to biologics is far different than the one Yoo hypothesizes and any new system would need to take those differences into account. 2/

Indeed, the settled regulatory rule is—and always has always been—that data and information concerning manufacturing processes as well as a product's safety and

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2/ Both the Barr and Yoo comments at times appear to treat biologics as if they were uniformly subject to the FDCA. See, e.g., Barr Comments at 17. But, most biologics are licensed exclusively under the PHSA. And, when Hatch-Waxman was enacted, it excluded those products from its scope. See 1984 U.S.C.C.A.N. 2686, 2712-14; Letter from Harry M. Meyer, Jr. Director, Center for Drugs and Biologics, FDA (Nov. 16, 1984) ("There is no specific provision in Title I that includes . . . biologicals . . . . The Act refers to generic versions of those drugs originally approved under Section 505(b) . . . of the Federal Food, Drug and Cosmetic Act. Biologicals are approved under the Public Health Service Act . . . . Accordingly, we do not consider these products to be covered by Title I."); 57 Fed. Reg. 17950, 17951 (Apr. 29, 1992) (ANDA provisions "inapplicable to . . . biological drug products licensed under 42 U.S.C. § 262.").

effectiveness, cannot be used to approve a subsequent application for a biologic.[3] Before 1984, that same rule applied to all drugs; however, Congress chose to alter the rule in certain respects through the Hatch-Waxman amendments to the FDCA. As explained below, the narrow exception that Congress carved out in Hatch-Waxman for using safety and effectiveness information in connection with the approval of certain generic drugs underscores that Congress did not alter the longstanding prohibition against using an innovator's trade secret data and information for reviewing and approving a generic drug or for using either trade secret or confidential commercial data and information in considering an application for a generic biologic.

More than 30 years ago, in a proposed rulemaking relating to disclosure of safety and effectiveness data under the FDCA, the FDA observed that:

> "Research data on the safety, functionality, and effectiveness of a wide variety of ingredients and products are submitted to FDA as part of various petitions and applications. Since 1938, FDA has taken the position that such data ordinarily represent valuable commercial property and trade secrets that must be retained as confidential and may not be disclosed to the public. The Attorney General's memorandum concluded that such research data are to be retained as confidential, and the House Report emphasized that, when the Government receives information such as this under a good faith pledge of confidentiality, the Government should keep its word.

37 Fed. Reg. 9128, 9130 (May 5, 1972) (emphasis added). [4]/

That rule was challenged by some drug companies on the ground that refusing to allow access to safety and effectiveness data effectively granted innovators a monopoly. 39 Fed. Reg. 44602, 44614 (Dec. 24, 1974). In response, the FDA observed that "Congress . . . weighs the need for release of certain information against the need for retaining it as confidential." Id. "With regard to trade secrets," the FDA continued, "Congress has concluded that the need to withhold such information outweighs the need to release it." Id. If subsequent manufacturers wanted to submit applications that relied on others' trade secret and confidential commercial data and information, they needed to lobby the Congress to change the statute. But FDA had "on a number of occasions pointed out to Congress the effect of this requirement, and has suggested that Congress

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[3]/ Just recently, the Eighth Circuit affirmed that manufacturing data and information concerning biologics are trade secrets under state law. See Wyeth v. Natural Biologics Inc., ---F.3d ---, 2005 WL 124269 (8th Cir. January 24, 2005).

[4] At the time, FDA considered safety and effectiveness data to fall within the definition of "trade secret" and discussed safety and effectiveness as "trade secrets." That position has since changed and the agency now defines them separately. See 21 C.F.R. 20.61(a) and (b).

consider whether this policy should be retained or changed. Congress has, to date, not taken action on this matter." Id. at 44634 (emphasis added).

Likewise, the FDA has emphasized that manufacturing trade secret and other confidential commercial data and information submitted in connection with a biologic will be kept confidential by the FDA and will not be disclosed to competitors or used by the FDA in considering a generic biologic. Genentech Petition at 23. Indeed, the FDA has made clear that there is no such thing as a "me too" biologic. See 39 Fed. Reg. at 44641.

For much of the FDA's history, it was not even possible for one applicant to use another applicant's safety and effectiveness information under either the PHSA or the FDCA. Since 1962, with limited exceptions, applicants under the FDCA must submit their own studies demonstrating safety and effectiveness. See 57 Fed. Reg. 17950 (Apr. 28, 1992). No applicant for licensing of a biologic under the PHSA has ever been allowed to rely on outside data—not even published studies – to establish safety and effectiveness. 21 C.F.R. § 601.2(a); see also 39 Fed. Reg. at 44641. Because each applicant for a biologic covered by the PHSA must support its own application with its own data, innovators reasonably expect that no other applicant may use an innovator's safety and effectiveness data or information to support a later application. [5]/

The Hatch-Waxman amendments of 1984 carved out a limited exception to the background rule that safety and effectiveness data may not be used or disclosed—although trade secrets, such as manufacturing data, remained inviolate. In order to facilitate the development of generic drugs, Hatch-Waxman created a carefully limited

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[5]/ Every biologics manufacturer must prepare and submit its own safety and effectiveness data. 21 C.F.R. 601.2(a). Because no subsequent biologics applicant may rely on an earlier manufacturer's safety and effectiveness data, 39 Fed. Reg. 44641 (Dec. 24, 1974); Letter from H. Meyer, Director, Center for Drugs and Biologics, FDA (Nov. 16, 1984), the FDA's regulations permit release of certain safety and effectiveness data. 21 C.F.R. 601.51. But if another manufacturer could benefit from the FDA's consideration of such safety and effectiveness information or the public disclosure of such information, then the use or disclosure of such information would violate the Trade Secrets Act and Section 301(j) as well as the FDA's own pronouncements. See 21 U.S.C. 331(j); see also August 20, 1996 letter from V. Zonana, HHS, to R. Theis at 3 (relying on Section 301(j) to deny release of "manufacturing methods or processes, production data, comparability data, and safety and effectiveness data" submitted with biologics application) (attached to Genentech Petition as exhibit 2). In an any event, as a practical matter, the FDA does not release safety and effectiveness data on biologics and it does not and could not rely on such data in approving subsequent biologics applications because, as the FDA has recognized, even subtle changes in the manufacturing process of a biologic can have a material effect on the safety or effectiveness of a product. See infra at __. Moreover, the agency's regulations prohibit the disclosure of confidential information on "[m]anufacturing methods or processes." 21 C.F.R. 601.51(f)(1).

process allowing prospective manufacturers of drugs subject to the FDCA to use the agency's conclusions about the drug's safety and effectiveness demonstrated by an innovator where the generic drug applicant can demonstrate that its proposed product is "the same" as the innovator. 21 U.S.C. 355(j)(2)(A). But biologics covered by the PHSA—i.e., all but a small category of biologics—were excluded from this carefully crafted exception. Manufacturers of biologics approved under the PHSA are therefore still responsible for providing their own safety and effectiveness data, as are all but a handful of manufacturers of biologics approved under the FDCA. See Serono v. Shalala, 158 F. 3d 1313 (D.C. Cir. 1998). And, as Genentech points out in its Petition, the agency's ability to review an application under the FDCA's Hatch-Waxman provisions for a generic version of a biologic product approved in the first instance under the FDCA is effectively constrained. The statute does not allow FDA to compare the generic product's manufacturing process against the innovator's process. See Genentech Petition at 21. Therefore, FDA cannot reach a scientifically sound conclusion about the degree to which the safety and effectiveness data about the innovator's product even applies to the generic version.

Moreover, in carving out a limited exception to the longstanding rule of confidentiality for safety and effectiveness data submitted for certain drugs, Hatch-Waxman ratified the FDA's regulations and procedures relating to the confidentiality of trade secret manufacturing and confidential commercial safety and effectiveness data and information submitted in connection with biologics that are not affected by Hatch-Waxman. See House Rep. No. 98-857 (Part I) at 36 (Sept. 6, 1984) ("[E]xcept as provided in this section, the Committee does not intend to change other regulations regarding Freedom of Information Act requests, trade secrets, and confidentiality of IND, NDA and master file safety and effectiveness information and data."); 130 Cong. Rec. S10988-89 (daily ed. Sept. 12, 1984) (Senator Hatch confirmed that it was his intent to ratify FDA's "policy and procedures" with respect to "release of information submitted to FDA by manufacturers"). That ratification effectively codified the FDA's prior interpretation of federal law as protecting innovators' trade secret and confidential commercial data and information. FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 144 (2000).

In Brown & Williamson, the FDA had taken the position through various regulatory actions and pronouncements that tobacco was beyond its ordinary regulatory jurisdiction. The Court concluded that Congress had "effectively ratified" that longstanding regulatory position through a series of statutes that created "a distinct regulatory scheme for cigarettes and smokeless tobacco." Id. at 155-156. So too here. As explained above, the FDA has long taken the position that trade secret and confidential commercial data and information submitted in connection with an innovator's drug application may not be used by FDA in connection with a subsequent application. When Congress created "a distinct regulatory scheme" under the Hatch-Waxman amendments with respect to the approval of certain drugs (though not biologics covered by the PHSA), Congress "effectively ratified" the longstanding rule of confidentiality with respect to trade secret and confidential commercial data and

information submitted by innovators in connection with drugs not covered by Hatch-Waxman.

Neither Barr nor Yoo effectively addresses the reliance that innovators historically have placed on the FDA's regulatory scheme. Nor do they address with any rigor our evidence about the proper interpretation of the statutory nondisclosure provisions contained in the FDCA. 21 U.S.C. 331(j); Genentech Petition at 12-13. Congress made clear that Section 301(j) of the FDCA was intended to safeguard manufacturers' property rights, S. Rep. No. 74-361, at 27 (1935), and the FDA has historically taken steps to protect such property. See 37 Fed. Reg. at 9130. Since then, Congress has enacted several other statutory provisions requiring the agency to protect manufacturers' trade secret data and information. See 21 U.S.C. 379; 360j(h)(4). All of these provisions, not to mention Hatch-Waxman itself, evince Congress's ratification of the longstanding regulatory rule that the FDA maintains the confidentiality of both trade secret and confidential commercial data and information submitted in connection with innovators' marketing applications.

The Barr And Yoo Comments Are Based On A Flawed Interpretation Of The Supreme Court's Decision in *Monsanto*

Both the Barr and Yoo comments attempt to draw support from the Supreme Court's decision in Monsanto. Yoo Letter at 5-7; Barr Comments at 11-14. However, the comments are premised on an erroneous understanding of that decision. In at least two key respects, Monsanto bolsters the conclusion that the FDA's use of trade secret or confidential commercial data and information submitted by an innovator to approve a generic biologic would constitute a taking.

First, Monsanto illustrates that the FDA's consideration of trade secret and confidential commercial data and information submitted by an innovator company in connection with a subsequent application directly implicates the Takings Clause of the Fifth Amendment. Monsanto involved a takings challenge to the EPA's consideration of data submitted by an applicant for registration of a pesticide under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) in evaluating a subsequent application. The Supreme Court concluded at the outset of its analysis that (1) trade secret data, including health, safety and environmental data, may constitute a protected property interest under the Fifth Amendment, see 467 U.S. at 1001-1003; and (2) that the Fifth Amendment was implicated if the EPA either "discloses those data" or simply "considers the data in evaluating another application." Id. at 1005.

Yoo suggests that in any procedure for generic biologics the FDA would not be relying on the confidential commercial safety and effectiveness data submitted in connection with the innovator's application, but rather only on "the public, non-trade secret fact that it concluded that the innovator drug was safe and effective." Yoo Letter at 8 (emphasis added). That suggestion is untenable. It is not feasible to divorce the FDA's decision to approve a biologic from either the trade secret manufacturing or

confidential commercial safety and effectiveness data and information underlying that application. That is because, in order to establish that the FDA's prior determination that a biologic is safe and effective applies with respect to a generic application, the subsequent applicant will have to prove that its product is the "same" as the innovator biologic and establish bioequivalence. There is no basis for the FDA to make a "sameness" determination about a biologic without considering the underlying trade secret manufacturing and confidential commercial safety and effectiveness data, regardless of whether that product is regulated under the FDCA or the PHSA. See Genentech Petition pp. 16-19. [6]/

Furthermore, as the FDA has recently stated, "[i]n the case of biological drugs, changes in the manufacturing process often lead to subtle unintentional changes in the product, resulting in altered pharmacokinetics." FDA, Guidance for Industry, Exposure-Response Relationships – Study Design, Data Analysis and Regulatory Applications (April 2003). As a result, in order to evaluate the safety or effectiveness of a biologic, the FDA must, among other things, compare the manufacturing processes used by the innovator and that of the generic applicant. See Biopharmaceuticals ("Follow-on" Protein Products): Scientific Considerations For an Abbreviated Approval Pathway, filed by GHPA December 8, 2004, to FDA Docket No. 2004N-0355, at 13. The FDA cannot do so without considering the trade secret manufacturing data submitted by an innovator in evaluating a generic application. As Monsanto recognizes, to the extent that the government has promised innovators that trade secret data will remain confidential, the agency's consideration of trade secret data directly implicates the protections of the Fifth Amendment.

Second, Monsanto underscores that the FDA's consideration of trade secret or confidential commercial data and information that is subject to the longstanding rule of confidentiality in approving a subsequent application would in fact give rise to a taking under the Fifth Amendment. That conclusion follows from an examination of the takings implications of the three different statutory and regulatory regimes that the Court considered in Monsanto: (1) pre-1972 FIFRA; (2) 1972-1978 FIFRA; and (3) post-1978 FIFRA.

Pre-1972. Before 1972, neither the statute nor the EPA gave any assurance that health and safety data submitted in connection with an application for registration would be kept confidential by the EPA. 467 U.S. at 991. To the contrary, the existing

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[6]/ Both the FDA and generic biologics proponents acknowledge that the Hatch-Waxman procedure of identifying "sameness" will not work for the vast majority of biologics. The significant difficulty in showing a biologic's "sameness" require a process different from that used for drugs. Indeed, even Barr has acknowledged that clinical testing would still be required for generic biologics. Law of Biologic Medicine 2004: Hearing. Before the Senate Comm. On the Judiciary, 108th Cong., 2d Sess. (June 23, 2004) (testimony of Carole Ben-Maimon, M.D., President and Chief Operating Officer, Barr Laboratories).

regulatory practice seemed to permit the use of such data in connection with a subsequent application. As the Court noted, there was "some evidence that the practice of using data submitted by one company during consideration of the application of a subsequent applicant was widespread and well known." Id. at 1009 & n. 14 (emphasis added). As a result, the Court concluded that the EPA's "consideration or disclosure of data" submitted prior to 1972 would "not effect a taking." Id. at 1013.

1972-1978. Between 1972 and 1978, the statute gave applicants an "explicit assurance that EPA was prohibited from disclosing publicly, or considering in connection with the application of another, any data submitted by an applicant if both the applicant and EPA determined the data to constitute trade secrets." Id. at 1011. As a result, the Court held that applicants who provided data to the EPA between 1972 and 1978 did so subject to the government's "express promise" that the data would remain confidential, and that the EPA's "consideration or disclosure" of such data in connection with another application would constitute a taking. Id. at 1011, 1013.

Post-1978. After 1978, the statute provided that the health, safety, and environmental data would remain confidential 10 years, but after 10 years the EPA was free to use the data in evaluating a subsequent application. Id. at 996 and 1006. As a result, the Court held that the EPA's use of data after the 10-year period had lapsed would not constitute a taking. Id. at 1013.

Both Yoo and Barr analogize the statutory and regulatory scheme with respect to the approval of biologics to the pre-1972 version of FIFRA. See Yoo Letter at 8-9; Barr Comments at 13, 15. That analogy is fundamentally flawed. As discussed above, the unbroken regulatory rule followed by the FDA is that all trade secret and confidential commercial data and information submitted in connection with an application for the approval of a biologic will not be used or considered in connection with a subsequent application. In that regard, the regulatory regime with respect to biologics is the exact opposite of the pre-1972 regulatory regime with respect to pesticides, where, as noted above, there was evidence of a "widespread and well-known" administrative practice of "using data submitted by one company during consideration of the application of a subsequent applicant." Id. at 1009.

In fact, the regulatory regime governing biologics subject to the PHSA is most directly analogous to the 1972-1978 statutory scheme discussed in Monsanto, where the Court found that the federal government had explicitly promised to keep the data submitted in connection with an application for registration secret. As discussed above, for decades the federal government has promised that it would maintain the confidentiality of both trade secret manufacturing and confidential commercial safety and effectiveness data and information submitted in connection with an application for a drug approval. The only exception that the government has made to that rule is for otherwise confidential commercial safety and effectiveness information about drugs covered by the Hatch-Waxman amendments of 1984.

Yoo argues that the only promise of confidentiality that can give rise to a taking under the Fifth Amendment is one that is "statutory in nature." Yoo Letter at 11. That argument fails for at least two reasons. First, the federal government's promise to keep trade secret and confidential commercial data and information submitted in connection with marketing applications confidential is statutory in nature. As discussed, the longstanding regulatory practice has been to maintain the confidentiality of all data submitted in connection with applications. That practice was adopted by an administrative agency (the FDA) operating well within the parameters of its statutory delegation of authority, and therefore has the effect of law. More to the point, in enacting the Hatch-Waxman amendments, Congress affirmatively ratified that longstanding regulatory regime, and Congress has enacted other statutes protecting the confidentiality of trade secret and confidential commercial data and information. See supra at __.

Second, and in any event, courts have recognized that a regulatory promise can give rise to a Fifth Amendment taking. See Tri-Bio Labs. v. United States, 836 F.2d 135, 140-141 (3d Cir. 1998) (FDA regulation was "provision of law" that supported reasonable investment-backed expectations); see also A.L. Pharma, Inc. v. Shalala, 62 F.3d 1484, 1489 (D.C. Cir. 1995). Although it is true that in Monsanto the Court pointed to the fact that between 1972 and 1978 the statute gave applicants an "explicit assurance" of confidentiality, 467 U.S. at 1011, the Court never stated that the only promise of confidentiality that could give rise to a taking was one explicitly set forth in a statute. At least where an agency has acted within its statutory mandate (as the FDA has done here), an agency's regulatory promise of confidentiality may give rise to a taking as well.

Furthermore, the application of Yoo's argument that only a statutory promise of confidentiality may give rise to a taking would lead to an absurd result here: that the FDA could for decades make explicit guarantees that trade secret and confidential commercial data and information submitted in connection with applications for biologics would be kept confidential, but that such guarantees could give rise to no protected interest under the Fifth Amendment. Nothing in Monsanto supports that counter-intuitive result. Nor, as explained next, does that conclusion find in support in the Penn Central analysis for regulatory takings.

Under A Proper Analysis, The FDA's Use Of An Innovator's Data and Information To Approve A Generic Biologic Would Constitute A Taking

Under a proper takings analysis, it is clear that the FDA's use of the trade secret manufacturing and confidential commercial data and information submitted by an innovator in approving a generic biologic would give rise to a taking proscribed by the Fifth Amendment. Under the Penn Central test for analyzing regulatory takings, the Supreme Court weighs three factors: (1) the character of the governmental action, (2) its economic impact, and (3) its interference with reasonable investment-backed expectations. Penn Central Transp. Co. v. City of New York, 438 U.S. 104, 124 (1978). Each of those factors points to a taking here.

1. Character of the Government Action. The FDA has asserted no valid regulatory interest for retroactively breaking its longstanding promise of maintaining the confidentiality of trade secret and confidential commercial data and information submitted in connection with an application for the approval of a biologic. Moreover, there is no basis for disproportionately imposing the costs of bringing generic biologics to the market on the innovator companies who have invested hundreds of millions of dollars in research and development in discovering and bringing new biologics to the public in the first place.

2. Economic Impact. The economic impact of a rule that permits the FDA to use the trade secret and confidential commercial data and information submitted by an innovator in considering the application of a generic biologic would be devastating from both the standpoint of the innovators of biologics that have already invested hundreds of millions of dollars in research and development efforts based in part on the agency's promise that such data would remain confidential, and from the standpoint of maintaining the necessary market incentives for companies to invest the time and money necessary to develop new, potentially life-altering biologics.

As the Supreme Court recognized in Monsanto, because a trade secret consists primarily of the right to exclude others, the economic value of that property is destroyed if others are given the right to use that information. 467 U.S. at 1011-1012. Whether the FDA uses innovators' trade secrets or confidential commercial data and information to benefit their competitors or discloses the same data and information to the public at large, it will destroy the economic value of that data and information. If the data and information is used, then the requisite economic impact exists. That is surely true in this context, where the trade secret and confidential commercial data and information submitted by innovators is typically the result of hundreds of millions of dollars of research and development efforts.

3. Reasonable Investment-Backed Expectations. The crux of any regulatory takings analysis in this context is whether the FDA's use of trade secret and confidential commercial data and information submitted by innovators in considering a generic biologic application would interfere with the reasonable investment-backed expectations of innovators. Because the unbroken regulatory practice has been to maintain the confidentiality of such data, the FDA's decision to break that promise with respect to trade secret and confidential commercial data and information that already has been submitted by innovators would destroy the reasonable investment-backed expectations of the companies that have invested the extraordinary time and expense necessary to discover, develop, and obtain the necessary regulatory approval of a new biologic.

Yoo and Barr suggest that innovators possess no "reasonable investment-backed expectation" that trade secret and confidential commercial data and information submitted by an innovator of a biologic will not be used to support another manufacturer's application. As discussed above, that argument is contradicted by the longstanding regulatory practice of maintaining the confidentiality of such data and

information and the Supreme Court's decision in Monsanto. In Monsanto, the Court held that where the government guarantees how it will use information it receives—including its "confidentiality and exclusive use"—then "this explicit governmental guarantee form[s] the basis of a reasonable investment-backed expectation." 467 U.S. at 1011. The existing statutory and regulatory scheme emphatically confers such a guarantee with respect to trade secret and confidential commercial data and information submitted to the FDA in connection with an application for approval of a biologic.

Yoo argues that "statutory silence in a heavily regulated industry places applicants on notice that they cannot form reasonable investment-backed expectations that submitted data will not be used by the agency in the future." Yoo Letter at 7. But the longstanding regulatory regime is not "silent" on the confidentiality of data and information submitted by innovators. To the contrary, as discussed above, the FDA has consistently read its own statutory mandate to forbid it from using innovator trade secret and confidential commercial data and information in considering a subsequent application, and Congress has ratified that practice.

At the same time, the mere fact that a company operates in a highly regulated industry does not prohibit the company from forming reasonable investment-backed expectations based on the government's own promises. Cienega Gardens v. United States, 331 F.3d 1319, 1350 (Fed. Cir. 2003); see also Palm Beach Isles Assocs. v. United States, 231 F.3d 1354, 1364 (Fed. Cir. 2000). Indeed, the industry for pesticides is highly regulated. But, as discussed, the Supreme Court in Monsanto held that companies that operate in that industry could form reasonable investment-backed expectations based on the regulatory promises of the government that it would maintain the confidentiality of data submitted in connection with applications for pesticide registration.

As Yoo points out (p. 7), in Monsanto, the Court observed that, "[i]n an industry that has long been the focus of great public concern and significant regulation, the possibility was substantial that the Federal Government, which had thus far taken no position on disclosure of health, safety, and environmental data concerning pesticides, upon focusing on the issue, would find disclosure to be in the public interest." 467 U.S. at 1008-09 (emphasis added). In the industry for biologics, however, the federal government has long taken a position on that issue: the government has for decades barred the disclosure of trade secret and confidential commercial data and information submitted by innovators. The participants of that industry were entitled to take the government at its word.

Allowing generic applicants to free-ride on an innovator's trade secret and confidential commercial data and information would amount to a forced transfer of the innovator's property to the generic manufacturer. Although doing so would fundamentally destroy a critical economic incentive for developing potentially life-saving or life-altering biologics and raise other policy concerns, Congress could—on a going-forward basis—adopt a regulatory regime that made clear to innovators that safety, effectiveness, or manufacturing data would not be kept secret by the FDA and, instead,

could be used by generic applicants. But any action by Congress or the FDA that would have the effect of retroactively revoking the government's longstanding promise of confidentiality with respect to the submission of such data would improperly divest innovator companies of the economic value of such data and require just compensation under the Fifth Amendment.

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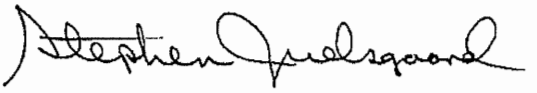
Respectfully submitted,



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Executive Vice President, General Counsel,
and Secretary