United States Court of Appeals
For the First Circuit

No. 18-2086

IN RE: LANTUS DIRECT PURCHASER ANTITRUST LITIGATION

CÉSAR CASTILLO, INC., on behalf of itself and all others similarly situated; FWK HOLDINGS LLC, on behalf of itself and all others similarly situated,

Plaintiffs, Appellants,

v.

SANOFI-AVENTIS U.S., LLC,

Defendant, Appellee,

SANOFI GMBH,

Defendant.

APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

[Hon. Judith G. Dein, U.S. Magistrate Judge]

Before

Torruella, Thompson, and Kayatta,
Circuit Judges.

Matthew W.H. Wessler, with whom Joshua Matz, Gupta Wessler PLLC, Thomas M. Sobol, Kristie A. LaSalle, Kristen A. Johnson, Hagens Berman Sobol Shapiro LLP, John D. Radice, Radice Law Firm, P.C., Joseph M. Vanek, David P. Germaine, John P. Bjork, Vanek, Vickers & Masini, P.C., Paul E. Slater, Matthew T. Slater, Sperling & Slater, P.C., Linda P. Nussbaum, Bradley J. Demuth, Nussbaum Law

Group, P.C., Juan R. Rivera Font, and Juan R. Rivera Font LLC were on brief, for appellants.

Benjamin C. Mizer, with whom Laura Diss Gradel, Julia E. McEvoy, Rosanna K. McCalips, Alisha M. Crovetto, and Jones Day were on brief, for appellee.

February 13, 2020

KAYATTA, Circuit Judge. The FDA maintains a publication called Approved Drug Products with Therapeutic Equivalence Evaluations, known in the industry as "the Orange Book." The Orange Book lists patents said by their owners to claim FDA-approved drugs. The listing of a patent in the Orange Book arms the patent-owning drug manufacturer with the ability to trigger an automatic, thirty-month suspension of the FDA's approval of a competitive product. The principal questions posed on this appeal are whether Sanofi improperly submitted a patent for listing in the Orange Book and, if so, whether Sanofi is potentially liable under the antitrust laws to drug purchasers who were allegedly harmed by the effective extension of Sanofi's monopoly. We answer "yes" to both questions and vacate the dismissal of the plaintiffs' complaint to the extent that the district court held otherwise.

I.

A.

When a drug manufacturer files an application for FDA approval of a new drug (a "new drug application," or NDA) or a supplemental application for approval of changes to an already-approved drug (a "supplemental new drug application," or sNDA), the manufacturer must

> file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to

> which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

21 U.S.C. § 355(b)(1).[1] The FDA reviews the submission for completeness and to see, in Sanofi's words, whether the patent "is not facially ineligible for listing." See 21 C.F.R. § 314.53(c)(2)(ii). Upon accepting the submission, the FDA then lists the patent in the Orange Book. Pointing to its "scarce resources," the FDA has expressly declared that it does not "review patent information for its accuracy and relevance." 59 Fed. Reg. 50,338, 50,343, 50,345 (Oct. 3, 1994). Rather, the agency requires the manufacturer to declare that the submitted patent claims the "drug substance," "drug product (composition/formulation)," or "one or more methods of using" the drug for which it is listed. 21 C.F.R. § 314.53(c)(2)(i)(M)–(O). The plaintiffs characterize the FDA's review of tendered Orange Book listings as purely "ministerial," noting that the FDA has refused to create any additional processes for "review[ing] the scope of [a submitted Orange Book] patent and its application to the approved drug

[1] The legal obligations of drug manufacturers at issue in this case are set out by the Hatch-Waxman Amendments, or the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98–417, 98 Stat. 1585 (codified as amended at 21 U.S.C. § 355 and 35 U.S.C. § 271(e)), which amended the Federal Food, Drug, and Cosmetic Act ("FDCA"), Pub. L. No. 75–717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301–397).

product" or for delisting patents in the Orange Book. 68 Fed. Reg. 36,676, 36,683 (June 18, 2003).[2]

The Orange Book listing comes into play when another manufacturer seeks FDA approval to sell a competing drug based on the safety and efficacy studies for the original, already-approved drug. See 21 U.S.C. § 355(b)(2); 21 C.F.R. § 314.54(a)(1)(iii). In its application, the aspiring competitor must certify for each patent listed in the Orange Book for the original drug that (1) the patent has expired, (2) the competing manufacturer will wait for the patent to expire before marketing its competing product, or (3) the listed patent is invalid, unenforceable, or will not be infringed. 21 U.S.C. § 355(b)(2)(A)(i)–(iv). The last of the foregoing certifications is referred to as a "Paragraph IV certification."

[2] The FDA does have a limited mechanism for reviewing the "accuracy or relevance of patent information submitted" for listing in the Orange Book. 21 C.F.R. § 314.53(f). Specifically, anyone may notify the Agency in writing about a potential problem. Id. § 314.53(f)(1). In the case of patents claiming the drug substance or drug product, the NDA holder may then be required either to "confirm the correctness of the patent information," or "withdraw or amend the patent information." Id. § 314.53(f)(1)(i)(A). There is no indication that any party attempted to use this process in this case. And in any case, as noted in In re Buspirone Patent Litigation, this process would not provide convincing evidence that "the FDA engaged in substantive review of the information." 185 F. Supp. 2d 363, 371-72 (S.D.N.Y. 2002). In fact, the regulation is clear that "[u]nless the NDA holder withdraws or amends its patent information in response to the patent listing dispute, the Agency will not change the patent information in the Orange Book." 21 C.F.R. § 314.53(f)(1)(i)(A).

A Paragraph IV certification has two direct effects on the resolution of any patent dispute between the original manufacturer and the putative competitor. First, the statute treats the filing of a Paragraph IV certification as an infringement of the listed patent, allowing the putative competitor to force the patentholder to acquiesce or sue without exposing the competitor to damages for actual infringement. See 21 U.S.C. § 355(c)(3)(C); 35 U.S.C. § 271(e)(2)(A). Second, if the patentholder initiates an infringement lawsuit within forty-five days of receipt of a Paragraph IV certification, the mere filing of the lawsuit triggers an automatic, thirty-month stay of FDA approval of the would-be competitor's application. 21 U.S.C. § 355(c)(3)(C). And while that thirty-month period may be shortened by resolution of the infringement action or order of the court, id., the status quo, the allocation of burdens, and the life-span of patent litigation can all work against any such shortening.

The plain text of the statute calls for the listing of patents "which claim[] the drug for which [an application is submitted] or which claim[] a method of using such drug." Id. § 355(b)(1). In its implementing regulations, the FDA makes it clear that "only" such patents are to be listed. 21 C.F.R. § 314.53(b)(1). The FDA also provides further guidance, to be discussed, infra, on what patents qualify as claiming a drug. See,

e.g., id. The FDA has noted that these requirements "reflect an attempt to balance two competing interests: [p]romoting competition between 'brand-name' or 'innovator drugs' and 'generic' drugs, and encouraging research and innovation." 68 Fed. Reg. at 36,676.

B.

In reviewing the dismissal of a complaint, see Fed. R. Civ. P. 12(b)(6), we assume that all pleaded facts and reasonable inferences drawn from those facts are true, Breiding v. Eversource Energy, 939 F.3d 47, 49 (1st Cir. 2019) (quoting Fothergill v. United States, 566 F.3d 248, 251 (1st Cir. 2009)). The complaint in this case, as amended, focuses on the drug insulin glargine, sold by Sanofi under the brand name "Lantus." Insulin glargine is a long-lasting and much-favored form of insulin that can be used to manage diabetes. In 2014, annual sales of Lantus products in the United States amounted to $7.87 billion.

Sanofi first obtained approval from the FDA to market Lantus for management of diabetes in 2000. With its original application, Sanofi submitted U.S. Patent No. 5,656,722 ("the '722 patent") for listing in the Orange Book. The '722 patent claimed the drug insulin glargine and was set to expire in August 2014, with its period of regulatory exclusivity ending in February 2015. Had Sanofi filed nothing else with the FDA, other companies would have been able to pursue requests for FDA approval to sell insulin

glargine products beginning in 2015 with the end of the '722 patent's grace period of exclusivity.

In 2006, Sanofi filed an sNDA to sell insulin glargine in a disposable injector pen device called the Lantus SoloSTAR. Sanofi had previously sold Lantus only in vials or cartridges for reusable injectors. The FDA reviewer evaluating the SoloSTAR product described it this way:

> The SoloStar injection system is a device that provides a method of accurately injecting a selected dose of insulin . . . . The device is intended to be used for self-injection by patients. . . . The dose is pre-selected by rotating a dosage selector at the rear end of the device. The number of selected insulin units is displayed in the dose window on the side of the pen. The dialing mechanism allows dosage in 1 insulin unit increments. It provides a maximum of 80 insulin units in one dosing. . . . The dose is delivered by pressing the injection button.

Sanofi sells the SoloSTAR pen for use with several active drugs in addition to insulin.

In 2007, the FDA accepted Sanofi's sNDA for the SoloSTAR and categorized it as a change to Lantus's labeling or container. In 2013, Sanofi submitted patents associated with the SoloSTAR to the FDA for listing in the Orange Book. While the complaint references a number of those patents, plaintiffs pare their arguments on appeal to U.S. Patent No. 8,556,864 ("the '864 patent"), named "Drive Mechanisms Suitable for Use in Drug Delivery Devices," which is set to expire in 2024.

In intellectual property law, a "patent claim" is "the portion of the patent document that defines the scope of the patentee's rights." Markman v. Westview Instruments, Inc., 517 U.S. 370, 372 (1996). The '864 patent contains ten claims, all concerning aspects of a "drive mechanism" that serves as a part of the SoloSTAR drug injector pen. The "drive mechanism" "enabl[es] the administration of medicinal products from" a pen injector's cartridge. Claim 1 sets out the attributes of the drive mechanism; Claim 2 describes a drive mechanism with slightly different attributes; Claims 3 through 7 describe different constructions of the mechanism in Claim 2; Claim 8 describes yet another variation on the drive mechanism; and Claims 9 and 10 describe alternative variations to the mechanics of Claim 8. The patent does not include a claim for an injector pen more broadly, though it does mention that the drive mechanism is intended for use in a "drug delivery device." Elsewhere the patent states that the technical field of the patent is "drive mechanisms suitable for use in drug delivery devices, in particular pen-type injectors." The patent does not mention insulin glargine or the Lantus SoloSTAR at any point. The patent's specification only briefly mentions diabetes and insulin, the latter as an example of the type of drug the device using the drive mechanism could dispense.

In 2013, competitor Eli Lilly planned to market a competing insulin glargine product, called Basaglar, in its own

injector pen, the KwikPen. Confronted with the Orange Book listing of the '864 patent, Lilly submitted a Paragraph IV certification stating that its Basaglar KwikPen product would not infringe that patent. Within forty-five days, Sanofi sued Lilly for patent infringement, seeking to bar Lilly from manufacturing or selling the Basaglar KwikPen until the last of the patents listed in the Orange Book for Lantus and the Lantus SoloSTAR expired in 2024. That lawsuit triggered the thirty-month stay of FDA approval for Basaglar under 21 U.S.C. § 355(c)(3)(C). In filing the lawsuit, Sanofi thus protected its monopoly from Lilly's competition for up to thirty months more, even if the KwikPen did not actually infringe any Sanofi patent. In September 2015, the parties settled the lawsuit, and Sanofi granted Lilly a royalty-bearing license to sell Basaglar beginning over a year later in December 2016.

Lilly was not the only would-be competitor in the insulin glargine market. In 2016 and 2017, Merck and Mylan both submitted applications to market insulin glargine in injector pens, along with Paragraph IV certifications on the patents that Sanofi had listed for the Lantus SoloSTAR. After it settled with Lilly, Sanofi also sued Merck and Mylan. The Merck lawsuit settled after a trial on some of the patents at issue. Stipulation of Dismissal (redacted), Dkt. 339, Sanofi-Aventis U.S. LLC v. Merck Sharp & Dohme Corp., No. 16-cv-00812 (D. Del. Nov. 1, 2018). A bench trial was held but not decided in the Mylan lawsuit in December 2019.

Minute Entry, Dkt. 528, Sanofi-Aventis U.S. LLC v. Mylan GmbH, No. 17-cv-09105 (D.N.J. Dec. 2, 2019).

The plaintiffs in this case are a putative class of direct insulin glargine purchasers who allege that Sanofi artificially restricted competition in the market for insulin glargine by impermissibly extending its monopoly over insulin glargine products. They allege that Sanofi improperly listed the '864 patent in the Orange Book, thereby delaying competition in the insulin glargine market and resulting in inflated prices. They also allege that Sanofi's lawsuit alleging infringement of the '864 patent was a "sham" that was initiated merely to trigger the automatic stay of FDA's approval of the KwikPen. They bring two claims under section 2 of the Sherman Act, 15 U.S.C. § 2, based on an unlawful scheme to monopolize and an attempt to monopolize the market for insulin glargine products.

The district court dismissed the plaintiffs' Sherman Act claims, reasoning that as a matter of law Sanofi's decision to list the '864 patent was reasonable and not "objectively baseless" given what the court deemed to be ambiguities in the FDA's listing requirements.[3] In re Lantus Direct Purchaser Antitrust Litig., 284 F. Supp. 3d 91, 104–05 (D. Mass. 2018). This appeal followed.

[3] The district court also determined that the plaintiffs' allegations that Sanofi's lawsuits against Lilly, Merck, and Mylan did not constitute impermissible serial petitioning. The

II.

To make out a violation of section 2 of the Sherman Act, a plaintiff must demonstrate, "(1) that the defendant possesses 'monopoly power in the relevant market,' and (2) that the defendant has acquired or maintained that power by improper means." Town of Concord v. Bos. Edison Co., 915 F.2d 17, 21 (1st Cir. 1990) (quoting United States v. Grinnell Corp., 384 U.S. 563, 570 (1966)). Here, all parties assume -- and so do we -- that the complaint adequately alleges that Sanofi possessed monopoly power in the relevant market. Our analysis thus turns on whether the complaint plausibly alleges that the challenged method by which Sanofi allegedly maintained that power, that is to say, submitting the '864 patent for listing in the Orange Book, was an "improper means" of maintaining that power. Id.; see also Ashcroft v. Iqbal, 556 U.S. 662, 678 (2009) (requiring "sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face'" (quoting Bell Atl. Corp. v. Twombly, 550 U.S. 554, 570 (2007))).

A.

We consider first whether, under the facts alleged by the plaintiffs, it was proper for Sanofi to submit the '864 patent for listing in the Orange Book. At first blush, the answer seems

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plaintiffs have abandoned those arguments on appeal, so we need not address them.

readily apparent: The statute and applicable regulations call for the listing of only patents that claim the pertinent drug or a method of using the drug, and the '864 patent does not even mention, much less claim, either insulin glargine or any method of using it.

Sanofi, though, points out that the term "drug" as used in the FDA's regulation includes not just the drug substance itself, but also the "drug product." 21 C.F.R. § 314.53(b)(1). FDA regulations further define a "drug product" as "a finished dosage form, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more ingredients." Id. § 314.3(b). Sanofi argues that the Lantus SoloSTAR is a "drug product" because it is a "finished dosage form," which the regulations define as "the physical manifestation containing the active and inactive ingredients that delivers a dose of the drug product." Id. This reading of the regulations finds support in FDA guidance, which has described the "appendix in the Orange Book" as "list[ing] current dosage forms for approved drug products," including "metered aerosols, capsules, metered sprays, gels, and pre-filled drug delivery systems." 68 Fed. Reg. at 36,680. Indeed, a "Frequently Asked Questions" page on the FDA website actually lists an "insulin injector pen" as an example of a "[p]refilled drug delivery system[]."

Working backward, then, Sanofi's principal argument goes like this: the Lantus SoloSTAR is an injector pen, and as such is a "pre-filled drug delivery system[]," meaning that it qualifies as a "dosage form," which under the regulations is a "drug product," which in turn is a "drug." Hence, Sanofi concludes that because the FDA approved the Lantus SoloSTAR as a "pre-filled drug delivery system," any patent claiming the Lantus SoloSTAR is a "patent which claims the drug for which" the sNDA was submitted.

Even if we accept Sanofi's chain of reasoning, however, and thus assume for the sake of argument that the Lantus SoloSTAR is a drug under the statute, there is still a vital link missing: the '864 patent does not claim or even mention the Lantus SoloSTAR. Indeed, though it claims a device intended for use in an injector pen, it does not claim any injector pen, nor even a method of using a pen.

Under the plain wording of the statute, proper filing of the '864 patent would require not only that it be a patent that claims a drug; it must be a patent that claims the drug (or a method of using the drug) "for which the applicant submitted" the sNDA. 21 U.S.C. § 355(b)(1). It therefore follows that because the claims of the '864 patent do not mention the drug for which the sNDA was submitted, the patent does not "claim the drug," and it was improper for Sanofi to have submitted it for listing in the Orange Book as a drug claiming either insulin glargine or the

Lantus SoloSTAR. The regulations clearly require a patent not to be submitted if it does not claim the drug for which the application was filed: "For patents that claim a drug product, the applicant must submit information only on those patents that claim the drug product, as is defined in § 314.3, that is described in the pending or approved NDA." 21 C.F.R. § 314.53(b)(1) (emphasis added).

Confronted with this gap between its reading of the law and its filing of a patent that does not claim the listed drug, Sanofi argues that the regulations also require listing in the Orange Book any patents that contain "integral components" of an approved drug product. According to this line of reasoning, because the drive mechanism is an integral part of the Lantus SoloSTAR, a patent that claims the drive mechanism claims a part of a drug product, and thus "claims the drug."

We see nothing in the statute or regulations that welcomes such a further expansion of the already stretched statutory terms, whereby an integral part of an injector pen becomes the pen itself, and in turn is a drug. One would not think, for example, that a patent claiming only a transmission system must be read as also claiming any car in which it is used.

The FDA has already passed on opportunities to stretch the statutory terms in this way. In 2003, the FDA addressed commentary to a proposed rule that "would not have allowed an

applicant to list a patent that claimed packaging." 68 Fed. Reg. at 36,680. Some of that commentary argued that "patents claiming devices or containers that are 'integral' to the drug product . . . should be submitted and listed." Id. The FDA acknowledged those comments but did not adopt them. See id. Instead it responded by reiterating that: "[t]he key factor is whether the patent being submitted claims the finished dosage form of the approved drug product." Id. And the '864 patent does not. Rather, it claims several versions of a device that can be combined with other components to produce the finished dosage form of the approved drug product.

Sanofi also argues that, because the language of the regulations suggests that multiple patents can be filed with an application, the regulations must contemplate submission of patents claiming components of a drug product[4] -- otherwise, Sanofi reasons, manufacturers would have to claim every part of a drug in a single patent in order to file it, and the plural language in the regulations would be meaningless. See, e.g., 21 C.F.R. § 314.53(b)(1) (referring to "those patents that claim the drug product," and those "patents that claim the drug substance"). But Sanofi does not explain why multiple patents could not all directly

[4] Sanofi does not make the same argument with regard to the statute, which itself employs the term "any patent." 21 U.S.C. § 355(b)(1).

claim a drug product. And in any case, the plaintiffs point out that some patents do claim all the components of a combination drug product, even for drug products similar to the Lantus SoloSTAR. Specifically, they point to the patent for Narcan, U.S. Patent No. 9,211,253, as well as the patent for the EpiPen, U.S. Patent No. 8,870,827. So even if in some cases only one patent can legitimately be listed as a patent claiming the drug product, that does not mean that the patent will necessarily be unable to claim all the important components of the drug. And in any event, even if we misunderstand Sanofi's rather cryptic point here,[5] the possibility that the statute does not accommodate all desired listings does not mean that we rewrite it.

At oral argument, Sanofi tried another argument. It pointed to the general definition of "drug" set forth at 21 U.S.C. § 321(g)(1), which states that the term includes, among other things, both "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals," and "articles intended for use as a component of any article specified" in the previous clause. 21 U.S.C. § 321(g)(1). The definitions included at 21 U.S.C. § 321 are "[f]or the purposes

[5] And if this is the case, then it is waived for lack of development. See United States v. Zannino, 895 F.2d 1, 17 (1st Cir. 1990) ("[I]ssues adverted to in a perfunctory manner, unaccompanied by some effort at developed argumentation, are deemed waived.").

of this chapter," referring presumably to Chapter 9 of Title 21, at which is codified the entire FDCA. The definition likely applies to the requirements under section 355, then, and it very clearly includes "components" of "articles intended for use in the" treatment of disease. Id. § 321(g)(1). Nevertheless, it is not clear how far this textual focus on Chapter 9's general definition of "drug" gets Sanofi. That definition of "drug" in section 321(g)(1) demonstrates that Congress knew that some drugs had "components"; thus the absence of any mention of "components" in the provisions setting out which patents should be filed cuts against any attempt to interpret the statute and its implementing regulations as requiring or allowing listing of patents that claim only components of a proposed drug. See 21 U.S.C. § 355(b)(1).

More importantly, even assuming that the drive mechanism claimed by the '864 patent is itself a drug, we still find Sanofi falling short of its goal because the drive mechanism is not the "drug for which [Sanofi] submitted" the sNDA. 21 U.S.C. § 355(b)(1). For that reason alone the patent for the drive mechanism does not qualify for listing in the Orange Book as claiming the Lantus SoloSTAR.

Sanofi also seeks to find support in communications between other drug manufacturers and the FDA. Sanofi points to requests for advisory opinions submitted by Ropes & Gray in 2006, Forest Laboratories in 2011, Novo Nordisk in 2012, and AstraZeneca

in 2007, all asking, in substance, "whether patents directed to drug delivery systems . . . that do not recite the approved active ingredient or formulation should be listed in the [Orange Book]." According to Sanofi, the FDA has not responded satisfactorily to any of the requests. Instead, the FDA has simply acknowledged that the Orange Book "was not designed to separately address combination product listings or to identify the specific type of drug delivery system" and that it "could benefit from enhanced listing capabilities." In response to one request from Forest Laboratories, the FDA also stated that it had "been unable to reach a decision . . . due to the need to address other Agency priorities" and noted the "numerous demands on the Agency's resources."

We find no warrant to read anything into the FDA's non-answer beyond a conclusion that it simply chose not to answer the question. To infer an answer, or even to infer that silence by the FDA indicates that the correct answer is uncertain, would be to force agencies to respond to all inquiries lest their silence be misunderstood. And even if one could infer an answer from silence, Sanofi points to no support for affording any deference to its chosen inference. Moreover, the fact that the Orange Book is not designed to separately address combination product listings hardly helps Sanofi's argument that the '864 patent was listable as claiming a component of a combination product. Nor does the

fact that some manufacturers view the FDA's guidance as outdated in that regard. The statute and regulations clearly require that only patents that claim the drug for which the NDA is submitted should be listed in the Orange Book. The '864 patent, which neither claims nor even mentions insulin glargine or the Lantus SoloSTAR, does not fit the bill.

B.

Having determined that the complaint adequately alleges that Sanofi should not have submitted the '864 patent for Orange Book listing, we turn to Sanofi's alternative argument, accepted by the district court, that submitting the '864 patent for listing was reasonable, and that Sanofi cannot be held liable under the antitrust laws for a reasonable mistake. Plaintiffs challenge this argument on both levels: they argue that reasonableness is not a defense, and they argue that the statute was sufficiently unambiguous so as to render Sanofi's filing unreasonable as a matter of law. For the following reasons we find that neither side is quite correct, and that further proceedings beyond a Rule 12 motion are necessary to determine whether Sanofi should be held liable under the Sherman Act for any antitrust injury caused by its improper submission of the '864 patent.

Generally in a section 2 case, we would examine the effects of a monopolist's improper conduct, rather that the reasons why it engaged in such conduct. See Barry Wright Corp. v. ITT

Grinnell Corp., 724 F.2d 227, 232 (1st Cir. 1983) (Breyer, J.) (observing that, though "[s]ome courts have written as if one might look to a firm's 'intent to harm' to separate 'good' from 'bad' [conduct]," this search for "improper intent" in reality "refer[s] to a set of objective economic conditions"); see also United States v. Microsoft Corp., 253 F.3d 34, 60 (D.C. Cir. 2001) (en banc) ("[I]n considering whether the monopolist's conduct on balance harms competition and is therefore condemned as exclusionary for purposes of § 2, our focus is upon the effect of that conduct, not upon the intent behind it."); Phillip E. Areeda & Herbert Hovenkamp, Antitrust Law: An Analysis of Antitrust Principles and Their Application ¶ 658f (4th ed. 2019) [hereinafter Areeda & Hovenkamp] ("[I]nquiries into subjective intent should be limited in § 2 cases."). Presumably for this reason, Sanofi does not point us to any section 2 cases holding that reasonableness generally immunizes monopolists from section 2 liability.[6]

[6] Sanofi does seem to argue that the "rule of reason" doctrine applies, but that doctrine developed in the context of section 1 claims and is not typically applied to claims under section 2. See Fraser v. Major League Soccer, L.L.C., 284 F.3d 47, 55-61 (1st Cir. 2002) (characterizing the rule as "section 1's rule of reason" and discussing whether it could be applied to evaluate claims of conspiracy between distinct members of the same franchise); MCI Commc'ns Corp. v. Am. Tel. & Tel. Co., 708 F.2d 1081, 1139 (7th Cir. 1983) ("The Rule of Reason is a rule of construction which applies to section 1 of the Sherman Act. The need for such a rule arose because a literal reading of section 1 would prohibit virtually every private contract. . . . [T]he Rule of Reason does not directly apply as such to the offense of monopolization under section 2 of the Sherman Act." (internal citations omitted)).

In this regulatory setting, however, there is some reason to consider the rationale for the monopolist's challenged conduct, rather than just the effects of that conduct. Under the Hatch-Waxman Amendments, Sanofi is subject to Congress's command to submit any patent that claims the drug for which it seeks approval. See 21 U.S.C. § 355(b)(1). And the improper failure to comply with that command could itself arguably have an anticompetitive effect by depriving potential competitors of notice and of the other procedural benefits that result from an Orange Book listing. Sanofi has pointed to one 1996 complaint seeking to charge a manufacturer with antitrust liability for not filing relevant patents in the Orange Book. The plaintiffs in that case alleged that they were damaged by the defendant's failure to list the patent because they spent money developing a potential generic competitor they would not have developed had they known of the original patent through an Orange Book listing. See Complaint, Mut. Pharm. Co. v. Hoechst Marion Roussel, Inc., No. CIV. A. 96-1409, 1996 WL 34406666 (E.D. Pa. Feb. 23, 1996) ("Had the '129 patent been listed in the Orange Book, [the plaintiff] would not have expended over $500,000.00 to develop its generic . . . product . . . .").[7] Sanofi therefore reasons that if liability flowed

[7] The parties appear to have settled the case after summary judgment briefing. See Stipulation of Dismissal, Dkt. 65, Mut.

from improper submission of patents for Orange Book listing, Sanofi and others seeking FDA approval would find themselves "between the horns of an insoluble dilemma: list -- or not -- at risk of treble damage claims" either way.

This may be something of an overstatement. It would appear that a company unsure about whether it must submit a patent for listing might protect itself from liability by submitting the patent and then not suing within forty-five days of any subsequent Paragraph IV certification, thereby ensuring that the mere listing would not slow down final FDA approval of a competitor's submission.

That being said, such a strategy would potentially sacrifice a benefit that Congress gave to patent holders in the Hatch-Waxman Amendments. So, in the end, Sanofi has a fair point in arguing that the plaintiffs' version of what would essentially be strict liability for improper Orange Book submissions could slightly tilt the regulatory balance Congress sought in this bespoke scheme at the intersection of the FDCA and patent law. See 68 Fed. Reg. at 36,676 (seeking a "balance between the innovator companies' intellectual property rights and the desire to get generic drugs on the market in a timely fashion").

Pharm. Co. v. Hoechst Marion Roussel, Inc., No. CIV. A. 96-1409, (E.D. Pa. July 1, 1999).

The fact that Sanofi must align its conduct with regulatory requirements does not, however, mean that Sanofi gets a free pass from antitrust scrutiny. Courts do not frequently find an implied repeal of antitrust law, except where there is a "plain repugnancy between the antitrust and regulatory provisions." Gordon v. N.Y. Stock Exch., Inc., 422 U.S. 659, 682 (1975) (quoting United States v. Phila. Nat'l Bank, 374 U.S. 321, 350-51 (1963)); see also MCI Commc'ns Corp. v. Am. Tel. & Tel. Co., 708 F.2d 1081, 1101-02 (7th Cir. 1983) (finding no immunity where "AT&T is not subject to conflicting requirements, nor would it be held liable for decisions which were not its own business judgment"); Town of Norwood v. New England Power Co., 202 F.3d 408, 422 (1st Cir. 2000) (noting "the default rule retaining antitrust liability"). There is no such repugnancy here where, far from seeking a contradictory result from the regulatory regime, the plaintiffs' antitrust claim relies upon obligations created by it.[8] Moreover, the FDA does not police the accuracy of an applicant's contention that a patent claims a drug, nor does the FDA profess to have any special expertise in construing patents.

[8] As a counter-example, see our recent opinion in Breiding, 939 F.3d at 54–57, in which we applied the filed-rate doctrine to claims challenging conduct that was expressly allowed in a FERC tariff. See also, e.g., In re Celexa & Lexapro Mktg. & Sales Practices Litig., 915 F.3d 1 (1st Cir. 2019); Gustavsen v. Alcon Labs., Inc., 903 F.3d 1 (1st Cir. 2018); In re Celexa & Lexapro Mktg. & Sales Practices Litig., 779 F.3d 34 (1st Cir. 2015).

See 68 Fed. Reg. at 36,683. Sanofi acknowledges as much: "Orange Book listings are not immune from antitrust scrutiny and might subject a patent holder to liability under certain circumstances."

Nevertheless, antitrust precedent anticipates the possibility that section 2 liability might work a bit differently in the regulatory context. As Areeda and Hovenkamp note, "even if the challenged conduct is not the proper implementation of regulatory policies, condemning conduct undertaken in a reasonable good faith effort to comply with such policies would punish regulated firms for trying to act consistent with those policies." Areeda & Hovenkamp, supra, ¶ 246a.

Several circuits have identified a defense to antitrust liability where the defendant's action was taken as part of a good faith, reasonable attempt to comply with a regulatory scheme. In MCI Communications, the Seventh Circuit held that "[i]n the particular context of an industry subject to extensive and rapidly changing regulatory demands, we believe that an antitrust defendant is entitled both to raise and to have the jury consider its good faith adherence to regulatory obligations as a legitimate antitrust defense." 708 F.2d at 1109–10; see also id. at 1138 ("An ideal instruction would very briefly explain . . . that a carrier has an obligation under the Communications Act to interconnect, but may deny interconnections if it determines that the public interest is to the contrary; and that if the carrier at

the time had a reasonable basis in regulatory policy to conclude, and in good faith concluded, that denial of interconnections is required by concrete, articulable concerns for the public interest, then there is no liability under the antitrust laws."). See also S. Pac. Commc'ns Co. v. Am. Tel. & Tel. Co., 740 F.2d 980, 1010 (D.C. Cir. 1984) ("[W]e agree with the standard articulated by the Seventh Circuit . . . ."); see also Phonetele, Inc. v. Am. Tel. & Tel. Co., 664 F.2d 716, 737–38 (9th Cir. 1981) (Kennedy, J.).

Though the aforementioned cases all deal with the Communications Act of 1934, and while recognizing that the regulatory overlay may be less extensive here, we nevertheless see no principled reason why the same defense should not arise from a reasonable, good-faith attempt to comply with the regulatory demands of the Hatch-Waxman Amendments. Deterring reasonable, good-faith attempts at compliance "would obviously impair the achievement of regulatory goals." Areeda & Hovenkamp, supra, ¶ 246a.

The defense recognized in the regulatory context of the communications industry is not quite the defense that Sanofi seeks. Sanofi asks for immunity if its proffered reading of the statute was objectively reasonable. But the precedent we have cited requires that the challenged conduct be both reasonable and in good faith. See MCI Commc'ns, 708 F.2d at 1138 (allowing the

defense "if the [defendant] at the time had a reasonable basis in regulatory policy to conclude, and in good faith concluded," that its actions were required by regulation); S. Pac. Commc'ns, 740 F.2d at 1010 (quoting the same). We adopt that two-pronged version of the defense here, to be proven by Sanofi on remand. See MCI Commc'ns, 708 F.2d at 1109–10 ("[W]e believe that an antitrust defendant is entitled both to raise and to have the jury consider its good faith adherence to regulatory obligations as a legitimate antitrust defense."); Phonetele, 664 F.2d at 737–38 ("If a defendant can establish that, at the time the various anticompetitive acts alleged here were taken, it had a reasonable basis to conclude that its actions were necessitated by concrete factual imperatives recognized as legitimate by the regulatory authority, then its actions did not violate the antitrust laws.").[9] Certainly the dilemma faced by companies seeking to comply with the Hatch-Waxman Amendments is no greater than the regulatory dilemmas presented by the "extensive and rapidly changing"

[9] One recent district court decision directly addressed the question of whether antitrust plaintiffs were required to plead facts alleging an absence of good faith in their prima facie case in order to avoid dismissal on the basis of this exception to antitrust liability. See In re Actos End-Payor Antitrust Litig., No. 13-CV-9244, 2019 WL 4805843, at *14-15 (S.D.N.Y. Sept. 30, 2019). At least in part because the defendant had acknowledged at oral argument that the exception was an affirmative defense to liability, the court determined that the complaint was not required to include allegations of bad faith in order to survive a motion to dismiss. Id.

regulation under the Communications Act in the other cases. MCI Commc'ns, 708 F.2d at 1109. Nor can we see any good reason to immunize improper, exclusionary conduct by a monopolist unable to show it was acting in good faith -- especially in the section 2 context, where reasonableness alone has never been considered to be a generally available defense to antitrust liability. See supra n.5.

Plaintiffs seem to argue that the allegations in the complaint necessarily defeat the reasonableness prong of any such defense. At this early stage of the lawsuit, however, the record does not yet contain any evidence about custom and practice in the industry, or what if any legal opinions Sanofi sought and obtained before submitting the patent. Indeed, Sanofi has yet to answer the complaint. And while we are reasonably confident of our reading of the statutory and regulatory texts, we cannot ignore either the complexity of that endeavor or the fact that at least one other district court has found it difficult to arrive comfortably at a similar conclusion. See Organon, Inc. v. Mylan Pharm., Inc., 293 F. Supp. 2d 453, 459–60 (D.N.J. 2003) (finding no liability where the defendant listed a patent claiming an "off-label" use of the drug because there was a "reasonable basis for the submission"). But see In re Buspirone Patent Litig., 185 F. Supp. 2d 363, 375–76 (S.D.N.Y. 2002) (finding that the defendant's improper listing of a patent in the Orange Book and subsequent

litigation to enforce it was "objectively baseless" under the Noerr-Pennington framework).[10] A statute can be unambiguous once carefully construed, yet nevertheless be reasonably susceptible to mis-readings until that unambiguous reading is explained. Occasionally, even courts that find a text unambiguous may split on the meaning of the text. See, e.g., Kasten v. Saint-Gobain Performance Plastics Corp., 563 U.S. 1, 16, 20–21 (2011) (majority finding that a statute supports one interpretation so unambiguously as to preclude use of the rule of lenity, with dissent finding a contrary interpretation of the statute so clear as to obviate any need to consider its purpose); Staples v. United States, 511 U.S. 600, 604–07, 624–25 (1994) (majority espousing one interpretation of the statute, with dissent arguing that it "unambiguous[ly]" means something different).

Conversely, the fact that the law in this area is complicated does not by itself mean that Sanofi's action was reasonable. Cf. Chevron, U.S.A., Inc. v. Nat. Res. Def. Council, 467 U.S. 837, 842–43 (1984) (anticipating that there are impermissible readings even of ambiguous statutes: "if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on

[10] See United Mine Workers of Am. v. Pennington, 381 U.S. 657 (1965); E. R.R. Presidents Conf. v. Noerr Motor Freight, Inc., 365 U.S. 127 (1961). The parties agree that the Noerr-Pennington doctrine does not apply to this issue.

a permissible construction of the statute"). An experienced and sophisticated drug manufacturer routinely works with such complexity. And in this instance no close reader could have reasonably thought that submitting the '864 patent was so clearly proper as to obviate the need for inquiry and advice.

We therefore hold that the facts and reasonable inferences found in the complaint describe an improper submission of the '864 patent for listing in the Orange Book; that the defenses to antitrust liability as a result of such an improper submission include proving that the submission was the result of a reasonable, good-faith attempt to comply with the Hatch-Waxman scheme; and that the record does not now allow for the adjudication of that defense as a matter of law.

C.

Finally, Sanofi briefly argues that even if its submission of the '864 patent was improper and not subject to any reasonableness defense, the plaintiffs could not win on their claims because the improper Orange Book listing could not alone have caused an antitrust injury. Antitrust causation, however, requires only that the complained-of activity be a "material" or "substantial" cause of the injury. Areeda & Hovenkamp, supra, ¶ 338a ("It is . . . enough that the antitrust violation contributes significantly to the plaintiff's injury, even if other factors amounted in the aggregate to a more substantial cause."). As best

we can tell, Sanofi's premise is that without the Orange Book listing of the '864 patent, the patent infringement litigation between Sanofi and its putative competitors, including its ultimate settlement with Lilly, would have proceeded and concluded exactly the same way as it did, such that the listing itself was not a substantial cause of the extension of Sanofi's monopoly. Even putting aside the sham-litigation claims, which the plaintiffs have abandoned on appeal, nothing in the operative complaint requires us to conclude that the automatic thirty-month freeze on FDA approval of the other companies' products had no plausible effect on the course of the underlying litigation. So we see no basis for affirming the dismissal of the complaint under Rule 12(b)(6) on this alternative basis.

III.

We reverse the district court's dismissal of the plaintiffs' claims as to Sanofi's alleged improper Orange Book listing of the '864 patent and remand for further proceedings in accord with this opinion.