INTELLECTUAL PROPERTY OWNERS

WHITE PAPER

APPLICATION OF INDUCED INFRINGEMENT LAW IN PHARMACEUTICAL PATENT LITIGATION

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I. INTRODUCTION

In this White Paper, we provide an overview of the statutory framework and relevant judicial decisions addressing induced infringement claims in different types of pharmaceutical patent infringement actions. We begin with an overview of the law governing such claims in the context of "Hatch-Waxman" infringement claims against a generic pharmaceutical product. We consider infringement claims based on Section 271(e)(2), based on the filing of an ANDA and service of a "Paragraph IV" Notice to the patent owner, as well as cases asserting induced infringement under Section 271(b).

We then look at cases addressing the two main scenarios for such claims: the first in which the generic product is arguably labeled for a use covered by the patent in suit, and the second in which all patented uses are off-label. We also consider the holdings and implications of the Supreme Court's recent decision in *Novo Nordisk v. Caraco*, which authorized generic defendants to bring a counterclaim to change the "use code" submitted by the patent owner to describe the uses covered by a patent listed with the U.S. Food and Drug Administration. In conclusion, we provide our thoughts about possible future areas of controversy in this important type of patent litigation.

II. BACKGROUND

A patent provides a right to exclude others from making, using, selling, offering for sale, or importing an infringing invention or its equivalent. While the Patent Act does not explicitly distinguish "direct" and "indirect" infringement, it has become customary to describe infringement under 35 U.S.C. § 271(a) as direct infringement. Under §271(a) a person directly infringes a patent by making, using, offering to sell, selling, or importing into the United States any patented invention, without authority, during the term of the patent. On the other hand, 35 U.S.C. § 271(b) and 35 U.S.C. § 271(c) together are grouped as "indirect" ways of infringing a patent. §271(c) relates to contributory infringement and is

beyond the scope of this White Paper. Rather, this White Paper focuses on the form of indirect infringement known as inducement of infringement.

Section 271(b) states: "Whoever actively induces infringement of a patent shall be liable as an infringer." In order to demonstrate inducement, the patentee must establish that there has been direct infringement and that the alleged infringer knowingly induced that infringement and possessed the specific intent to encourage another's infringement.

First, therefore, no party can be liable for induced infringement unless a direct infringement of the patent occurred. And, second, induced infringement requires a showing of intent, namely intent to lead the direct infringer to infringe. Liability for induced infringement requires that the inducing infringer knew or should have known that its actions would induce infringement.

Importantly, the Federal Circuit recently held it is not necessary that a single entity perform all steps of a claimed method in order to find induced infringement. Overruling prior precedent, the Federal Circuit held that a defendant may be liable for induced infringement where the defendant induced one or more entities to perform all of the claimed steps. *Akamai Technologies, Inc. v. Limelight Networks, Inc.*, 692 F.3d 1301 (Fed. Cir. 2012) (en banc) (reaffirming the proposition that all steps of a claimed method must still be performed in order to find induced infringement).

Claims for inducing patent infringement have particular significance in the pharmaceutical industry. Pharmaceutical patents often consist of method claims for treating a disease or administering a drug. Direct infringers of these types of patent claims are patients or prescribing physicians. As a result, patent owners often turn to a theory of induced infringement in order to assert these types of claims against competitors. The competitor does not, itself, use the drug. Rather, the competitor's infringement is indirect, by encouraging and causing the direct infringement by others.

By law, pharmaceutical products must be sold with labeling that states the U.S. Food and Drug Administration-approved indications for using the product, as well as instructions for administering the

product and summaries of clinical studies done on the drug that are relevant to the safe and effective administration of the product. The statements in these labels are often the most relevant evidence in any litigation regarding a competitor's intent to induce infringement of a method patent.

A pharmaceutical product's labeling is also relevant to whether a claim of induced infringement can be brought against a competitor under Section 271(e)(2), which permits the patent owner and the holder of an approved new drug product (the NDA holder) to bring suit against a potential generic competitor filing an Abbreviated New Drug Application (ANDA) or "paper" NDA under Sections 505(j) or 505(b)(2) of the Hatch-Waxman Act. In order to start an action under § 271(e)(2), the ANDA applicant must be seeking approval for a drug whose use is claimed in a patent previously listed in the FDA's Orange Book by the NDA holder. In the ANDA, the ANDA applicant must copy the labeling of the NDA holder.

Thus, induced infringement in an ANDA context generally provides an allegation from the NDA holder and patent owner that if the ANDA is approved, the ANDA applicant would induce infringement under 35 U.S.C. § 271(b). When the patent at issue claims a method of using a drug for an approved indication, an inducement theory should be straightforward. This so-called "on-label" induced infringement occurs as a result of the patient using the drug in accordance with the FDA-approved label. When the ANDA applicant seeks permission to sell its competing product with a label that instructs doctors and patients to use the drug for the infringing indication, a theory of liability under induced infringement should follow. As will be discussed in detail herein, however, the analysis for on-label induced infringement is not always so straightforward.

In addition, however, drug products commonly have multiple or alternative uses, often referred to as "off-label" uses. Such uses include not only different therapeutic indications which are wholly separate from the label, but also indications that are closely related or complementary to the approved use, despite falling outside the express language of the label. For patent claims covering these uses, a

patent owner will allege that an ANDA applicant, wishing to achieve the broadest use of a competing product, must intend for doctors and patients to use the ANDA product for all possible indications, thereby encompassing the off-label uses.

An additional complicating factor is the FDA's regulations regarding the listing of method patents as covering an approved new drug product. The FDA relies on the patent owner to describe the methods covered by the listed patents. If a potential generic competitor is seeking approval for the use of a generic drug for an approved indication that is not covered by any listed patent, where other approved indications are covered by listed patents, the generic competitor can seek approval for only the unpatented method by filing a so-called "Section (viii) carve-out label". Under this procedure, the ANDA applicant can try to avoid seeking approval for its generic drug product for any use covered by a listed patent, even though the generic drug product may be dispensed by pharmacies for all of the approved indications, including the patented ones.

If an ANDA applicant that is sued for infringement under § 271(e)(2) believes that the patent information provided by the patent owner to the FDA describing the patented methods is incorrect in some respect, it can file a counterclaim against the patent owner for an order requiring the patent owner to correct the information submitted to FDA. The scope of this counterclaim was recently expanded by the Supreme Court, and raises additional questions regarding the scope and progress of litigation based on induced infringement allegations.

This White Paper reviews the relevant case law that illustrates the different results that can result for induced infringement claims depending on what the label says, and discusses recent case law regarding induced infringement allegations that allege an intent to induce infringement of methods that are not expressly instructed by the product's label.

III. Scenario No. 1: Patent in Dispute Arguably Covers All or Part of the On-Label or Approved Use

In the first scenario, we examine inducement allegations made by plaintiffs whose method-of-use patents cover all or part of the treatments that are permitted by the FDA. The Federal Circuit has found that the requisite specific intent to induce infringement can be inferred when a party submits an application to the FDA containing a proposed label that will cause at least some users to infringe the asserted method claims. *See Eli Lilly & Co. v. Actavis Elizabeth LLC*, 435 Fed. Appx. 917 (Fed. Cir. 2011); *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042 (Fed. Cir. 2010). As discussed below, some courts have also suggested that intent may also be inferred based on marketing activities or the funding of clinical studies. *See AstraZeneca LP*, 633 F.3d at 1060; *Genentech v. Trustees of the University of Pennsylvania*, 2012 WL 1670167, *13 (N.D.Cal., May 14, 2012).

In *Eli Lilly & Co. v. Actavis Elizabeth LLC*, the district court found requisite evidence that Actavis had a specific intent to induce infringement based on statements it made in its proposed product labeling. 676 F. Supp.2d 352 (D.N.J. 2009). Eli Lilly's asserted patent claimed the use of the drug atomoxetine to treat ADHD — the only use that was permitted by the FDA. Accordingly, in submitting its ANDA, Actavis was required to include a label that instructed the proper application of the drug for treatment of ADHD. *Id.* at 376.

Actavis asserted that it had no intent to induce others to infringe Eli Lilly's patent. *Id.* at 377. Instead, it planned to market atomoxetine as a "commodity," without encouraging any particular use of the drug. *Id.* Actavis also alleged that it could not be liable for the instructions in its proposed product label to use the drug in an infringing manner because it had been required by the FDA to include them. *Id.* at 378. Finally, Actavis maintained that doctors prescribe atomoxetine for a number of non-infringing uses in addition to ADHD. *Id*.

The district court granted summary judgment of infringement, finding that Actavis induced infringement of the asserted patent. *Id.* at 378. The court reasoned that specific intent to infringe could be inferred from Actavis's product labeling, even where that labeling was required by the FDA. *Id.* at

378. The Federal Circuit affirmed the ruling on induced infringement, noting they "have long held that the sale of a product specifically labeled for use in a patented method constitutes inducement to infringe that patent . . . ." *Eli Lilly & Co.*, 435 Fed. Appx. at 926.

In *AstraZeneca LP v. Apotex, Inc.*, the district court similarly found specific intent on the part of Apotex to induce infringement based on its proposed product label. 633 F.3d 1042, 1049. AstraZeneca's product label stated that the recommended starting dose may be administered as either the total daily dose once-daily or in individual doses twice daily. AstraZeneca's patented method was directed to the once-daily treatment of asthma with budesonide. Apotex filed an ANDA for the twice-daily treatment of asthma with budesonide, deleting the explicit references to once-daily dosing from its proposed label. *Id.* at 1047. Apotex's proposed generic label, however, included an FDA-mandated warning that patients should "titrate down" to the lowest effective dose of the medication to avoid any adverse effects from excessive use of the medication. *Id.* at 1047. The district court determined that this would cause some users to infringe because they would need to administer budesonide once-daily if they followed the label's instructions to titrate down from the lowest twice-daily dose. *Id.* at 1057. The district court also found that, despite being aware of the infringement problem presented by its proposed label, Apotex proceeded with its plans to distribute its generic product. *Id*. at 1060

In affirming the district court's finding that AstraZeneca would likely prove induced infringement at trial, the Federal Circuit agreed that Apotex possessed the specific intent to induce infringement because its label would inevitably lead some users to practice the claimed method. *Id*. at 1060. The court rejected Apotex's assertion that it faced the Hobson's choice of either complying with FDA requirements and risking a patent infringement suit or removing the downward-titration language, which would ensure that its ANDA would not be approved. *Id.* at 1061. Instead, the Federal Circuit found that there was no such dilemma as "Apotex was free to submit a Paragraph III certification and

wait until the patents expired before distributing its generic drug or file a Paragraph IV certification and challenge infringement and validity of the asserted claims." *Id*. at 1061.

In *Genentech v. Trustees of the University of Pennsylvania*, the district court denied Genentech's motion for summary judgment of no induced infringement, holding that a reasonable jury could find specific intent based on Genentech's product label and other "active steps" taken by Genentech that could be found to encourage direct infringement. 2012 WL 1670167 at *12-14. University of Pennsylvania's patent claimed a method for preventing transformation of a potential breast cancer cell that overexpresses cell surface protein p185 ("p185") into a cancer cell by treatment with anti-p185 antibodies. *Id*. at *2. In addition to being indicated for the treatment of cancer, Genentech's anti-p185 antibody drug Herceptin is approved for use in reducing the risk of cancer recurrence in patients who have been diagnosed with primary breast cancer and have been treated by surgical removal of their tumor. *Id*. at *1. The University claimed that Genentech's Herceptin drug could be administered in an infringing manner to patients consistent with the second indication because Herceptin acts on p185 overexpressing isolated tumor cells that are not cancer cells and prevents their transformation into cancer cells. *Id.* at 2.

Genentech argued that there are substantial noninfringing uses of Herceptin because the University admitted that "only a minority of that [treated] population may possess the [non-cancer] cells on which its claimed invention operates to prevent transformation…." *Id.* at 17. The court rejected Genentech's argument, finding that "even where a product has substantial noninfringing uses, an accused can still be liable for inducement if the patentee establishes the alleged inducer's affirmative intent that the product be used to infringe." *Id*. at *13 (citing AstraZeneca, 633 F.3d at 1059) (internal quotation marks omitted)). The court reasoned "AstraZeneca demonstrates that, to find induced infringement, the Court need not find that the drug label teaches infringement in every instance, so long as the language would inevitably lead *some* consumers to practice the claimed method." *Id*.

The court noted that in addition to the product label, other evidence of "active steps" taken to induce direct infringement may be used to prove affirmative intent to induce infringement. *Id*. The court found that the following additional evidence was relevant: (1) Genentech actively markets Herceptin to prevent "recurrence" and to keep patients "cancer free," (2) Genentech's parent company, Roche, funded a sophisticated molecular biological study of patients establishing that Herceptin acts on p185 overexpressing noncancerous tumor cells, and (3) Genentech represents to the public that Herceptin targets cancerous and noncancerous tumor cells alike. *Id.* at *13. In denying Genentech's motion for summary judgment, the court concluded a jury could find that Genentech induced infringement because it knew Herceptin acted on noncancerous cells, that this infringed the asserted method claims, and that Genentech nonetheless continued to encourage the use of Herceptin. *Id.* at *13-14.

IV. SCENARIO No. 2: Patent in Dispute Covers Undisputed Off-Label Use (no patent covering on-label use).

In an opinion of first impression, in *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed. Cir. 2003), the Federal Circuit addressed "whether it is an act of infringement under 35 U.S.C. § 271(e)(2)(A) to submit an ANDA seeking approval to make, use, or sell a drug for an approved use if any other use of the drug is claimed in a patent, or if it only an act of infringement to submit an ANDA seeking approval to make, use, or sell a drug if the drug or the use *for which FDA approval is sought* is claimed in a patent." *Id*. at 1354 (emphasis in original). The court determined that it was the latter and held 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." *Id*. at 1354-55.

In that case, Apotex Corp. ("Apotex") filed an ANDA seeking approval to market a generic formulation of gabapentin upon the expiration of Warner-Lambert Company's ("Warner-Lambert")

epilepsy method patent. *Id*. at 1352. Apotex sought approval to market gabapentin only for the same indication for which Warner-Lambert's Neurontin (R) was approved (i.e. "adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy"). *Id*. Apotex also filed a paragraph IV certification stating that its proposed manufacture, use and sale of gabapentin for the treatment of partial seizure would not infringe another Warner-Lambert method patent relating to the treatment of certain neurodegenerative diseases, such as stroke, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis ("ALS") and Parkinson's disease. *Id*. Such uses were all off-label.

Warner-Lambert filed an infringement action under 35 U.S.C. § 271(e)(2)(A), alleging that Apotex's submission of the ANDA was an act of infringement of the neurodegenerative method patent. *Id*. at 1353. Although the FDA had not approved the use of gabapentin for any of the indications that were claimed in the patent, and the promotion of unapproved uses by NDA or ANDA holders is prohibited under 21 C.F.R. § 202.1(e)(4), Warner-Lambert argued that "patients will use the Apotex Defendants' gabapentin for all purposes for which Warner-Lambert's Neurontin (R) product has been and customarily is used, and doctors will prescribe the Apotex Defendants' gabapentin product for such uses, including the treatment of neurodegenerative diseases." *Id.*

At the close of discovery, the District Court granted summary judgment of noninfringement for Apotex and the Federal Circuit affirmed the decision. The Federal Circuit stated that the "FDA does not grant across-the-board approval to market a drug. Rather, it grants approval to make, use, and sell a drug for a specific purpose for which that drug has been demonstrated to be safe and efficacious." *Id*. at 1356. That approved use is "the *only* use for which an ANDA applicant can seek approval." *Id*. (emphasis in original). "[B]ecause an ANDA may not seek approval for an unapproved or off-label use of a drug under 21 U.S.C. § 355(j)(2)(A)(i), it necessarily follows that 35 U.S.C. § 271(e)(2)(A) does not apply to a use patent claiming only such a use." *Id*.

The Court further held that "Congress clearly intended to limit actions for infringement of method-of-use patents under § 271(e)(2)(A) to 'controlling use patents,' or patents that claim an approved use of a drug. An ANDA applicant, who necessarily 'piggybacks' on the approved NDA of the innovator, can only apply to sell the approved drug, which, in this case, is no longer under patent, and to market it for the use for which the FDA has indicated that the drug is safe and efficacious, for which use the patent here has also expired." *Id*. at 1362.

Because Apotex did not submit an application to sell a drug for treatment of neurodegenerative diseases, which was the only use covered by the patent involved in this case, the Court concluded that Apotex was entitled to summary judgment of noninfringement. *Id*. The Court also addressed the paragraph IV certification that Apotex filed and determined that it was unnecessary – "a certification need not be provided for a patent claiming a use for which the ANDA applicant is not seeking approval, *i.e.*, a use not covered by the NDA." *Id*. at 1361. The Court noted that although Apotex formally labeled it as a paragraph IV certification, with respect to the neurodegenerative method patent, Apotex's statement "was effectively a statement of non-applicable use pursuant to 21 U.S.C. 355(j)(2)(A)(viii)," *Id*. at 1360, also referred to as a "Section (viii) carve-out."

Soon after its *Warner-Lambert* decision, the Federal Circuit relied on it to affirm another district court's grant of summary judgment in favor of defendants that had filed ANDAs relating to uses that were not covered by the patents at issue. In *Allergan, Inc. v. Alcon Laboratories, Inc.*, 324 F.3d 1322, (Fed. Cir. 2003), Allergan, Inc. ("Allergan") filed an action against Alcon Laboratories, Inc. ("Alcon") and Bausch & Lomb, Inc. ("B&L"), alleging that they infringed two of Allergan's patents by submitting ANDAs seeking approval for the production and sale of a generic version of brimonidine for the reduction of intraocular pressure. *Id*. at 1324. As in *Warner-Lambert*, the drug itself was not patented, and the FDA had not approved the drug for the uses claimed in the patents at issue. *Id*. at 1324. The patents at issue claimed a method of neural protection and a method of protecting the optic nerve, both by

administering brimonidine. *Id*. at 1324. The Federal Circuit determined that *Warner-Lambert* controlled the case, and that under that decision, "Allergan is precluded from suing Alcon and B&L under section 271(e)(2) for inducing infringement of the [patents at issue], 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." *Id*. at 1334.

The Federal Circuit recently revisited this issue in *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316 (Fed. Cir. 2012), and provided additional guidance regarding what would constitute an approved use, such that an ANDA submission seeking approval to make, use, or sell a drug for such use would constitute an act of infringement under 35 U.S.C. § 271(e)(2)(A). In *Bayer v. Lupin,* the defendants Lupin, Ltd. *et al.* (collectively "Lupin") had filed ANDAs to market generic versions of Yasmin, an oral contraceptive produced and marketed by the plaintiffs Bayer Schering Pharma AG and Bayer HealthCare Pharmaceuticals, Inc. (collectively "Bayer"). The ANDAs sought FDA approval for the generic versions of Yasmin for use as oral contraceptives. After paragraph IV certifications and notice letters by Lupin, Bayer sued, alleging infringement under § 271(e)(2)(A) of one of its Orange Book-listed patents, U.S. Patent No. 5,569,652 ("the '652 patent"). *Id.* at 1319.

The '652 patent claims methods of simultaneously achieving an contraceptive effect, an anti-androgenic effect, and an anti-aldosterone (also known as anti-mineralocorticoid) effect in a female patient in need thereof by administering dihydrospirorenone (an active compound contained in Yasmin) to the patient. *Id.* at 1319-20. Thus, the '652 patent did not cover the use of Yasmin for contraception alone. In contrast, the only use set forth in the "Indications and Usage" section of the Yasmin label attached to the FDA's approval letter was for preventing pregnancy in women who decide to use an oral contraceptive. *Id.* at 1320.

However, Bayer argued that its label for Yasmin showed that the FDA actually approved the drug for simultaneously obtaining all three effects specified in the claims of the '652 patent, and thus,

because the similar label to be used by Lupin instructs the use of the drug to obtain all three effects, the defendants were liable for inducing infringement. *Id.* at 1321. Bayer argued that the label instructs such use, because the "Pharmacodynamics" subsection of the "Clinical Pharmacology" section of the label mentions that one of the active ingredients in Yasmin, drospirenone, has anti-mineralocorticoid activity and mentions that preclinical studies have shown that drospirenone has anti-androgenic activity. *Id.* at 1322.

The Federal Circuit rejected Bayer's argument, affirming the district court's dismissal of patent infringement claims against Lupin. *Id.* at 1321. The Federal Circuit stated that, while the label mentions potential anti-mineralocorticoid and anti-androgenic activities, it does not recommend or suggest to a physician that the drug is safe and effective for inducing these effects in patients in need thereof. *Id.* at 1322, 1324. The court noted, *inter alia,* the FDA labeling regulation, 21 C.F.R. § 201.57, which requires indications to be supported by evidence from "adequate and well-controlled studies," and requires that indications and usages "must not be implied or suggested in other sections of the labeling" if not in the Indications and Usage section. *Id.* at 1322-23. The court held that absent a recognition in the label that the FDA had found the relevant indications safe and effective, the "label cannot instruct (and the ANDA proposed label cannot induce infringement of) the method of use claimed in the '652 patent." *Id.* at 1324.

Finally, a recent District Court case addressing related issues also merits discussion. In *AstraZeneca UK Limited v. Watson Laboratories*, Civil Action No. 10-915-LPS; (D. Del. March 23, 2012), Judge Stark dismissed certain claims of AstraZeneca UK Limited ("AstraZeneca") against defendant, Watson Laboratories ("Watson"), alleging that Watson infringed two method of use patents under 35 U.S.C. § 271(e)(2), because, similar to the cases discussed above, Watson had filed a Section 505(b)(2)(B) Statement certifying that it was not seeking FDA approval for the indications covered by the two patents. *Id*. at 6. In reaching that decision, the court considered the allegation in AstraZeneca's

complaint that Watson's Section 505(b)(2)(B) Statement was "erroneous or improper" and rejected AstraZeneca's allegation as "conclusory and speculative." *Id*. at 7.

In that same opinion, Judge Stark also addressed a motion to dismiss filed by EGIS Pharmaceuticals PLC ("EGIS"), Watson's development partner. *Id*. at 7. After Watson's filing of a Paragraph 4 certification as to U.S. Patent No. RE37,314 (the "'314 Patent")[1], AstraZeneca had claimed that EGIS would induce the infringement of the '314 Patent upon the approval of Watson's NDA. *Id*. at 7-8. The court rejected all of EGIS's arguments regarding the '314 Patent. First, the court rejected EGIS's argument that FDA approval of Watson's NDA was "too remote and speculative to establish an Article III case or controversy." *Id*. at 8 (citing *Allegan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322, 1331-32 (Fed. Cir. 2003). Second, the court rejected EGIS's argument that AstraZeneca's claim was "improperly directed against activities protected by the Section 271(e)(1) safe harbor" in light of the Federal Circuit's decision in *Forest Labs., Inc v. Ivax Pharms., Inc.*, 501 F.3d 1263, 1272 (Fed. Cir. 2007). Id. at 9. Finally, the court rejected EGIS's argument that under *Allergan*, Section 271(e)(2) does not permit the assertion of induced infringement claims for composition patents such as the '314 Patent against a development partner like EGIS. *Id*. The court stated that this argument "overlooks the Federal Circuit's decision in *Forest*, which stated, 'Section 271(e)(2) may support an action for induced infringement' without limitation as to any particular types of patents or defendants." *Id*. at 9 (*quoting Forest*, 501 F.3d at 1272). The court determined that AstraZeneca had "adequately alleged in its Second Amended Complaint that EGIS is a prime mover responsible for the events that will lead up to Watson's eventual FDA approval." *Id*.

Thus, collectively, the decisions discussed in this section of this White Paper, *Warner-Lambert v. Apotex* and the subsequent decisions, make it clear that the key to determining whether a use, for

[1] The '314 Patent claims rosuvastatin compounds and pharmaceutical compositions containing such compounds. Id. at 1.

which approval is sought by an ANDA filer, is an approved use sufficient to qualify the submission of the ANDA as an act of inducing infringement under § 271(e)(2)(A), is whether the label recommends or suggests to a physician that the drug is safe and effective for such use, and in order for the label to do so, the use must appear in the Indications and Usage section of the label. Absent such a recommendation and suggestion in the label, a claim of inducing infringement by the NDA holder will be dismissed, and the appropriate action by an ANDA filer regarding such a use is not a paragraph IV certification, but, rather, a "Section (viii) carve-out" pursuant to 21 U.S.C. § 355 (j)(2)(A)(viii).

V. *Caraco*-type Counterclaims To Correct Listed Patent Information Including Use Codes

As illustrated in sections III and IV, uses or use codes (description of method-of-use patents listed in the Orange Book, 21 C.F.R. §§314.53(c)(2)(ii)(P)(3), (e)) are central to inducement-based causes of action under the Hatch-Waxman Act. It is thus instructive to review the controlling authority on the statutory interpretation of use codes as "patent information," thereby providing ANDA filers a means to correct listed use codes via counterclaims in ANDA litigation. The Supreme Court's April 17, 2012 decision in *Caraco Pharmaceutical Laboratories, Ltd. v. Novo Nordisk A/S*, 132 S.Ct. 1670 (2012) provides such authority. The Court in that decision gives guidance for the construction and application of relevant provisions in the 2003 Medicare Prescription Drug Improvement and Modernization Act, which amends the Hatch-Waxman Act.

Specifically, and as touched on in section II above, the statute in question mandates that an NDA holder or sponsor list patents claiming pharmaceutical products and their uses by patent number and expiration date. For method-of-use patents, use codes are also required to be listed in the Orange Book. If an ANDA applicant seeks approval to sell a generic drug for a previously approved use that is not covered by the listed use codes, an ANDA filer or generic manufacturer can submit what is called a "Section viii statement" – pursuant to 21 U.S.C. §355(j)(2)(A)(viii) – "carving out" the patented uses covered by the use codes, in order to obtain approval of the ANDA. Significantly, under the statute, an

ANDA filer is authorized to file a counterclaim in ANDA litigation to challenge the accuracy of the "patent information" listed by the NDA holder. *See* 21 U.S.C. §355(j)(5)(C)(ii)(I). However, before *Caraco*, it was disputed whether this counterclaim provision is properly construed to allow an ANDA filer to correct use codes, and if so, under what circumstances and to what extent.

The *Caraco* case has a long history, culminating in the Supreme Court overturning the Federal Circuit, and most recently the Federal Circuit on remand modifying the trial court's mandatory injunction to correct Novo's use codes. *Novo Nordisk A/S v. Caraco Pharmaceutical Laboratories, Ltd.*, 688 F.3d 766 (Fed. Cir. 2012).

By way of background, the facts in the case have to do with Novo Nordisk's branded Type 2 diabetic drug PRANDIN©, a.k.a. repaglinide. Novo had two patents listed in the Orange Book for PRANDIN©, one drawn to the pharmaceutical product (Reissue Pat. No. RE 37,035, "RE '035") and the other the method of using repaglinide in combination with metformin (US Pat. No. 6,677,358, "USP '358"). The product patent RE '035 expired in 2009, and the use patent USP '358 will expire in 2018. PRANDIN© has two other approved uses that are not covered under Novo's patents: (1) in combination with thiazolidnediones and (2) as monotherapy.

In filing an ANDA for repaglinide, Caraco submitted a Paragraph III certification with respect to RE '035, and a Paragraph IV certification with respect to USP '358. On the basis of Caraco's Paragraph IV certification, Novo sued Caraco for infringement under 35 U.S.C. § 271(e)(2). Caraco later submitted an amended ANDA to the FDA with a Section viii statement that it would not seek approval for repaglinide in combination with metformin. This proposed "carve-out" label was supposed to satisfy the FDA for the approval of Caraco's ANDA. However, around the same time Novo changed the use code for the '358 patent from U-546 to U-968, the latter being "a method for improving glycemic control in adults

with Type 2 diabetes," to conform it to FDA's statement of PRANDIN's only approved use. This changed use code was no longer limited to repaglinide in combination with metformin.

In light of the changed use code, the FDA rejected Caraco's proposed "carve-out" label. Consequently, Caraco filed a counterclaim seeking an order from the trial court to reinstate the use code to U-546. The trial court granted summary judgment on Caraco's counterclaim. The Federal Circuit, in its first review of the case, reversed the trial court, holding that the statute does not permit an ANDA filer to request an order compelling a NDA holder to change its use code. *Novo Nordisk A/S v. Caraco Pharmaceutical Laboratories, Ltd.*, 601 F.3d 1359 (Fed. Cir. 2010). In reaching its holding there, the Federal Circuit found that "patent information" was limited to the "patent number and the expiration date" and did not include use codes. *Id.* at 1367. The Federal Circuit also held that an ANDA filer could not assert its counterclaim if *any* approved method is covered in the listed patents.

The case went on appeal in the Supreme Court, and by a unanimous decision the Supreme Court overturned the Federal Circuit, holding that an ANDA filer is permitted to challenge inaccurate use codes under the counterclaim provision. Resorting to statutory context, the Court found that use codes qualify as "patent information" under the statute, as they are "pivotal" to the implementation of the statutory scheme. 132 S.Ct. at 1683-1684. The Court also emphasized that one patented use should not foreclose other unpatented uses for an ANDA filer, thereby clarifying the statutory interpretation of "an approved method." More broadly, the Court rejected the notion advanced by Novo that the counterclaim provision is intended only to enable an ANDA filer to remove an incorrectly listed patent from the Orange Book. Instead, the Court pointed out that by the counterclaim provision Congress intended to provide generic drug manufacturers a means to correct inaccuracies in branded drugs' patent listings.

On remand from the Supreme Court, and on the issue whether the trial court abused its discretion by dictating the change of the use code to Novo, the Federal Circuit held that it did and

ordered the lower court to modify its injunction to allow for Novo to rewrite its use code consistent with the Supreme Court's holding. 601 F.3d 1359 at 1367.

Given the fairly recent date of the *Caraco* decision, cases would likely take some time to percolate through the system where an ANDA filer may seek to change a NDA holder's listed use code via counterclaims in ANDA litigation. At the time of this writing, there has not been any ANDA case citing *Caraco* to change use codes via a counterclaim pursuant to 21 U.S.C. §355(j)(5)(c)(ii)(I).

Interestingly, *Caraco*'s facts fall within the first scenario discussed above in section III, where the listed patent is deemed to cover part of the approved uses. But, unlike in *AstraZeneca v. Apotex* or *Genentech v. Trustees of the University of Pennsylvania*, the approved uses for repaglinide, albeit all for the same indication, are for different combinatory therapies or monotherapy, and are thus arguably independent in terms of possible implications for inducement. Put another way, a generic label for one combinatory therapy, standing alone, would generally not evidence a "specific intent" for the ANDA filer to induce a patient to use the drug as a monotherapy or in a different combinatory therapy. The same kind of analysis cannot be applied to labels and approved uses involving different dosage forms, as in *AstraZeneca,* or different aspects of the mechanism of action, as in *Genentech*.

VII. Conclusion

Court decisions provide considerable guidance in this complicated area of the law. Resolution of patent infringement disputes alleging induced infringement requires a complete understanding of the particular factual scenario at issue. We expect courts will continue to see new scenarios and issue decisions that will provide even more guidance in the future.