

No. 10-844

IN THE
Supreme Court of the United States

CARACO PHARMACEUTICAL LABORATORIES, LTD. AND
SUN PHARMACEUTICAL INDUSTRIES, LTD.,
Petitioners,

v.

NOVO NORDISK A/S AND NOVO NORDISK INC.,
Respondents.

On Writ of Certiorari to the
United States Court of Appeals for the Federal Circuit

**BRIEF OF AMICI CURIAE
ALLERGAN, INC., SHIRE PHARMACEUTICALS, INC.,
MEDICIS PHARMACEUTICAL CORP., AND
SOMAXON CORP. IN SUPPORT OF RESPONDENTS**

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INTEREST OF AMICI CURIAE INNOVATOR PHARMACEUTICAL COMPANIES¹

Amici Curiae are so-called “innovator” or “branded” pharmaceutical companies. Collectively, *amici* and companies similarly situated to *amici* invest tens of billions of dollars annually on the research and development of new drugs, as well as new indications and uses for “old” drugs. The latter is a growing and increasingly important area of interest for pharmaceutical manufacturers, physicians and patients.

Through exhaustive and expensive clinical research, the branded pharmaceutical industry has been able to discover new indications and “re-purpose” old drugs to eliminate and/or reduce the occurrence and effects of serious diseases and illnesses. This research involves substantial risks. The reward for taking these risks is patent protection on the newly discovered indications, without which innovator companies would be unable to recoup their investments.

The Hatch-Waxman Act and the 2003 amendments to it take into account these risks and rewards and carefully balance the interests of innovator pharmaceutical companies with the

¹ Pursuant to Rule 37.6, *amici* certify that no counsel for a party authored this brief in whole or in part and that no person or entity, other than *amici* or its counsel, has made any monetary contribution to the preparation or submission of this brief. The parties have consented to the filing of this brief. A letter acknowledging consent by petitioners accompanies this brief, and respondents have filed a letter with the Clerk of the Court providing blanket consent to the filing of *amicus* briefs.

interests of their generic competitors. Caraco, and the *amici* in support of a reversal of the Federal Circuit's decision (collectively, "Caraco"), propose a reading of 21 U.S.C. § 355 that threatens, not furthers, this balance. Caraco attempts to circumscribe the process set forth in the statute and delay method of use patent infringement inquiries until *after* generic drugs come on to the market, when the market for the innovator product has already been destroyed by the generic product. It does this by taking a construct of the FDA, namely Orange Book use codes, and conflating it with the carefully constructed "pre-launch" patent protection scheme established under the Act. This is contrary to the Act's language and purpose, whose patent provisions are designed to resolve such disputes *before* the generic is launched.

In addition to being contrary to the Act's purpose, the relief requested by Caraco is likely to cause satellite litigation in every pharmaceutical method of use patent case surrounding the wording chosen by the branded manufacturer for its Orange Book use codes. Rather than the simple, administrative tools they were designed to be, use codes may come to look like patent claims that will have to be interpreted by FDA in the context of drug labeling. As all parties and *amici* agree, FDA is ill equipped to assess patent claims and their scope or to make infringement decisions about generic drugs.

Accordingly, the undersigned innovator pharmaceutical companies respectfully urge this Court to affirm the Federal Circuit's decision.

SUMMARY OF ARUMENT

The Federal Circuit correctly held that “the terms of the counterclaim provision do not authorize an order compelling the patent holder to change its use code narrative.” *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 601 F.3d 1359, 1366 (Fed. Cir. 2010), *cert. granted (mem.)*, 131 S. Ct. 3057 (U.S. June 27, 2011) (No. 10-844). This is so not only for the reasons and support found in the Federal Circuit’s opinion, but also, because the “use code” is a creation of the FDA, and not of the Hatch-Waxman Act or Congress. For FDA purposes, use codes are used as regulatory surrogates for actual patent claims. Properly viewed, they allow FDA to render summary decisions on the scope of generic ANDA applicant’s request for approval as an adjunct to, not replacement of, the notice and litigation procedures carefully laid out in the Hatch-Waxman Act.

Unlike the objective patent information required by statute (patent number and expiration date), use codes required by regulations are highly subjective and thus, not easily addressed by courts under the counterclaim provisions. Indeed, if Caraco were correct that it and/or any generic could ask a court to enjoin a patent holder to change the “use code” for an approved dug product, use codes would begin to look like patent claims. FDA would then need to evaluate if and how these patent claim-like use codes relate to approved indications and generic ANDA applicants’ proposed labels. This is not a task that FDA is equipped to undertake.

Use codes are not patent claims. They are approved indications covered by patent claims. They are provided to FDA and subsequently published in

the Orange Book. They are not, nor are they intended to be, legally determinative of infringement. Caraco seeks to change this in an effort to avoid the Hatch-Waxman protections by carving out the approved use specifically claimed in an unexpired patent, obtaining FDA approval while bypassing the statutory provisions requiring patent certification and notice to the innovative pharmaceutical company pre-launch, and heading to market with a generic drug that is substitutable for *all* indications, including those that infringe the unexpired patent. This has the potential to render valueless method of use patents covering newly discovered indications, strongly dis-incentivizing innovator pharmaceutical companies from the pursuit of additional uses for safe and effective drugs. Surely, such a glaring “loophole” in Hatch-Waxman’s pre-launch patent protection scheme is not what Congress intended.

Further, Caraco’s argument that a properly drafted “use code” would allow generic entry more swiftly is based on an incorrect reading of the statute. As the plain language of the statute makes clear, every ANDA is required to contain a patent certification “and” a section viii statement when the latter is applicable, i.e., where there is a listed method of use patent that does not claim or cover every approved indication, for each Orange Book listed patent. Congress did not intend for generics to simply bypass the procedure for method of use patents’ certifications by “carving out” approved uses, particularly when approved generics are adjudged therapeutically equivalent to the branded drug product by FDA, and are thus fully substitutable for the branded product, regardless of the narrower label of the generic. Method of use patents listed in the

Orange Book, regardless of use codes, should be treated the same as compound and formulation patents where patent certifications alleging non-infringement are required. There is no cogent reason why method of use patents need not be certified and infringement not considered pre-launch via the mechanism set forth by the Hatch-Waxman Act. At a minimum, this issue needs further study by the Court of Appeals before the “use code” counterclaim issue should be decided.

ARGUMENT

A. Finding New Uses For “Old” Drugs Is A Critical Area Of Emerging Innovation

Caraco argues that branded pharmaceutical companies have overstepped appropriate boundaries or “manipulated” the Hatch-Waxman Act by the conduct at issue in this case. Nothing could be further from the truth. As explained below, it is generic companies that have overstepped and improperly taken advantage of the section viii provisions in the statute. Contrary to the Hatch-Waxman Act’s language and purpose, generic companies are “carving out” patented uses from their labels, securing approval of such so-called “skinny labels”, and then receiving from FDA so-called “A” ratings, which allow their products to be substituted for not just the un-patented use for which the generic drug received approval, but also for the patented use that the generic has “carved out” from its label. Terry G. Mahn, *Skinny Labeling and the Inducement of Patent Infringement*, UPDATE, Nov./Dec. 2010, at 39. As a consequence, generic drug companies effectively receive the benefit of having the patented

use on the label without paying the price of having to defend a pre-market case for patent infringement under the Hatch-Waxman Act.

This situation highly dis-incentivizes innovator pharmaceutical companies from researching and pursuing approval of new indications for previously approved drugs. The discovery of new indications and uses for old drugs should be encouraged, not discouraged by a crabbed reading of the Hatch-Waxman Act that conflates an FDA construct – “use codes” – with infringement determinations in a court of law.

The research and development costs for bringing a new drug to market are estimated to be \$1.3 billion. Ted Agres, *New Life for Old Drugs*, DRUG DISCOVERY & DEVELOPMENT, Aug. 1, 2011, *available at* <http://www.dddmag.com/article-New-Life-for-Old-Drugs-72911.aspx>. It often takes 10-15 years to bring a new drug to market. *Id.* And, there is a slim rate of success – 5%. *Id.* Drug repurposing, i.e., finding a new indication for an old drug, is a way of lowering these costs of drug development and getting new therapies to patients more quickly. Amy D. Marcus, *Researchers Show Gains in Finding Reusable Drugs*, WALL ST. J., August 18, 2011, *available at* <http://online.wsj.com/article/SB10001424053111903639404576514542144726276.html?>. More specifically, costs and failure rates are reduced as the starting point is often an already approved compound with established safety and bioavailability profiles, proven formulation and manufacturing routes, and well-characterized pharmacology. As a result, these compounds can enter clinical trials more

quickly and receive FDA approval on a more expedited basis.

New uses of old drugs have been recognized as “a growing area of interest” and “as a way of lowering costs of drug development and getting therapies to patients more quickly.” Marcus, *supra*. As the National Institute of Health (NIH) has explained, drug repurposing allows “[e]xpansion of a drug’s clinical use to new indications.” Christopher P. Austin et al., *The NCGC Pharmaceutical Collection: A Comprehensive Resource of Clinically Approved Drugs Enabling Repurposing and Chemical Genomics*, 80 SCIENCE TRANSLATIONAL MEDICINE, April 27, 2011, at 1. And, while “many examples exist of successful repurposing, only recently has the concept of large-scale, even comprehensive, examination of the disease applications of clinically used drugs been considered.” *Id.* at 10.

Examples of drug repurposing include Requip® (ropinorole) and Mirapex® (pramipexole), manufactured by GlaxoSmithKline and Boehringer-Ingelheim, respectively. Initially, both of these drugs were approved for use solely in Parkinson’s disease. Extensive further research led to the development of these drugs for use in restless leg syndrome (a disease affecting 8% of the population). Sara H. Sleight & Cheryl L. Barton, *Repurposing Strategies for Therapeutics*, 24 PHARMACEUTICAL MEDICINE 151, 153 (2010).

Another oft-cited example of an innovator pharmaceutical company repurposing an “old” drug is the revitalization of thalidomide by Celgene in the United States. Thalidomide was originally prescribed in the 1950s for nausea and insomnia in

pregnant women. It caused severe birth defects and was taken off the market in 1961. In a surprising 1965 article, an Israeli doctor reported that thalidomide alleviated complications of leprosy. Jacob Sheskin, *Thalidomide in the Treatment of Leprosy Reactions*, 6 CLINICAL PHARMACOLOGY & THERAPEUTICS 303–06 (1965). It was also later discovered that thalidomide had antiangiogenic and immunomodulatory effects. Agres, *supra*. These findings prompted an innovator company, Celgene, to risk the capital required to secure approval from the FDA of new uses of the previously banned Thalidomide. Celgene was successful and received approval from FDA to market Thalomid® (thalidomide) as a treatment for leprosy in 1998. Since its approval, Thalomid® has become a flagship product for Celgene, now with an additional indication for multiple myeloma. In addition, through controlled clinical trials and FDA compassionate-use programs, the drug has been found to be effective in treating a myriad of disorders, including certain mycobacterial and autoimmune diseases, HIV and AIDS-related afflictions, and cancer.

Simply put, these kinds of new uses for drugs will not be developed by innovator pharmaceutical companies without the ability to enforce patent rights on the new methods of use. Bringing these new uses to market is very expensive (only 40% less than the new drug), and FDA exclusivities related to them (three years only, *see* 21 C.F.R. § 314.108

(2010))², provide only limited value. Agres, *supra*. “While the FDA will give market exclusivity for a new indication, there is little to prevent physicians from prescribing a generic version in its place.” *Id.* As a result, as Atul Butte, M.D., Ph.D., assistant professor of medicine at Stanford University School of Medicine noted “[h]ighlighting new uses for off-patent drugs may be exciting, but it is a challenge for companies to get enough value out of it to fund clinical trials It’s an unanswered question right now.” According to Drug Discovery & Development, it is a question to which the National Institute of Health (NIH) is seeking to help answer with an initiative to find ways to make “repurposing more practical and less burdensome.” *Id.*

B. “Use Codes” Are Constructs Of The Food & Drug Administration, Not Statutory Requirements

Section 505 of the Hatch-Waxman Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355), regulates the approval process for drugs in the United States. As part of this approval process, innovator pharmaceutical companies filing a New Drug Application (“NDA”) are required to identify all patents and their

² When a drug is approved for a new indication, Hatch-Waxman provides for three years of so-called “label exclusivity.” Pub. L. No. 98-417, § 101, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355(j)(5)(F)(iv)). Unlike the exclusivities for newly-discovered molecules, this type of exclusivity does not stop a generic manufacturer from filing an ANDA during the period of the exclusivity (though FDA could not approve it). *Id.* Because it can take years to recover the investment required to undertake patient clinical trials and obtain FDA approval for any new use, 3 years of data exclusivity is simply inadequate for recouping these investments. Patent protection is essential.

respective expiration dates that claim the drug or an approved method of using the drug. *See* 21 U.S.C. §§ 355(b)–(c).

Under the FDA’s authority to promulgate regulations for the efficient enforcement of this statute, the FDA separately requires an innovator pharmaceutical company to submit Form 3542 to the FDA identifying the patent number and the expiration dates of any applicable patents. If a patent claims one or more approved methods of using the drug, Form 3542 also requires “a description of the approved indication or method of use” also known as the “use code.” *See* Form FDA 3542: Patent Information Submitted Upon and After Approval of an NDA or Supplement 3 (rev. Oct. 2010), *available at* <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048345.pdf>. The FDA publishes a list of approved drugs, along with applicable patents and any associated use codes in its Approved Drug Products With Therapeutic Equivalence Evaluation, *i.e.*, the Orange Book.

Nowhere in the statute or legislative history of the Hatch-Waxman Act are use codes and descriptions required. This is hardly surprising given that use codes are intended to compliment the patent information provided to FDA by branded manufacturers and published in the Orange Book. Use codes are designed to give notice to both FDA and interested generic drug companies of the patents the innovator pharmaceutical company believes cover uses that have been approved by FDA. *See* Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,683 (June 18, 2003) (“Use codes are intended to alert ANDA and 505(b)(2)

applicants to the existence of a patent that claims an approved use.”).

“Use codes” were thus not intended to be debatable, or as Caraco requests – *litigious* – issues. If the brand’s assertion, through its use code, that a particular method of use was approved turned out to be erroneous, the counterclaim provision of Hatch-Waxman, as it already existed, would take care of the problem. A generic applicant could seek de-listing of the patent as not covering an approved use, and that would be the end of it. 21 U.S.C. § 355(j)(5)(C)(ii)(I) (2006) (permitting a “counterclaim seeking an order requiring the [patent] holder to correct or delete information submitted by the holder ... on the ground that the patent does not claim ... an approved method of using the drug”). As use codes were envisioned by FDA, there is no need to litigate them.

Indeed, litigating over the particular words of a use code will result in a quagmire and will create a flurry of satellite litigations that are not in the courts’ or the public’s interest. FDA currently accepts the use code submitted by the innovator company and publishes it in the Orange Book. Its role in this regard is ministerial. Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. at 36,683. (FDA stated that “it is more efficient and accurate” to ask the NDA holder to provide “the exact use code description to be published in the Orange Book.” *Id.* FDA further said that “[i]n addition to the absence of any statutory basis for a substantive agency review of patents, we have long observed that we lack expertise in patent matters. . . . [O]ur patent listing role remains ministerial.” *Id.*).

If Caraco's relief is granted, a permissible counterclaim to change the "use code" description will first be filed with a court. If the counterclaim is successful, the innovator will be directed to change the published use code. But, to what? It is only by happenstance that, in the case at bar, there is another use code to adopt if Caraco is successful – namely, the original use code that Novo had submitted. In most cases, however, that will simply not be the case. A brand will properly list a patent in the Orange Book and provide its use code to the FDA, which will adopt it. That will be all that there is. If a generic company then challenges that use code in Court as insufficiently descriptive of a patent, unlike in the case at bar, there will not be an alternative use code to adopt. Either the district court will have to re-write the use code, or FDA will. Neither is in an appropriate position to do so.

Further, if that happens, the innovator pharmaceutical company will appeal immediately. As the appeal is pending, and there is potential loss of the Hatch-Waxman's Act 30-month stay of approval on the generic's proposed drug product (provided by Congress so that any patent infringement issues would be litigated pre-launch), FDA will need to become less "ministerial" and compare the new use code to the carved out indication, making a substantive determination as to whether the two are commensurate in scope and if the carve-out is allowable under section viii. This is not a determination FDA is equipped to make. Moreover, the innovator company may concurrently file a citizen's petition with FDA arguing that the carve-out should not be allowed. The unsuccessful

party before FDA on that issue may then sue FDA in district court. Further appeals will likely follow.

But despite the inevitable number of court and FDA proceedings sparked by these counterclaims and potential changes to use codes, none will address patent infringement. In fact, the patent infringement issue will take a back seat to determining the propriety of certain “use code” language: only after resolution of the “use code” issues, will patent infringement cases proceed. *See e.g., AstraZeneca LP v. Apotex, Inc.*, 623 F. Supp. 2d 579 (D.N.J. 2009). This is inefficient and a waste of the courts’ and parties’ resources, and, is inconsistent with Hatch-Waxman. Satellite litigations, like those inevitable under Caraco’s requested relief, can and should be avoided.

C. Because Label Carve-Outs Result In Infringement of the Very Patents That Are Designed to Be Carved Out, Limiting the Counterclaim to Whether a Patent Is Properly Listed Is Appropriate

While the general rule that a generic drug must be labeled for the same conditions of use as the approved innovator drug is skirted when carve-out labels are approved, the same cannot be said for infringement liability. This is so because despite FDA’s rules permitting drugs to be marketed only for approved uses—i.e., in the context of a generic “carve-out,” the non-patented use—the drugs may still be prescribed, dispensed and used in an infringing manner. In fact, most are.

This is a result of FDA’s therapeutic equivalence rating and generic substitution practices. When a

generic drug is approved by the FDA it receives a therapeutic equivalence rating of A or B. Mahn, *supra*. The "A" code, which is most commonly given, indicates that the generic is therapeutically equivalent to the branded product; products receiving such code can be "*substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the [branded] product.*" Drugs@FDA Glossary of Terms, <http://www.fda.gov/Drugs/informationondrugs/ucm079436.htm#T> (last updated Jan. 7, 2010) (defining "therapeutic equivalence (TE)") (emphasis added). There is no limitation of this therapeutic equivalence to any particular approved use.

While state laws and regulations vary in their approach to the management of generic drug substitution, in practice, pharmacists in nearly every state use these "A" ratings in the Orange Book as the primary basis for generic drug substitution determinations. Mahn, *supra*. In fourteen states, pharmacies are required to substitute "A"-rated generics for branded prescriptions (unless prescribing physician indicates no substitution). *Id.* All other states have laws or regulations that leave the selection of equivalent generic drugs completely to the discretion of the pharmacists making the substitution decisions. *Id.* Pharmacists and personnel on the boards of pharmacy routinely rely on "A"-rated generics listed in the Orange Book when making those substitution decisions. *Id.*

Despite these substitution practices, the pharmacist, prescribing physician and/or patient often have no idea what uses are approved on an A-rated generic. This is not surprising as there is no

compendium tracking or publishing such information. The consequence is that generics approved by FDA with labels carving out certain methods of use are treated identical to generics that did not carve out those uses (as well as the branded product). As a result, in the case at bar, there can be no dispute that Caraco's proposed generic drug will be prescribed and dispensed for the use it proposes to carve out. This is so even though Caraco will technically not have approval for that use.

The approval process and substitutability of generic ANDAs with carve-outs already disincentivizes branded manufacturers from developing new uses of old drugs. This would worsen if the patent counterclaim provision is not narrowly construed. If a patent is listed properly in the Orange Book, a dispute over a use code should not be the gate-keeper to whether or not litigation over the patent should be allowed to proceed.

D. The Hatch-Waxman Act's Policy of Resolving Patent Disputes Before Market Launch Supports The Federal Circuit's Decision

As the Federal Circuit correctly found, permitting Caraco to counterclaim for a narrower use code is contrary to the central policy aim of the Hatch-Waxman Act, *i.e.*, to strike a balance between the interests of generic and innovator manufacturers. *Novo*, 601 F.3d at 1364–65.

The Hatch-Waxman Act was intended to promote innovation by innovator pharmaceutical companies while also promoting early and efficient access to generic drugs. *See Prepared Statement of the FTC Regarding Competition in the Pharmaceutical*

Industry Before the S. Comm. on Judiciary, 108th Cong. (2003) (statement of Timothy J. Muris, Chairman, Fed. Trade Comm'n), *available at* <http://www.ftc.gov/os/2003/06/030617pharmtestimony.htm>. The Act specifically permits generic drug companies to partially circumvent patent restrictions and accelerate FDA approval so that they can bring generic products to market as soon as the innovator drug companies' patents expire or are found invalid or not infringed. *See* 35 U.S.C. § 271(e); *see also Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 675–78 (1990).

Before the Act, generic drug manufacturers would be liable for infringement of viable innovator patents under 35 U.S.C. § 271(e) by actions such as seeking approval of proposed generic drug products. The Act, however, created a safe harbor provision whereby generic drug manufacturers no longer have to wait until the expiration of the branded drug patents to begin their development of a generic drug product and/or to begin the abbreviated drug approval process. This provision significantly reduced the amount of time for generic entry. *Id.*

One of the “*quid pro quos*” of this so-called “safe harbor” in Hatch-Waxman is the patent litigation provisions of the statute. These provisions generally provide that, if a generic manufacturer wishes to challenge an innovator patent, that process will play out before the generic product comes to market. Integral to this process is the 30-month stay on approval that results when the generic applicant provides a paragraph IV certification and the branded company files a lawsuit within 45 days. By so doing, the branded company is afforded a single

opportunity to litigate the challenged patents without fear of having its market destroyed – i.e., before the generic company comes to market. This is only fair since it is the branded company that has invested in the patented product and the generic company seeks to copy it. *See generally* Robin J. Strongin, *Hatch-Waxman, Generics, and Patents: Balancing Prescription Drug Innovation, Competition, and Affordability* (Nat'l Health Policy Forum, Background Paper, 2002), *available at* http://www.nhpf.org/library/background-papers/BP_HatchWaxman_6-02.pdf.

While Caraco and its *amici*, including the government, deride this 30-month stay as causing delay; that is the point of it. The generic company receives the benefit of a safe harbor provision partaking in infringing activities while copying the branded drug without having to face an infringement suit until later. Moreover, the reality is that the 30-month stay does not delay anything. This time period coincides with the average time for FDA approval of an ANDA, causing little to no delay before the generic drug gets to market. *See* K.L. Spear M.D., President, Spear Pharmaceuticals and GPHA Board member, Comments at the FDA Public Meeting on Generic Drug User Fees (Sept. 17, 2010), *available at* <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM226833.pdf>.

The resolution of any infringement claims prior to the generic drug products launch was a clear intention of the Act as it encourages the development of new drugs and the protection of valid patents. In fact, courts have recognized that, in pharmaceutical cases like this, “the incentive for discovery and

development of new products [would be] adversely affected” by “shifting market benefits to the infringer while litigation is pending for patents that are likely to withstand the attack.” *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008).

Indeed, if a generic drug is permitted to enter the market before even consideration of patent infringement issues, the financial hardship falls on the innovator pharmaceutical company alone and the balance created by the Act is no longer maintained. In effect, the generic gets all the benefits of the Act – including the ability to rely on the innovator’s research, data and creation of the market – without paying any of the price.

Market research has shown that generic drugs typically capture approximately 80-90% of the prescriptions of the branded drug within six months of the generic’s launch. FED. TRADE COMM’N, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION 12 (2009). The loss of market share for branded companies occurs very quickly and often can never be regained. Moreover, it results in significant changes to the branded company including loss of jobs and research and development monies. These losses are irreparable. *See e.g., Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008) (finding loss of revenue and market share caused by generic entry constitutes irreparable harm); *Bio-Technology Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1566 (Fed. Cir. 1996) (finding that loss of revenue, goodwill, and research and development support constitute irreparable harm); *see also AstraZeneca LP v. Apotex, Inc.*, 623 F. Supp. 2d 579, 612 (D.N.J. 2009) (finding that “the damage caused

by a loss in personnel and the impact this would have on the company are indeed significant and unquantifiable”).

For example, in *Pfizer, Inc. v. Teva Pharmaceuticals, USA, Inc.*, 429 F.3d 1364, 1382 (Fed. Cir. 2005), the Federal Circuit affirmed the district court’s grant of a preliminary injunction enjoining the sale of an infringing generic drug, noting that “while the statutory framework . . . does seek to make low cost generic drugs available to the public, it does not do so by entirely eliminating the exclusionary rights conveyed by pharmaceutical patents. Nor does the statutory framework encourage or excuse infringement of valid pharmaceutical patents.”

Further, the public interest favors protecting valid patents by preventing premature entry of generic drugs into the market. The mere “selling [of] a lower priced product does not justify infringing a patent. Were that to be a justification for patent infringement, most injunctions would be denied because copiers universally price their products lower than innovators.” *Payless Shoesource, Inc. v. Reebok Int’l Ltd.*, 998 F.2d 985, 991 (Fed. Cir. 1993); *see also Pfizer*, 429 F.3d at 1382. Indeed, in the pharmaceutical industry, the public policy is best served by protecting patent rights in order to encourage investment in research and development:

Although companies . . . which do not engage in significant amounts of research and development, consequently might be able to undercut the prices offered by pharmaceutical manufacturers that devote large sums to invention and product

improvement, this type of short-term competition does not, at least in the considered opinion of the Congress, serve the public interest. Instead, Congress has determined that it is better for the nation in the long-run to afford the inventors of novel, useful, and nonobvious products short-term monopolies on such products than it is to permit free competition in such goods.

Eli Lilly & Co. v. Premo Pharm. Labs., Inc., 630 F.2d 120, 138 (3d Cir. 1980).

Significantly, FDA has already shown that it is ill-equipped to resolve disputes ahead of time through its application of section viii: FDA has permitted section viii carve-outs that have resulted in infringement. For example, in *AstraZeneca LP v. Apotex, Inc.*, 623 F. Supp. 2d 579 (D.N.J. 2009), Apotex submitted an ANDA referencing AstraZeneca's drug Pulmicort Respules and "carved out" the patented method of use covering once-daily administration. FDA approved the ANDA based on the section viii statement, i.e., "carve out," and Apotex launched its generic product. One day later, AstraZeneca filed a declaratory judgment action and a motion for a preliminary injunction on the grounds that, among other things, the generic drug and its proposed label would induce users to infringe the patented method covering once daily administration despite the "carve-out" by Apotex. The district court found for AstraZeneca. The Federal Circuit affirmed. *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042 (Fed. Cir. 2010). This case confirms that patent infringement remains a separate inquiry from whether a carve-out is appropriate on a generic label;

it also demonstrates that FDA does not have the capacity to render reliable decisions on patent scope and infringement.

Caraco's position in this case will perpetuate cases such as *AstraZeneca* by asking FDA to make determinations that are better left to the patent holder and the courts. Leaving the counterclaim provision out of the use code quagmire will leave approval of drug products to FDA and patent issues to district courts. This Court should reject Caraco's argument and keep the regulatory scheme promulgated by FDA separate from patent inquiries.

E. Underlying This Case is FDA's Erroneous "Either/Or" Policy, Which, in Violation of the Statute, Invites Carved Out Indications In Lieu Of Patent Certifications

A generic drug manufacturer seeking approval for a generic drug product files an Abbreviated New Drug Application ("ANDA") and the requirements for its application are governed by 21 U.S.C. § 355(j) (2006).

Relevant to the instant case is the statutory requirement for an ANDA to contain:

(vii) *a certification*, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; **and**

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, **a statement** that the method of use patent does not claim such a use.

21 U.S.C. §§ 355 (j)(2)(A)(vii)–(viii) (2006) (emphasis added).

The plain language of the statute thus requires **both** a certification **and** a section viii statement when the ANDA applicant is seeking approval for a use not claimed by the method of use patent. Nowhere in its language does the statute imply that a section viii statement can replace the certification required by 21 U.S.C. §355 (j)(2)(A)(vii); *see also* H.R. REP. NO. 98-957, pt. 1, at 22 (1984).

This reading is further confirmed by the legislative history: “if there are indications which are claimed by any use patent and for which the applicant is not seeking approval, then an ANDA must state that the applicant is not seeking approval

for those indications which are claimed by such use patent. For example, the listed drug may be approved for two indications. ***If the applicant is seeking approval only for Indication No. 1, and not Indication No. 2 because it is protected by a use patent, then the applicant must make the appropriate certification and a statement*** explaining that it is not seeking approval for Indication No. 2.” H.R. REP. NO. 98-957, pt. 1, at 22 (1984) (emphasis added).

The House Report further clarifies that an ANDA cannot be approved if it is missing any of the elements required under § 505(j)(2)(A) and gives as an example, a missing patent certification, thereby indicating that a certification is needed in all ANDAs. *Id.*³

FDA policy diverges from the statute’s clear language and legislative intent. Specifically, it ignores the term “and” and implements an “either/or” policy treating sections vii and viii as mutually exclusive.

This FDA policy was addressed in *Purepac Pharmaceutical Co. v. Thompson*, 238 F. Supp. 2d 191 (D.D.C. 2002), *aff’d* 354 F.3d 877 (D.C. Cir. 2004), and *TorPharm, Inc. v. Thompson*, 260 F. Supp. 2d 69 (D.D.C. 2003) *aff’d by Purepac Pharm. Co. v. Thompson*, 354 F.3d 877 (D.C. Cir. 2004). *See also Warner-Lambert Co. v. Apotex Corp.*, No. 98-C-

³ Section viii of the statute requires ANDA applicant to inform FDA how and why the proposed generic label will differ from the innovator product label. FDA relies on this information to assess the label and indications for which the generic is seeking approval without having to assess patents and claims.

4293, 2001 WL 1104618 (N.D. Ill. Sept. 14, 2001), *aff'd*, 316 F.3d 1348 (Fed. Cir. 2003); *Allergan, Inc. v. Alcon Labs., Inc.*, 200 F. Supp. 2d 1219 (C.D. Cal. 2002), *aff'd*, 324 F.3d 1322 (Fed. Cir. 2003). Yet, in each of those cases, the courts simply deferred to FDA and reviewed the statute in instances where the patented uses were “unapproved.” That is, the ANDA applicant would not be seeking approval of the patented use as it was not an approved use for even the innovator product at that time. The instant case, as well as others like it, including the *AstraZeneca* case, give rise to a different problem with FDA’s “either/or” policy.

First, to be listed in the Orange Book, the method of use patent must claim at least one approved FDA use that is indicated for in the brand products label. *Applications for FDA Approval to Market a New Drug*, 68 Fed. Reg. at 36,681 (“If an NDA applicant or holder or patent owner intends to submit information on a patent that claims a method of use, the patent must claim a use that is described in the NDA. If we have already approved the NDA, the patent must claim a method of use that is in the labeling of the approved NDA.”). This requirement alone makes the *Warner-Lambert* gabapentin cases and *Allergan* case anomalies. *See Warner-Lambert*, 316 F.3d at 1354–55 (concluding that “it is not an act of infringement to submit an ANDA for approval to market a drug for a use when neither the drug nor that use is covered by an existing patent, and the patent at issue is for a use not approved under the NDA”); *Allergan*, 324 F.3d at 1334 (finding that “Allergan is precluded from suing Alcon and B & L under section 271(e)(2) for inducing infringement of the ‘415 and ‘741 patents, because Alcon and B & L

are not seeking FDA approval for the uses claimed in the patents and because the uses claimed in the patents are not FDA-approved”).

After a section viii statement is filed with FDA, under current FDA practice and policy, FDA compares the proposed generic label to the use code and description of the patented method of use. If FDA determines that the label sufficiently carves out the patented method of use, the section viii statement and label can be approved and FDA does not require patent certification. This approval can occur without notice to the patent holder and/or the innovator pharmaceutical company holding the NDA. This is directly contrary to the language of the statute and the legislative history. *See* 21 U.S.C. §§ 355 (j)(2)(A)(vii), (viii); H.R. REP. NO. 98-957, pt. 1, at 22 (requiring an ANDA applicant not seeking approval for certain patent-protected indications for use to submit a certification addressing each Orange Book-listed patent *and* a statement concerning the proposed omitted indication for use.) The result, the generic company obtaining approval and bringing its generic product to market without having given the patentee an opportunity to assess infringement, is also contrary to the policy aims of the Act. Indeed, as discussed above, it disincentives innovator pharmaceutical companies from researching and seeking approval of new indications as the balance of the Act is undermined.

Generic and innovator pharmaceutical companies must resolve any disputes concerning patents in private litigation. Efficient resolution of these disputes occurs when the procedures set forth in 21 U.S.C. § 355 are followed. This is the appropriate

avenue for method of use patents, regardless of whether the use may be carved out of the ANDA-filer's label. Indeed, requiring patent certifications for all patents in the Orange Book, branded and generic companies alike will simply follow the mechanism set forth in the statute and determine infringement and validity issues for method of use patents as is done for compound and formulation patents.⁴

Amici respectfully request that this Court reject FDA's "either/or" policy and require the language of the statute be followed for patent all Orange Book listed patents or, in the alternative, remand to the appellate court for further consideration of this issue. In doing so, the policy aims of Hatch-Waxman will be furthered.

⁴ Contrary to Caraco's assertions, requiring a certification and a section viii statement for each listed Orange Book patent will not result in undue delay for generic entry. Rather, it will allow the innovator pharmaceutical company to assess the generic's proposed carved out indication and assess whether its noninfringement contentions based on that carve out are agreeable. Caraco's argument assumes that an innovator pharmaceutical company will frivolously litigate a patent. Such assumption is inappropriate and should not be accepted by the Court.

CONCLUSION

Given the emerging importance of new uses of old drugs, the counterclaim provision of the Hatch-Waxman Act should be narrowly construed in a way that is consistent with the careful balance the Act provides between branded and generic manufacturers. “Use codes” litigation was simply not envisioned by the Hatch-Waxman Act’s framers, nor is there any good reason to permit it. Indeed, opening up the counterclaim provision to allow “use code” litigation has the potential to open a Pandora’s box of satellite litigation that will be a waste of resources. The Federal Circuit should be affirmed.

Respectfully Submitted,

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