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Practice Tips for Patentees Asserting Method-of-Treatment Claims Involving Divided Infringement



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Do physicians ''condition participation'' of drug therapy based on patients' compliance with drug manufacturer instructions regarding how to take drugs? Do physicians withhold medically necessary drug therapy from patients when patients fail or refuse to take a drug in accordance with the instructions in the label?

You might think these are syllabus topics for an advanced course in medical ethics. But under recent decisions of the U.S. Court of Appeals for the Federal Circuit, these are the questions that federal district courts have been asked to grapple with in method-of-treatment patent cases involving claims of ''divided infringement.''

In cases of divided infringement, in which a single party does not perform all of the steps of a patented method, claims for infringement depend on whether all steps of a patented method can nonetheless be attributed to one party. The Federal Circuit defined a framework for this inquiry in *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 797 F.3d 1020, 116 U.S.P.Q.2d 1344 (Fed. Cir. 2015) (en banc), holding that such liability may be found only in cases where a single entity ''directs'' or ''controls'' each step of the recited method. Although the Federal Circuit explained that the type of conduct sufficient to amount to the required ''direction or control'' is something that is to be decided on a case-by-case basis, thus far, the *only* factual scenario that has been deemed sufficient by the Federal Circuit is one where the single entity ''conditions participation in an activity or receipt of a benefit upon performance of . . . [the] steps of a patented method.''

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Such a framework is seemingly a good fit for cases involving *computer*-related methods—where the actors have no choice but to perform certain steps to take advantage of available services. But does this make sense in the *pharmaceutical* and *biotechnology* context—where the actors retain a certain degree of discretion in their roles (e.g., physicians devising a course of treatment for their patients).

Just one Federal Circuit decision since *Akamai* has involved a divided infringement analysis in the context of method-of-treatment claims. This article explores the *Akamai* framework and how the Federal Circuit has applied it in the method-of-treatment context, while considering whether there is a framework that is better suited for method-of-treatment cases. This article also provides practice tips for practitioners to follow if they encounter a case of divided infringement in the method-of-treatment context.

I. *Akamai v. Limelight*

In *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 797 F.3d 1020, 116 U.S.P.Q.2d 1344 (Fed. Cir. 2015) (en banc) (per curiam), the Federal Circuit ''unanimously set forth the law of divided infringement.'' *Id.* at 1021. The case has a long history. In 2006, Akamai Technologies filed suit against Limelight Networks for infringement of a patent that claims methods for delivering content over the Internet. *Id.* at 1024. The parties agreed that Limelight performed every step of the claimed methods, except for the ''tagging'' and ''serving'' steps, which were performed by Limelight's customers. *Id.* After instructing the jury that Limelight is responsible for its customers' performance of those steps if Limelight directs or controls their activities, the district court overturned a jury finding of infringement by Limelight. *Id.*

On appeal, the Federal Circuit affirmed. *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 629 F.3d 1311, 1320, 97 U.S.P.Q.2d 1321 (Fed. Cir. 2010). The Federal Circuit then granted en banc review and reversed, finding that Limelight was liable for induced infringement under 35 U.S.C. § 271(b), and it was therefore unnecessary to resolve whether a single party would be liable for direct infringement. *Akamai Techs. Inc. v. Limelight Networks, Inc.*, 692 F.3d 1301, 1308-1309, 1319, 104 U.S.P.Q.2d 1799 (Fed. Cir. 2012) (per curiam).

The Supreme Court granted certiorari and reversed, holding that a finding of induced infringement requires an underlying act of direct infringement. *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111, 2117-2218, 110 U.S.P.Q.2d 1681 (2014). The Supreme Court declined to address the question of when a party may be liable for direct infringement in a case of divided infringement. *Id.* at 2120.

On remand from the Supreme Court, a Federal Circuit panel applied a rigid approach to divided infringement and held that there was no infringement where the plaintiff failed to show that the defendant's ''customers were acting as agents of or otherwise contractually obligated to'' the defendant or ''that they were acting in a joint enterprise when performing the tagging and serving steps.'' *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 786 F.3d 899, 915, 114 U.S.P.Q.2d 1749 (Fed. Cir. 2015).

The en banc Federal Circuit reversed the panel and unanimously reinstated the jury verdict. *Akamai Techs.*, 797 F.3d at 1024. The en banc court explained that ''[d]irect infringement under § 271(a) occurs where all steps of a claimed method are performed by or attributable to a single entity.'' *Id.* at 1022. The Federal Circuit examined the circumstances where a ''single entity'' may be held responsible for direct infringement when more than one actor is involved in practicing the steps of a method claim. *Id.* The court held that ''*an entity [is] responsible for others' performance of method steps* in two sets of circumstances: (1) *where that entity directs or controls others' performance*, and (2) where the actors form a joint enterprise.'' *Id.* (emphasis added).

The Federal Circuit concluded that ''a single entity directs or controls the acts of another'' so that ''liability under § 271(a) can . . . be found when an alleged infringer [1] *conditions participation in an activity or receipt of a benefit upon performance of a step or steps of a patented method* and [2] *establishes the manner or timing of that performance*.'' *Id.* at 1023 (emphases added). According to the court, ''In those instances, the third party's actions are attributed to the alleged infringer such that the alleged infringer becomes the single actor chargeable with direct infringement.'' *Id.* In so ruling, the court stressed that its decision applied to ''the facts presented by th[at] case.'' *Id.* at 1023. ''In the future, other factual scenarios may arise which warrant attributing others' performance of method steps to a single actor.'' *Id.*

II. Divided Infringement in the Context of Method-of-Treatment Claims

Such a different ''factual scenario[]'' arises in the method-of-treatment context, where the ''conditioning participation'' and ''establishing the manner or timing'' of performance test does not seem to be as neat of a fit. Since *Akamai*, only one Federal Circuit decision has evaluated divided infringement in the method-of-treatment context.

A. *Eli Lilly v. Teva Parenteral Medicines*

In *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 121 U.S.P.Q.2d 1277 (Fed. Cir. 2017), the Federal Circuit reviewed a district court decision to apply *Akamai* to find the defendant pharmaceutical companies liable for inducing direct infringement by treating physicians. The case involved the Food and Drug Administration-approved method of administering the chemotherapy drug pemetrexed disodium. *Id.* at 1362-1363. Like many other chemotherapies, pemetrexed is administered through an intravenous infusion, typically at a hospital or infusion center. ''Eli Lilly markets pemetrexed under the brand name ALIMTA®,'' which is indicated for the treatment of certain types of lung cancer and mesothelioma. *Id.* at 1362.

Teva filed Abbreviated New Drug Applications (ANDAs) with the FDA seeking approval to launch a generic version of the drug. *Id.* Eli Lilly sued Teva for induced infringement of U.S. Patent No. 7,772,209, which, among other things, claims a method of administering pemetrexed after pretreatment with folic acid. *Id.* Claim 12 is representative:

> 12. An improved method for administering pemetrexed disodium to a patient in need of chemotherapeutic treatment, wherein the improvement comprises:
>
> a) *administration of between about 350 ìg and about 1000 ìg of folic acid* prior to the first administration of pemetrexed disodium;

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. . .

c) administration of pemetrexed disodium.

The purpose of the vitamin pretreatment regimen is to reduce toxic side effects that were associated with pemetrexed therapy. *Id.* at 1365. Unlike the infusion of pemetrexed itself, which is administered at a hospital or infusion center by a healthcare professional, the pretreatment with folic acid is self-administered by the patient. *Id.* at 1362. Because different actors perform each step of the claimed method—a patient for the pretreatment step and a healthcare professional for the pemetrexed step—there could only be direct infringement under a theory of ''divided'' infringement. *Id.*

The district court found such infringement by treating physicians, holding that ''the factual circumstances are sufficiently analogous to those in *Akamai* to support a finding of direct infringement by physicians under § 271(a), and thus inducement of infringement by [d]efendants under § 271(b).'' *Id.* at 1041. The court concluded that ''the physician directs or controls the patient's administration of folic acid such that performance of all the claimed steps, including the administration of folic acid, can be attributed to . . . the physician.'' *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 126 F. Supp. 3d 1037, 1042-1043, 2015 BL 273790 (S.D. Ind. 2015).

On appeal, the main infringement issue was therefore whether all of the patented steps could be attributed to a physician. At the Federal Circuit, the parties agreed ''that no single actor performs all steps of the asserted claims; rather, the steps are divided between physicians and patients. Though physicians administer vitamin B12 and pemetrexed, patients self-administer folic acid with guidance from physicians.'' *Eli Lilly & Co.*, 845 F.3d at 1362.

The Federal Circuit returned to the *Akamai* test to determine whether physicians ''direct or control'' the performance of patients. *Eli Lilly & Co.*, 845 F.3d at 1364. Specifically, the Federal Circuit examined whether physicians ''condition participation'' in the patented treatment upon performance of the patients' self-administration of the folic acid step, and whether they establish the manner or timing of that performance. *Id.* at 1365. The court defined the benefit to be conditioned as the patented pemetrexed treatment, and held that the record evidence supported a finding that physicians ''condition'' that treatment on the patients' administration of folic acid. *Id.* at 1365-1366. Specifically, the court ruled that the product labeling combined with certain expert testimony showed that taking folic acid is an ''absolute'' requirement before a pemetrexed treatment. *Id.* at 1366-1368.

B. A Different Approach

Although the Federal Circuit applied the *Akamai* ''conditions participation'' framework in *Eli Lilly*, that approach is not the most logical in the context of method-of-treatment cases involving divided infringement. Under the Hatch-Waxman Act, a patentee can file a patent infringement action based on the submission of an ANDA ''for a drug claimed in a patent or the use of which is claimed in a patent.'' 35 U.S.C. § 271(e)(2)(A) (A similar patent infringement regime exists under the Biologics Price Competition and Innovation Act, whereby a patentee can file a patent infringement action based on the submission of an application for a biosimilar version of a ''biological product claimed in a patent or the use of which is claimed in a patent.'' 35 U.S.C. § 271(e)(2)(C).).

The act of infringement is hypothetical, as no generic product has been sold. Accordingly, in the case of method-of-treatment patents where the claims are ''divided'' such that patients perform certain steps, the best approach to determining whether a doctor directs or controls the patient's performance should focus, in the first instance, on the labeling of the proposed generic drug. Because the Hatch-Waxman Act authorizes infringement actions to be brought before the ANDA products are sold, the infringement analysis must assume that the ANDA labeling accurately describes how the products will be used once approved. *See, e.g.*, *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569, 42 U.S.P.Q.2d 1257 (Fed. Cir. 1997) (''[T]he question of infringement must focus on what the ANDA applicant will likely market if the application is approved, an act that has not yet occurred.''). ''The pertinent question'' when assessing induced infringement by a defendant pharmaceutical company in method-of-treatment cases is therefore ''whether the proposed label instructs users to perform the patented method. If so, the proposed label may provide evidence of . . . affirmative intent to induce infringement.'' *AstraZeneca LP v. Apotex Inc.*, 633 F.3d 1042, 1060-1061, 97 U.S.P.Q.2d 1029 (Fed. Cir. 2010).

When a proposed ANDA label tracks a patented method-of-treatment claim, courts should assume that doctors will prescribe the ANDA product in accordance with its label and that patients will follow those label-based instructions as well. In such circumstances, courts should find that the ''direction or control'' standard for divided infringement is satisfied. Although it is of course possible that *some* physicians might not follow the approved method or that *some* patients may not follow their doctor's directions—that is not an issue of infringement, but a question of damages in cases where they are available. When patients take a drug product according to the directions in the label, they can be presumed to be doing so under the ''direction or control'' of their doctors.

The *Akamai* court specifically anticipated that ''other factual scenarios may arise which warrant attributing others' performance of method steps to a single actor.'' *Akamai Techs.*, 797 F.3d at 1023. The method-of-treatment context is just such a scenario. Accordingly, courts should adopt the label test.

III. Practice Tips

In asserting a method-of-treatment claim, practitioners who represent patent owners should take the following steps in order to maximize their chances of prevailing in litigation:

■ *Strive for a finding of direct infringement without relying on theories of divided infringement.* One way to prevail in a method-of-treatment claim is to prove direct infringement without relying on theories of divided infringement. Before the district court in *Eli Lilly v. Teva Parenteral Medicines*, the patentee argued that the patient's taking of folic acid ''constitutes the physician 'administering' the folic acid.'' 126 F. Supp. 3d at 1042. The court decided that ''whether or not this satisfied the definition of 'administer' is not relevant,'' because the

court found infringement under the *Akamai* divided infringement framework. *Id.*

However, practitioners who represent patentees should consider whether they can make claim construction arguments so that all claimed steps can be attributed to a single actor. This practice tip actually starts before litigation with the patent prosecution process. As more medical treatments require self-treatment regimens, patentees should consider how they can frame their claims to attribute all steps of method-of-treatment claims to a single actor.

■ *Prepare litigation strategy to fit evidence and arguments into* Akamai's *''conditions participation'' and ''establish manner or timing'' framework*. On appeal in *Eli Lilly & Co.*, the Federal Circuit noted certain evidence that was especially persuasive to the district court in finding that ''physicians 'condition' pemetrexed treatment on the administration of folic acid,'' and that they ''establish[] [the] manner or timing of that performance.'' 845 F.3d at 1366-1367. Among that evidence was the ''Physician Prescribing Information,'' which ''explains that folic acid is a '[r]equirement for [p]remedication' in order 'to reduce the severity of hematologic and gastrointestinal toxicity of [pemetrexed],' '' and ''instructs physicians not only to tell patients to take folic acid orally, but also to take '400 [ug] to 1000 [ug] [of folic acid] once daily beginning 7 days before the first dose of [pemetrexed].' '' *Id.* (alterations in original). The court also looked to the ''Patient Information'' that ''informs patients that physicians may withhold pemetrexed treatment.'' *Id.* The court did not limit itself to the statements in the drug label, but also considered evidence of how the brand drug was actually used in practice. The court noted that ''Eli Lilly's expert . . . testified that it is 'the physician's responsibility to initiate the supplementation' of folic acid'' and that ''the product labeling shows that taking folic acid is 'an absolute requirement.' '' *Id.* The expert testified ''that if a physician realizes that a patient did not follow his or her instructions to take folic acid, then the 'doctor will not give the pemetrexed.' '' *Id.* The patentee also elicited an admission from the defendants' expert that ''it is 'standard practice' . . . that a patient 'must have taken their required folic acid in order to have the pemetrexed administered.' '' *Id.*

The takeaways from the *Eli Lilly* case are that while practitioners who represent patentees should emphasize the product labeling, they should also look *beyond* the label for evidence of how the drug is actually used in practice to support a conclusion that the doctor ''conditions participation'' in a treatment and ''establishes the manner or timing'' of that treatment. In addition, practitioners should rely on expert testimony to explain the physician's role in treatment.

■ *Preserve arguments for a new approach to establishing ''direction or control.''* Finally, practitioners must remember that the *Akamai* court specifically anticipated that ''other factual scenarios may arise which warrant attributing others' performance of method steps to a single actor.'' 797 F.3d at 1023. As a result, practitioners should preserve arguments to allow a court to look beyond the specific ''conditions'' framework set forth in *Akamai*. As previously explained, an approach that relies on the product label may make more sense in the context of method-of-treatment claims.

Practitioners should therefore argue that when a product label tracks a patented method-of-treatment claim, the ''direction or control'' standard for divided infringement is satisfied.

IV. Conclusion

Cases of divided infringement in the method-of-treatment context are an odd fit for the *Akamai* ''conditions participation'' framework. Nonetheless, in the one method-of-treatment decision since *Akamai*, the Federal Circuit shoehorned the fact pattern into that ''conditions participation'' framework. A ''direction or control'' divided infringement test that relies on the proposed generic label could be used in future cases. Therefore, in cases where a product label tracks a patented method-of-treatment claim, courts should find that the ''direction or control'' standard for divided infringement is satisfied.

Practitioners who represent patentees in such actions should devise a litigation strategy that (1) aims for a claim construction that allows for a finding of direct infringement without relying on theories of divided infringement; (2) develops evidence that fits into the *Akamai* ''conditions participation'' framework; and (3) argues for application of a new test that better fits the method-of-treatment context.

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