IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PERNIX IRELAND PAIN DAC and PERNIX THERAPEUTICS, LLC,	§	
	§	
Plaintiffs,	§	
	§	
v.	§	Civil Action No. 16-139-WCB
	§	
ALVOGEN MALTA OPERATIONS LTD.,	§	
	§	
Defendant.	§	

MEMORANDUM OPINION AND ORDER

Before the Court are various pretrial motions filed by plaintiffs Pernix Ireland Pain DAC and Pernix Therapeutics (collectively, "Pernix") and defendant Alvogen Malta Operations Ltd. ("Alvogen"). The motions include Defendant Alvogen Malta Operations Ltd.'s Motion for Summary Judgment of Invalidity Under 35 U.S.C. § 101, Dkt. No. 111; Plaintiffs' Motion for Summary Judgment of No Invalidity Under 35 U.S.C. § 101, Dkt. No. 114; Defendant Alvogen Malta Operations Ltd.'s Motion for Summary Judgment of Invalidity by Anticipation, Dkt. No. 115; Plaintiffs' Motion for Summary Judgment of Infringement, Dkt. No. 118; and Alvogen Malta Operations Ltd.'s Motion To Strike and Exclude Pernix's Late-Disclosed Infringement Theory, Dkt. No. 125. The Court heard argument on the motions on May 11, 2018. Alvogen's motion for summary judgment of invalidity under section 101 is DENIED, and Pernix's motion for summary judgment of no invalidity under section 101 is GRANTED. Alvogen's motion for summary judgment of invalidity by anticipation is DENIED. Pernix's motion for summary judgment of infringement is DENIED. Alvogen's motion to strike Pernix's late-disclosed infringement theory is GRANTED.

BACKGROUND

In this Hatch-Waxman Act lawsuit arising under 35 U.S.C. § 271(e)(2)(A), Pernix has accused Alvogen of patent infringement. Pernix's claims of infringement are based on Alvogen's filing of its Abbreviated New Drug Application ("ANDA") with the United States Food and Drug Administration ("FDA"), seeking authorization to sell hydrocodone bitartrate extended release capsules as generic versions of Pernix's hydrocodone formulation, which is sold under the name Zohydro.

For purposes of the trial in this case, Pernix has asserted nine claims from two of the patents that protect Pernix's Zohydro product. The asserted claims are claims 1–4, 11, 12, 17, and 19 of Pernix's U.S. Patent No. 9,265,760 ("the '760 patent"), and claim 1 of Pernix's U.S. Patent No. 9,339,499 ("the '499 patent"). Pernix's patents are directed to methods of treating pain in patients with hepatic impairment, i.e. comprised liver function. The patents explain that the liver is responsible for most of the body's capacity to metabolize opioids. Because of the importance of the liver in clearing opioids from the body, patients with hepatic impairment who take opioids for pain relief are often prescribed reduced dosages of the drugs so as to avoid an unsafe build-up of the opioids in the patients' systems. See '760 patent, col. 2, ll. 41–66.

The patented invention encompasses formulations of extended release hydrocodone that have release profiles that are similar for both healthy and hepatically impaired patients. For that reason, the starting dose does not need to be adjusted for a patient with hepatic impairment relative to one without hepatic impairment.

All nine of the claims asserted in this case recite a "method of treating pain in a patient having mild or moderate hepatic impairment," and all nine include the step of "administering to the patient having mild or moderate hepatic impairment an oral dosage unit having hydrocodone

bitartrate as the only active ingredient, wherein the dosage unit comprises an extended release formulation of hydrocodone bitartrate."

While the claims generally cover the same subject matter, they differ in a few respects, and can be separated into three groups. First, in addition to the "administering" step, claim 1 of the '760 patent includes the limitation "wherein the starting dose is not adjusted relative to a patient without hepatic impairment." Second, claims 2–4 and 11 of the '760 patent all depend on claim 1, and each of those dependent claims recites different components of the release profile, i.e., the way a patient's body breaks down the drug, as measured by the maximum concentration of drug in the patient's blood (C_{max}) and the measure of total exposure of the drug over time ($AUC_{0-inf.}$). Specifically, each claim adds that the dosage unit does not result in increasing the maximum or total exposure of hydrocodone in subjects with mild or moderate hepatic impairment by more than a certain amount relative to subjects not suffering from mild or moderate hepatic impairment. Finally, claims 12, 17, and 19 of the '760 patent, and claim 1 of the '499 patent, are likewise directed to methods of treating pain in a patient having mild or moderate hepatic impairment. Each of those claims includes limitations regarding the release profile of the dosing unit, but that group of claims does not include or incorporate a limitation that the starting dose is not adjusted relative to a patient without hepatic impairment.

DISCUSSION

I. Alvogen's Motion to Strike

Alvogen's motion to strike is addressed to only the first two sets of claims—claims 1–4 and 11 of the '760 patent. Alvogen contends that in Pernix's recently filed motion for summary judgment of infringement, Pernix added a theory of infringement that was not disclosed in its amended infringement contentions or discussed in the report of its infringement expert. Pernix's

new theory, according to Alvogen, is that a patient can directly infringe claims 1–4 and 11 of the '760 patent acting alone, and that it is not necessary for Pernix to show joint infringement by both the prescribing physician and the patient in order to prove direct infringement of those claims. Pernix contends that in addition to its theory of joint infringement by the physician and patient, it has consistently asserted the theory that the patient can infringe alone—without the need for joint action by the physician—since the outset of the case and that it should not be foreclosed from presenting that theory at trial.

A. Pernix's Theories of Direct Infringement

The two theories of direct infringement of claims 1–4 and 11 of the '760 patent on which Pernix seeks to rely are: (1) joint direct infringement by the physician and the patient; and (2) single-party direct infringement by the patient alone. Under the theory of joint direct infringement, Pernix contends that the physician and the patient jointly infringe claims 1–4 and 11 when the physician prescribes and directs a hepatically impaired patient to take extended release hydrocodone bitartrate, in which the starting dose is not adjusted relative to a patient without hepatic impairment, and the patient takes the drug as directed. Under the theory of single-party direct infringement, Pernix contends that the patient alone, when taking the unadjusted dose of hydrocodone bitartrate, directly infringes those claims.

Pernix did not explicitly spell out any theory of infringement in the complaint. The complaint, however, referred to direct infringement by "physicians, health care providers, and/or patients," and thus was broad enough to encompass both the joint-infringement and the patient-alone theories of direct infringement. See Second Am. Compl., Dkt. No. 37, ¶ 40; id. ¶ 41 ("On information and belief, Alvogen specifically intends that physicians, health care providers, and/or patients will use the Alvogen Generic Product in accordance with the instructions

provided by Alvogen to directly infringe one or more claims of the '760 [patent]"); id. ¶ 48 ("The use of the Alvogen Generic Product by physicians, health care providers, and/or patients prior to patent expiry will directly infringe one or more claims of the '760 patent.").

In its initial infringement claim charts, Pernix made clear that its theory of liability was based on induced infringement. However, Pernix did not explicitly state whether the direct infringement necessary to establish liability for induced infringement was the product of direct infringement by the patient alone or joint infringement by the patient and the prescribing physician. Instead, Pernix's infringement contentions focused on Alvogen's acts of inducement; Pernix asserted that "Alvogen's Draft Label provides instructions for administering its proposed generic product to treat pain in patients having mild or moderate hepatic impairment." Dkt. No. 125-2, Ex. A, at 1. As to the requirement that the "starting dose is not adjusted relative to a patient without hepatic impairment," the infringement contentions stated: "Alvogen's Draft Label instructs physicians that the starting dose of Alvogen's proposed generic product is not adjusted for patients with mild or moderate hepatic impairment relative to a patient without hepatic impairment." Id.

During the claim construction process, the parties focused on two phrases from the claims: "administering to the patient" and "wherein the starting dose is not adjusted relative to a patient without hepatic impairment." Pernix argued that "administering" meant "prescribing, dispensing, giving or taking (such that what is prescribed, dispensed, given or taken is actually taken into the patient's body." See The Parties' Revised Final Joint Claim Chart, Dkt. No. 58-1, at 1. Pernix argued that the "wherein the starting dose is not adjusted" phrase was a limitation that meant "the dose prescribed to a patient with mild or moderate hepatic impairment when

initiating treatment is not reduced due to that hepatic impairment relative to the dose prescribed to a patient without hepatic impairment when initiating treatment." Id. at 2.

In both the briefing and the argument on the claim construction dispute, Pernix made clear that it construed the "wherein the starting dose is not adjusted" limitation to be directed to the actions of the prescribing physician. For example, in its answering claim construction brief, Pernix wrote that the disputed phrase "is a step that is integral to the claimed method and its infringement, requiring action to be taken by the physician, namely administering (prescribing) the same starting dose of drug to a hepatically impaired patient that would be administered to one that is not impaired." Dkt. No. 65, at 2. Similarly, in the claim construction oral argument before Judge Sleet, Pernix contended that the "wherein the starting dose is not adjusted" limitation "tells a physician how to dose the drug." Dkt. No. 68, at 5:24–25; see also id. at 13:10–14 ("'[W]herein the starting dose is not adjusted relative to a patient without hepatic impairment' tells the physician to give the same dose to a hepatically impaired patient that would be given to an unimpaired person."); id. at 14:12–14 ("[T]his language is the only language in the claim that tells the physician what to do and tells an accused infringer why they infringe.").

Judge Sleet issued a claim construction order construing the two disputed terms on August 3, 2017. Dkt. No. 69. First, he construed the term "administering" to mean "delivering into the body." Id. at 1. When adopting that construction, he rejected Pernix's argument that "administering" should include the acts of prescribing or dispensing (by a physician or health care provider). Second, he construed the phrase "starting dose is not adjusted relative to a patient without hepatic impairment" to mean that "the dose prescribed to a patient with mild or moderate hepatic impairment when initiating treatment is not reduced due to that hepatic impairment relative to the dose prescribed to a patient without hepatic impairment when initiating treatment."

Id. at 2. In so doing, Judge Sleet adopted Pernix's proposed construction of that term. He also agreed with Pernix's position that the "starting dose is not adjusted" phrase is a limitation of the claim. Id. at 2 n.2.

Following the claim construction order, Pernix served an amended infringement claim chart for claims 1–4 and 11 of the '760 patent. Dkt. No. 125-3, at 1–2. The only change made in the new infringement contentions for those claims was the addition of the following language for both the "administering" and "starting dose is not adjusted" limitations: "Physicians direct and/or control their patients' administration of a starting dose of Alvogen's proposed generic product in such a manner as to condition the receipt of treatment on the patient's administration of the prescribed starting dose. Further, the physician establishes the manner and timing of the patients' administration of the starting dose." Id., Ex. A, at 1–2.

When it filed its brief in support of its motion for summary judgment of infringement in March 2018, Pernix stated for the first time that it intended to prove the direct infringement component of induced infringement either by showing direct infringement by the patient alone or by showing joint direct infringement by the patient and the prescribing physician. Dkt. No. 120. Alvogen immediately protested by filing the present motion to strike and exclude Pernix's theory that direct infringement could be shown by proof of direct infringement by the patient alone. Dkt. No. 125.

In its motion, Alvogen argues that the amended infringement contentions effectively abandoned that theory of direct infringement and that it was too late for Pernix to attempt to revive it. Pernix responds that it never withdrew the theory of patient-only direct infringement, because it never withdrew any of the language of its original infringement contentions. Instead, Pernix contends that it merely added new language to the infringement contentions after Judge

Sleet's claim construction order and thus preserved both the "patient-only" theory of direct infringement and the "patient-physician" theory of joint direct infringement. Dkt. No. 148, at 4–6.

B. Pernix Has Not Preserved a "Patient-Only" Theory of Direct Infringement

The Court agrees with Alvogen that Pernix may not pursue its patient-only theory of direct infringement. Until Pernix filed its summary judgment motion in March of this year, Pernix's position as to infringement of claims 1–4 and 11 of the '760 patent was based on a theory of joint direct infringement by both the patient and the physician. Pernix's amended infringement contentions contained no reference to the patient-only theory of direct infringement. Instead, the amended contentions focused on the role of the physician in the alleged direct infringement; thus, joint infringement was the only theory of direct infringement set forth in the amended infringement contentions.

Similarly, the arguments made by Pernix's counsel during the claim construction process make quite clear that Pernix's theory of direct infringement contemplated that the physician would be the person who would be responsible for determining that the "starting dose is not adjusted relative to a patient without hepatic impairment." See Dkt. No. 65, at 2 (The language of the "starting dose is not adjusted" limitation requires "action to be taken by the physician," i.e., prescribing "the same starting dose of drug to a hepatically impaired patient that would be administered to one that is not impaired.").

The absence of any reference to the patient-only theory of direct infringement in the report of Dr. Gudin, Pernix's infringement expert, is particularly telling. In the portions of his report directed to the issue of direct infringement, Dr. Gudin repeatedly emphasized that the physician "will direct a patient with mild or moderate hepatic impairment to take the same

starting dose . . . as a patient without hepatic impairment," and that "the dosage form will be self-administered by the patient as directed by the physician." Dkt. No. 125-4 ¶ 69; see also id. ¶ 70 ("[A] physician following the Alvogen Draft Label does treat patients, and it is the physician who determines the starting dose to be given, and the physician who controls the dose that the patient will receive through writing a prescription for a particular dosage strength."); id. ¶ 73 ("[W]hen a physician directs a patient with mild or moderate hepatic impairment to take a particular dose of the Alvogen Proposed ANDA Product, and the patient takes that dose, the physician and patient jointly practice the claimed method."); id. ¶ 77 ("When a physician directs a patient with mild or moderate hepatic impairment to take a particular dose of the Alvogen Proposed ANDA Product, and the patient takes that dose, the physician and patient jointly practice 'a method of treating pain in a patient having mild or moderate hepatic impairment.'"); id. ¶ 83 ("In summary, all of the elements of claim 1 of the '760 Patent are met when physicians direct patients with mild or moderate hepatic impairment to self-administer Alvogen's Proposed ANDA Product according to the instructions in the Alvogen Draft Label, and patients self-administer the Alvogen Proposed ANDA Product according to the physician's instructions.").

Pernix asserts that Dr. Gudin's report contains references to the patient-only theory of direct infringement, but the citations to the report on which Pernix relies do not support that assertion. Dkt. No. 148, at 5–6. Pernix first cites a section of Dr. Gudin's report in which he summarized general legal principles as he understood them. He stated that "I further understand from counsel that if no single actor performs all steps of the method of treatment claims (e.g., a physician determines the dose to be administered, but the patient self-administers the drug), direct infringement occurs if the acts of one actor are attributable to the other." Dkt. No. 125-4 ¶ 49. Contrary to Pernix's argument, that general statement of law does not constitute a

contention that in this case the patient alone is directly infringing the relevant '760 patent claims. In fact, later in that same paragraph, Dr. Gudin made clear that the application of the general principles he recited was to joint direct infringement by the physician and the patient. He wrote: "As discussed in further detail below, for the claims of the Patents-in-Suit, the patient's receipt of the prescribed dose of drug (through the doctor's prescription) is conditioned upon the understanding that the patient will use the drug as directed, and it is the physician who dictates the manner and timing of the patient's self-administration of the drug." Id.

Pernix also cites a portion of Dr. Gudin's report in which he stated that he understood Alvogen's argument to be that it does not infringe the claims of the '760 patent because different actors perform the separate steps of selecting a starting dose and administering the drug. Id. ¶ 72. Dr. Gudin's answer to that contention is telling. He did not respond by saying that the patient infringes through his conduct alone, but instead stated that Alvogen's argument ignores that "when a physician directs a patient with mild or moderate hepatic impairment to take a particular dose of the Alvogen Proposed ANDA Product, and the patient takes that dose, the physician and patient jointly practice the claimed method." Id. ¶ 73. It is thus clear that, as of the time that it submitted its amended infringement contentions and Dr. Gudin's expert report, Pernix was not pursuing a patient-only theory of direct infringement, even as an alternative to the joint direct infringement theory.

C. Pernix's Failure to Raise Its Patient-Only Theory is Not Excused

Pernix's final argument is that, even if it did not present a patient-only direct infringement theory in its amended infringement contentions and in Dr. Gudin's expert report, it should be permitted to raise that theory now, even though discovery in the case is closed, expert reports and depositions have been completed, and trial is only a month away. In so arguing,

Pernix relies on a line of cases holding that a sanction such as excluding a theory of infringement is an extreme sanction that should not lightly be imposed, and that the following factors should be considered in determining whether to bar a party from asserting a belatedly presented theory: (1) prejudice or surprise to the objecting party; (2) the ability of that party to cure the surprise; (3) whether the default would disrupt the orderly and efficient presentation of the case; and (4) bad faith or willfulness on the part of the defaulting party. Dkt. No. 148, at 3 (quoting Meyers v. Pennypack Woods Home Ownership Ass'n, 559 F.2d 894, 904–05 (3d Cir. 1977)); see also id. at 6–11.

The first answer to Pernix's argument is that, quite apart from any default on Pernix's part, the claim language does not support a patient-only theory of direct infringement. Relying on the recent opinion from this district in Orexigen Therapeutics, Inc. v. Actavis Laboratories FL, Inc., 282 F. Supp. 3d 793 (D. Del. 2017), Pernix contends that although the "wherein the starting dose is not adjusted" phrase is a limitation of claims 1–4 and 11 of the '760 patent, it merely states a background condition for the administration of the hydrocodone composition, and that identifying the starting dose "is a predicate to performing the claimed administering step, which is performed by the patient." Dkt. No. 120, at 13; see also id. ("While a physician must determine and prescribe the dose of the drug product before a patient can administer it, as in Orexigen, that action will already have been completed prior to performance of the claimed method (i.e., prior to the patient 'administering' the drug product).").

That argument goes nowhere. It is certainly true that the physician must make a determination regarding the dose that the patient should take before the patient performs the administration step. But it is commonplace for the steps in a method claim to have to be performed in a particular order in order for the method to work as intended. If the phrase

"starting dose is not adjusted relative to a patient without hepatic impairment" had been drafted to read "the prescribing physician does not adjust the starting dose relative to a patient without hepatic impairment," there would be no question that infringement would require joint action by the physician and the patient. The fact that the claim limitation calls upon the physician to refrain from doing something (not adjusting the dosage limitation) instead of affirmatively doing something (such as directing that the dosage be cut in half for hepatically impaired patients) does not alter the fact that action by the physician is required to infringe the claim. The step is simply written in the passive voice in order not to limit the identity of the party that determines that an unadjusted dose should be given to the patient with hepatic impairment.

The Orexigen case on which Pernix relies is inapplicable. In that case, the pertinent claim language referred to administering a compound to a person "who has been diagnosed as suffering from overweight or obesity." 282 F. Supp. 3d at 812. Judge Andrews found that the claims containing that language involved "the single step of administering the drug to a patient who has already been diagnosed," and that the diagnosis was not a step of the claimed methods. Id. In this case, by contrast, the step of not adjusting the starting dose relative to a patient without hepatic impairment is properly characterized as both a limitation and a step of the methods recited in the asserted claims.

Even setting aside the legal flaw in Pernix's patient-only direct infringement theory, the Court would reject Pernix's argument that it should be allowed, at this late juncture, to present a new patient-only theory of direct infringement. In light of Pernix's consistent reliance on the theory joint direct infringement by patient and physician, and in particular in light of Pernix's expert's failure to present a theory of patient-only direct infringement, it would be unfair to require Alvogen to respond to that theory at trial. Alvogen's expert did not address that theory,

and Alvogen (understandably) did not conduct discovery directed at that theory, which it otherwise could have done, such as by examining Pernix's expert on that issue and having its own expert address the issue.

Pernix argues that it is inconsequential that Alvogen's expert has not had the opportunity to address the patient-only theory of direct infringement, since that theory raises only an issue of law. As Alvogen points out, however, there are important factual components to that theory that Alvogen might well have wanted its expert to address, such as whether the patient ever sets the dose amount when taking a drug such as extended release hydrocodone and whether Alvogen's Draft Label for its proposed ANDA product encourages the patient—as opposed to the physician—to carry out the dosing step of the asserted claims.

The need for additional discovery, including in all likelihood a supplemental report from Alvogen's infringement expert, would be burdensome to Alvogen and would potentially disrupt the trial schedule. While Alvogen could likely do the work necessary to prepare a supplemental report and conduct whatever further investigation and discovery would be necessary to prepare for the patient-only theory of direct infringement, it would be able to do so only by diverting resources from trial preparation at a critical point in the pretrial process. The Court accordingly finds that allowing Pernix to raise the patient-only theory belatedly would be prejudicial to Alvogen, would potentially disrupt the trial, and would be curable, if at all, only through the expenditure of time and resources by Alvogen that it should not have to bear at this point in the process. While the Court does not find bad faith or willful disregard of a court order by Pernix, the Court nonetheless regards the balance of factors as favoring Alvogen, particularly in light of the fact that Pernix will still be able to press its joint direct infringement theory, which has been its main theory of liability on claims 1–4 and 11 of the '760 patent since the outset of the case.

Alvogen's motion to strike Pernix's late-disclosed patient-only infringement theory as to infringement of claims 1–4 and 11 of the '760 patent, Dkt. No. 125, is therefore GRANTED.

II. Pernix's Motion for Summary Judgment of Infringement

Pernix has moved for summary judgment of infringement on both the first and second sets of claims that are at issue in this case. Dkt. No. 118. Pernix argues that Alvogen is liable for infringement under 35 U.S.C. § 271(e)(2)(A) on the ground that Alvogen has submitted an application to the FDA for a drug the use of which is claimed in a patent.

In order to prove that Alvogen will be liable for induced infringement, Pernix must show that Alvogen will induce a party or parties to directly infringe the asserted claims. Limelight Networks, Inc. v. Akamai Techs., Inc., 134 S. Ct. 2111, 2117 (2014); Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd., 887 F.3d 1117 (Fed. Cir. 2018). To make that showing, Pernix must prove that Alvogen will possess "specific intent to encourage another's infringement and not merely that the defendant [will have] knowledge of the acts alleged to constitute infringement." Vanda, 887 F.3d at 1129 (quoting DSU Med. Corp. v. JMS Co., 471 F.3d 1293, 1306 (Fed. Cir. 2006) (en banc in relevant part)).

In order to prove the direct infringement of a method claim that is a necessary component of an inducement case, the plaintiff must show that all steps of the claimed method have been (or, in the Hatch-Waxman context, will be) performed by or attributable to a single entity. Akamai Techs., Inc. v. Limelight Networks, Inc., 797 F.3d 1020, 1022 (Fed. Cir. 2015) (en banc). Where no single actor performs all the steps of a method claim, joint direct infringement occurs if "the acts of one are attributable to the other such that a single entity is responsible for the infringement." Eli Lilly & Co. v. Teva Parenteral Meds., Inc., 845 F.3d 1357, 1364 (Fed. Cir. 2017) (quoting Akamai, 797 F.3d at 1022). In that setting, the plaintiff must show either

that the parties are (or will be) engaged in a joint enterprise or that one party directed and controlled the infringing activity of the other (or will do so). Id. To show that one party directed and controlled the infringing activity of another, the plaintiff must prove that the alleged infringer "conditions participation in an activity or receipt of a benefit upon performance of a step or steps of a patented method and establishes the manner or timing of that performance." Akamai, 797 F.3d at 1023.

As to the first two sets of claims (claims 1–4 and 11 of the '760 patent), Pernix argues that Alvogen's application will result in infringement based on the following analysis: First, Pernix argues that there is no genuine dispute that patients and physicians will act as a single entity in directly infringing those claims.[1] Second, Pernix argues that Alvogen will be liable for induced infringement because, if the ANDA product becomes commercially available, Alvogen will induce patients and physicians to engage in direct infringement, with the specific intent to do so. As to the final set of claims (claims 12, 17, and 19 of the '760 patent and claim 1 of the '499 patent), Pernix argues that there is no genuine dispute that (1) patients will directly infringe those claims when they self-administer the drug; and (2) Alvogen will induce the patients to infringe those claims with the specific intent to do so.

A. Claims 1–4 and 11 of the '760 Patent

1. Joint Direct Infringement

In the case of the relationship between a physician and a patient, joint direct infringement of a claimed method occurs if the physician "directs or controls" the patient so that the patient's acts are attributable to the physician. Eli Lilly, 845 F.3d at 1364. The Federal Circuit explained in Eli Lilly & Co. v. Parenteral Medicines, Inc., that the requisite degree of direction and control

[1] The Court does not discuss Pernix's struck patient-only theory of direct infringement.

occurs if the physician "conditions participation in an activity or receipt of a benefit" on the patient's performance of one or more steps of the claimed method, and the physician "establishes the manner or timing of that performance." Id. (emphasis omitted) (quoting Akamai, 797 F.3d at 1023).

Pernix's theory of joint direct infringement is based on the assertion that the prescribing physician will direct and control the patient's self-administration of the accused product. The showing of joint direct infringement is made more difficult in a typical Hatch-Waxman Act case such as this one, where the ANDA product is not yet on the market and where the determination of joint direct infringement is necessarily predicated not on the past conduct of physicians and patients, but on whether physicians are likely to direct patients to engage in infringing conduct and whether the physicians' directions to the patients are sufficient to direct or control the patients' infringing conduct.

Pernix argues that there is no disputed factual question regarding the physician's control and direction of the infringing actions of a patient when the physician prescribes an unadjusted starting dose of Alvogen's hydrocodone extended release composition to a patient with mild or moderate hepatic impairment. As support for that contention, Pernix relies on the proposed label for Alvogen's ANDA product ("Alvogen's Label"); on testimony from Alvogen's infringement expert; and on consent forms that are used in some instances to ensure that patients will administer opioid medications as prescribed. Dkt. No. 120, at 13–15.

Pernix points out that Alvogen's Label directs physicians to "[i]nstruct patients how to properly take Hydrocodone Bitartrate Extended Release Capsules." Dkt. No. 121-1, Ex. C, at Alvhydro-PTX00013463. The Label also directs patients, when taking the capsules, to "[t]ake

Hydrocodone Bitartrate Extended Release Capsules exactly as prescribed by your healthcare provider." Id. at Alvhydro-PTX00013465.

Pernix also notes that Alvogen's infringement expert, Dr. Candiotti, testified that physicians "give instruction and guidance as to when to take the medication and how to take it." Dkt. No. 121-1, Ex. F, at 158:15–17. Dr. Candiotti further acknowledged that some physicians use a consent form when prescribing opioid drugs. On one such form, offered as evidence in support of Pernix's motion, the patient is asked to state "I will take these medications only as prescribed and will not change the amount or dosing frequency without authorization from my physician," and that "I understand and agree that failure to adhere to these policies will be considered noncompliance and my result in the cessation of opioid prescribing by my physician and possible dismissal from this clinic." Id. at 139:15–141:13.

In its response, Alvogen argues that Pernix's evidence does not show that physicians will necessarily control and direct patients in taking the extended release hydrocodone composition because there is no evidence that physicians will "condition" continued treatment on the patient's administering Alvogen's ANDA product as prescribed. See Akamai, 797 F.3d at 1023. In addition, Alvogen argues that physicians typically have no means of verifying that patients are adhering to the physicians' directives regarding patient adherence to the prescribing directions. Dkt. No. 143, at 9–13.

Although it is clear that a physician gives instructions to a patient as to dosing levels and practices, the extent to which those instructions constitute "direction and control" of the patient's infringing conduct turns on factual questions such as whether the physician conditions receipt of a benefit—continued treatment for chronic pain—on the patient's performance of the administering step, i.e., administering the drug as prescribed. In support of its assertion that the

facts are undisputed on that issue, Pernix cites the fact that because hydrocodone is a controlled substance, physicians enter into agreements with their patients requiring the patients to take the drug as prescribed by the physician, and thus exercise control and direction over the patient's conduct in that regard. In addition, relying on the deposition testimony of Alvogen's infringement expert, Pernix argues that physicians establish the timing and manner in which the patients administer the drug.

While Pernix's evidence could support a finding that physicians exercise direction and control over the self-administration of hydrocodone extended release formulations by patients, the evidence on that issue is not so compelling as to justify the entry of summary judgment in Pernix's favor. Rather, the Court concludes that the issue turns on disputed facts, the resolution of which must await trial.

2. Inducement of Infringement by Alvogen's Label

Because Pernix's theory of liability for Alvogen on all of the asserted claims depends on inducement of infringement, Pernix must prove not only the elements of direct infringement, but also the elements of inducement. Proof of induced infringement, for claims 1–4 and 11 of the '760 patent, requires Pernix to show that Alvogen's actions will induce joint direct infringement by physicians and patients and that Alvogen will engage in those actions with the specific intent to do so. See Eli Lilly, 845 F.3d at 1368; Takeda Pharm. USA, Inc. v. West-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015). In the context of patent infringement litigation involving pharmaceuticals, the Federal Circuit has held that "the sale of a product specifically labeled for use in a patented method constitutes inducement to infringe that patent." Eli Lilly & Co. v. Actavis Elizabeth LLC, 435 F. App'x 917, 926 (Fed. Cir. 2011).

In a Hatch-Waxman Act case where the act of infringement under section 271(e)(2)(A) consists of the filing of an ANDA for a method of treatment protected by a patent, "[t]he pertinent question is whether the proposed label [of the ANDA product] instructs users to perform the patented method." AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1060 (Fed. Cir. 2010). In that setting, the Federal Circuit has explained, "[t]he label must encourage, recommend, or promote infringement." Takeda, 785 F.3d at 631. Evidence that a proposed label will "inevitably lead some consumers to practice the claimed method" can suffice to support a finding of specific intent to induce infringement. AstraZeneca, 633 F.3d at 1060; Novartis Pharm. Corp. v. Breckenridge Pharm., Inc., 248 F. Supp. 3d 578, 585 (D. Del. 2017). Put another way, the question is whether the instructions in the label "teach an infringing use . . . such that we are willing to infer from those instructions an affirmative intent to infringe the patent." Takeda, 785 F.3d at 631 (emphasis omitted); Rhodes Pharm. L.P. v. Indivior, Inc., No. 16-cv-1308, 2018 WL 326405, at *7 (D. Del. Jan. 8, 2018).

Pernix relies on Alvogen's Label and testimony by Alvogen's expert, Dr. Candiotti, to support its contention that there is no disputed question of fact regarding the issue of inducement. Pernix quotes the Alvogen Label, which states: "No adjustment in starting dose . . . is required in patients with mild or moderate hepatic impairment." Dkt. No. 121-1, Ex. C, at Alvhydro-PTX00013439, 13445, 13455. The label further directs the patient as follows: "Take . . . exactly as prescribed by your healthcare provider." Id. at Alvhydro-PTX00013465. And Pernix cites Alvogen's expert, who testified that the Alvogen Label constitutes a "dosing recommendation" that "tells you how to dose" Alvogen's ANDA product in patients with mild or moderate hepatic impairment. Id., Ex. F, at 174:4–9.

For its part, Alvogen argues that its Label does not encourage, recommend, or promote administering Alvogen's ANDA product to parties with mild or moderate hepatic impairment, nor does it encourage prescribing the ANDA product to patients with mild or moderate hepatic impairment without adjusting the starting dose relative to the dosage prescribed to a normal patient. Inferring specific intent to induce infringement from a pharmaceutical label, Alvogen argues, requires recommending, encouraging, or promoting an infringing use, not merely describing an infringing mode as a possible alternative. Alvogen contends that the portions of its Label to which Pernix points merely describe the effects of Alvogen's ANDA product on patients with mild or moderate hepatic impairment and do not do not encourage, recommend, or promote the use of the claimed methods in treating such patients.

Alvogen distinguishes the Eli Lilly case on which Pernix relies on the ground that in that case the ANDA label "provided direct and fervent instructions for patients to perform the claim step of administering folic acid," Dkt. No. 143, at 18, which was essential to the safe use of the chemotherapy procedure in which the folic acid was involved. By contrast, Alvogen argues, Alvogen's label merely "describes" the use of the product in patients with hepatic impairment, and therefore does not reflect "an affirmative intent to infringe the patent." Id. (quoting Eli Lilly, 845 F.3d at 1368). Nor, according to Alvogen, does the Alvogen label recommend, promote, or encourage the non-adjustment of the starting dose for patients with hepatic impairment. Alvogen contends that the label merely "informs physicians that they may or may not adjust the starting dose in patients with mild or moderate hepatic impairment." Id. at 19.

The Court concludes that this issue presents an issue of fact for trial and cannot be resolved on summary judgment. Alvogen's expert testified that the Alvogen Label gives "instruction and guidance" as to the dosing for patients with hepatic impairment, but stopped

short of saying that the Label would give directions to the physician. See Dkt. No. 121-1, Ex. F, at 172:6–19. In the absence of more unequivocal evidence on the issue of specific intent and inducement, the Court regards the matter as inappropriate for summary judgment.

B. Claims 12, 17, and 19 of the '760 Patent and Claim 1 of the '499 Patent

In order to prove that Alvogen's ANDA product will infringe claims 12, 17, and 19 of the '760 patent and claim 1 of the '499 patent, Pernix must show that Alvogen will induce infringement by patients with mild or moderate hepatic impairment to administer an extended release hydrocodone formulation having a release profile that satisfies the release profile limitations of those claims. Unlike for claims 1–4 and 11 of the '760 patent, Pernix is not required to show joint direct infringement by the patient and a physician, but only need prove inducement of direct infringement by the patient.

Moreover, the proof of inducement required to show induced infringement of claims 12, 17, and 19 of the '760 patent and claim 1 of the '499 patent is less demanding than the proof required to show induced infringement of claims 1–4 and 11 of the '760 patent. While claims 1–4 and 11 of the '760 patent require proof that Alvogen's Label induces physicians to direct and patients to administer an unadjusted starting dose of an extended release formulation of hydrocodone, claims 12, 17, and 19 of the '760 patent and claim 1 of the '499 patent do not require a showing of inducement to administer an unadjusted starting dose. Instead, the latter claims only require inducement to treat pain in a patient with mild or moderate hepatic impairment by administering an oral dosage unit having hydrocodone bitartrate as the only active ingredient, where the dosage unit results in a particular pharmacokinetic release profile in the relevant patient population.

Nonetheless, Pernix must demonstrate that Alvogen's Label will induce hepatically impaired patients to use Alvogen's ANDA product for the treatment of pain. That issue raises a question of fact: whether the Alvogen Label would encourage a patient with mild or moderate hepatic impairment to use Alvogen's ANDA product to inhibit pain.

In an effort to show that the factual issue of inducement could not reasonably be decided in Alvogen's favor, Pernix cites portions of Alvogen's Label as well as excerpts from the report and deposition of Alvogen's infringement expert, Dr. Candiotti. In particular, Pernix contrasts the portions of Alvogen's Label that refer to patients with mild or moderate hepatic impairment with the portions addressing severe impairment. The "Dosage and Administration" section of the Label provides, in pertinent part, as follows: "Patients with Severe Hepatic Impairment: Initiate dosing with 10 mg every 12 hours and titrate carefully, while monitoring for respiratory depression. No adjustment in starting dose with Hydrocodone Bitartrate Extended Release Capsules is required in patients with mild or moderate hepatic impairment." Dkt. No. 121-1, Ex. C, at Alvhydro-PTX00013439.

Similarly, a section of the Label entitled "Dosage Modification in Patients with Severe Hepatic Impairment," provides: "Patients with severe hepatic impairment may have higher plasma concentrations of hydrocodone than those with normal function. Therefore, initiate therapy with 10 mg every 12 hours and titrate carefully, while monitoring for respiratory depression, sedation, and hypotension. No adjustment in starting dose with Hydrocodone Bitartrate Extended Release Capsules is required in patients with mild or moderate hepatic impairment." Id. at Alvhydro-PTX00013445. Finally, a section of the Label entitled "Hepatic Impairment" provides: "No adjustment in starting dose with Hydrocodone Bitartrate Extended Release Capsules is required in patients with mild or moderate hepatic impairment. Patients with

severe hepatic impairment may have higher plasma concentrations than those with normal hepatic function . . . . Therefore, a dosage reduction is recommended for patients with severe hepatic impairment . . . . Monitor patients with severe hepatic impairment closely for respiratory depression, sedation and hypotension . . . ." Id. at Alvhydro-PTX00013455.

Pernix also relies on the general statement in the "Medication Guide" section of Alvogen's Label that directs patients as follows: "Do not change your dose. Take Hydrocodone Bitartrate Extended Release Capsules exactly as prescribed by your healthcare provider." Id. at Alvhydro-PTX00013465. To the same effect, Pernix notes that Dr. Candiotti admitted that the medication guides in Alvogen's Label are Alvogen's "instructions to the patient," in which Alvogen "is saying, 'Do not change your dose. Take the medication exactly as prescribed by your health care provider.'" Dkt. 121-1, Ex. F, at 71:17–72:7. Dr. Candiotti acknowledged that the Label gives "direction to not change your dose and to take the pills exactly as prescribed." Id. at 146:5–6.

Alvogen argues that Pernix's evidence does not justify entry of an order of summary judgment on claims 12, 17, and 19 of the '760 patent and claim 1 of the '499 patent. With respect to the references to hepatic impairment in Alvogen's Label, Alvogen points out that the Label contains explicit directions for patients with severe hepatic impairment (e.g., "Initiate dosing with 10 mg every 12 hours and titrate carefully, while monitoring for respiratory depression."), but does not use directory language when referring to patients with mild or moderate hepatic impairment (e.g., "No adjustment in starting dose with Hydrocodone Bitartrate Extended Release Capsules is required in patients with mild or moderate hepatic impairment."). With respect to Dr. Candiotti's testimony and the Medication Guide in Alvogen's Label, Alvogen explains that the statements on which Pernix relies simply advise the patient to comply

with the prescribing physician's directions, which does not constitute direct evidence of an intent by Alvogen to induce hepatically impaired patients to use Alvogen's ANDA product.

Alvogen contends that, at most, its Label and Dr. Candiotti's testimony indicate that Alvogen has not affirmatively sought to discourage such patients from using its ANDA product. Thus, rather than demonstrating intentional inducement, Alvogen argues that the statements in its Label on which Pernix relies merely describe an infringing mode without "recommending, encouraging, or promoting an infringing use, or suggesting that an infringing use should be performed." Takeda, 785 F.3d at 631 (citations, quotation marks, and alterations omitted).

Finally, citing Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1365 (Fed. Cir. 2003), and Vita-Mix Corp. v. Basic Holding, Inc., 581 F.3d 1317, 1329 (Fed. Cir. 2009), Alvogen notes that where, as here, a product has substantial non-infringing uses, intent to induce infringement cannot be inferred simply because the defendant is aware that some users of its product may be infringing the patent. Instead, in such a case, the plaintiff must "show[] statements or actions directed to promoting infringement." AstraZeneca, 633 F.3d at 1059 (quoting Ricoh Co. v. Quanta Computer Inc., 550 F.3d 1325, 1341 (Fed. Cir. 2008)).

As noted, the question whether the evidence of particular statements by an accused infringer evinces a specific intent to induce infringement is a question of fact. And on that factual issue, the reports of Pernix's expert, Dr. Gudin, and Alvogen's expert, Dr. Candiotti, are in conflict. Dr. Gudin states that in his view Alvogen's Label provides instructions to physicians regarding the use of Alvogen's ANDA product in the treatment of patients with mild or moderate hepatic impairment. Dkt. No. 144-2, ¶¶ 50–53. Dr. Candiotti, by contrast, views the pertinent portions of Alvogen's Label as not promoting, encouraging, or recommending that physicians prescribe Alvogen's ANDA product for patients with mild or moderate hepatic impairment, but

as merely responding to the FDA's guidance requiring a drug manufacturer to conduct a hepatic impairment study, and to report the results of that study on its label when hepatic metabolism has a substantial role in the elimination of the drug from the body. Dkt. No. 121-1, Ex. E, ¶¶ 67–68.

Given the conflict between the views taken by the two experts, the Court concludes that the inducement issue presents a disputed issue of fact. While a factual question can be resolved on summary judgment if a reasonable finder of fact could reach only one conclusion as to that question, the Court does not regard the evidence offered at this juncture as compelling such a conclusion on the issue of inducement as to claims 12, 17, and 19 of the '760 patent and claim 1 of the '499 patent. Moreover, the Court notes that the inducement question turns on an issue of specific intent and "[t]he issue of intent is particularly inappropriate for resolution by summary judgment because evaluating state of mind often requires the drawing of inferences from the conduct of parties about which reasonable persons might differ." Justofin v. Metro. Life Ins. Co., 372 F.3d 517, 524 (3d Cir. 2004) (quotation marks omitted); see also Sanofi v. Watson Labs. Inc., 875 F.3d 636, 644 (Fed. Cir. 2017) (stating, regarding induced infringement in a Hatch-Waxman Act case, that "intent is a factual determination that may rest on circumstantial evidence"); Impax Labs., Inc. v. Actavis Labs. FL, Inc., No. 15-cv-6934, 2018 WL 1863826, at *13 (D.N.J. Apr. 18, 2018) (same). Resolution of this issue will therefore have to await trial.[2]

[2] The fact that this is a summary judgment proceeding in a case that will be tried to the Court requires the Court to engage in a somewhat artificial exercise: for purposes of summary judgment, the Court is required to determine, drawing all reasonable inferences in Alvogen's favor, whether the evidence of inducement proffered during the summary judgment proceedings is sufficient to require a finding of inducement as a matter of law; whereas after trial, the Court will be required to determine whether the evidence of inducement offered at trial is sufficient to require a finding of inducement as a matter of fact. Given the different nature of the inquiry at those two procedural steps, and the different evidence that the Court is likely to have before it at each stage, the Court could well reach a different result on the factual issue following the trial.

Accordingly, Pernix's motion for summary judgment of infringement with respect to each of the asserted claims, Dkt. No. 118, is therefore DENIED.

III. Alvogen's Motion for Summary Judgment of Anticipation

Alvogen has moved for summary judgment of invalidity for anticipation under 35 U.S.C. § 102. In its motion, Alvogen relies on two prior art references, U.S. Patent Appl. No. 2006/0240105 ("Devane") and U.S. Patent No. 8,808,740 ("Huang").

A. Huang as Prior Art

The parties dispute whether Huang is prior art. In addition to raising that issue in its opposition to Alvogen's motion, Dkt. No. 141, at 27–28, Pernix has filed a motion in limine to preclude Alvogen from relying on Huang as prior art, Dkt. No. 137, and it has sought to exclude the testimony of one of Alvogen's experts on the ground that his opinion cites Huang as prior art, Dkt. No. 135, at 5–7. The Court concludes that factual disputes preclude a determination as a matter of law whether Huang is prior art. The Court therefore will not enter summary judgment of invalidity based on Huang.[3]

The patents-in-suit claim priority to, inter alia, U.S. Provisional Appl. No. 61/677,601, which was filed on July 31, 2012. The application for the Huang patent was filed on December 21, 2011. Because Huang predates the filing date of the provisional application for the patents in suit, Huang qualifies as prior art unless Pernix can show that the patents in suit are entitled to an earlier priority date. See Loral Fairchild Corp. v. Matsushita Elec. Indus. Co., 266 F.3d 1358,

[3] For the same reason, the Court has denied Pernix's motion in limine to preclude Alvogen from relying on Huang as prior art and Pernix's motion in limine to exclude the testimony of Alvogen's expert, Dr. Mayersohn, on the ground that his expert report treats Huang as prior art. The Court orally denied both of those motions on the record at the motions hearing held on May 11, 2018.

1361 (Fed. Cir. 2001) ("[The patentee] bear[s] a burden of production to present evidence of its asserted actual reduction to practice prior to the filing date of its patent application.").

In an effort to establish a priority date before the filing date for the Huang application, Pernix argues that the inventors of the '760 and '499 patents reduced the inventions of those patents to practice no later than November 2, 2011.[4] Dkt. No. 137, at 4–5. Specifically, Pernix relies on a draft of a clinical study report, dated November 2, 2011. That report included the results of testing that compared the pharmacokinetic profile of hydrocodone in normal individuals and in individuals suffering from mild or moderate hepatic impairment. See Dkt. No. 138-1, Ex. E, at 178. The draft report concluded that "subjects with mild or moderate hepatic impairment are likely to experience slightly higher hydrocodone exposure after administration of HC-CR, compared to subjects with no hepatic impairment. Overall, the increase in exposure is likely to be modest and would not warrant a priori dose adjustment in these populations." Id. at 117–18. The study described in the draft report was performed using "HC-CR 20 mg," id. at 117, which Pernix has confirmed was an extended release hydrocodone formulation that was previously disclosed in the prior art Devane application, see Dkt. No. 163-3, at 3–8.

In support of its argument that the inventors reduced their invention to practice by November 2, 2011, Pernix points to deposition testimony from two of the three inventors of the patents-in-suit. See Dkt. No. 138-1, Ex. G, at 142:13–148:21 (deposition of inventor Andrew Hartman, testifying that the invention of "using a controlled release formulation of hydrocodone

[4] Huang claims priority to U.S. Provisional Application No. 61/426,306, which was filed on December 22, 2010. Pernix argues that Huang is not entitled to that priority date, because Alvogen has not shown that the provisional application provides support for the claims in Huang in compliance with 35 U.S.C. § 112. Dkt. No. 137, at 3 (citing Dynamic Drinkware, LLC v. Nat'l Graphics, Inc., 800 F.3d 1375, 1381 (Fed. Cir. 2015)). For purposes of this motion, Alvogen has not argued that Huang is entitled to the filing date of its provisional application. Dkt. No. 164, at 4 n.3.

in which no adjustment to starting dose would be necessary for patients with mild or moderate hepatic impairment" was discovered "mid to late summer" of 2011, before the November 17, 2011 date of the final clinical study report); Dkt. No. 138-1, Ex. F, at 112:22–120:13 (deposition of inventor Christopher M. Rubino, discussing the draft study in general terms).

Reduction to practice is a legal issue based on underlying factual determinations. Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d 588, 592 (Fed. Cir. 1997). "To demonstrate an actual reduction to practice, the [patentee] must have: (1) constructed an embodiment or performed a process that met all the limitations of the claim and (2) determined that the invention would work for its intended purpose." Nintendo of Am. Inc. v. iLife Techs., Inc., 717 F. App'x 996, 1002 (Fed. Cir. 2017) (quoting In re Steed, 802 F.3d 1311, 1318 (Fed. Cir. 2015)); see also Estee Lauder, 129 F.3d at 593 ("It is well-settled that conception and reduction to practice cannot be established nunc pro tunc. There must be contemporaneous recognition and appreciation of the invention represented by the counts." (quoting Breen v. Henshaw, 472 F.2d 1398, 1401 (CCPA 1973))).

Alvogen makes two arguments about why Huang is prior art to the patents-in-suit, notwithstanding Pernix's arguments about the inventors' conception and reduction to practice. First, Alvogen argues that "Pernix's motion relies solely on the deposition testimony of one of the three named inventors, Andrew Hartman, to demonstrate that conception of the alleged invention predates Huang." Dkt. No. 164, at 3. Alvogen contends that "when a party seeks to prove conception via the oral testimony of a putative inventor, the party must proffer evidence corroborating that testimony." Id. (quoting Singh v. Brake, 317 F.3d 1334, 1340–41 (Fed. Cir. 2003)). That argument is unpersuasive. Pernix relies not only on the testimony of Mr. Hartman, but also on the draft study and the testimony of his co-inventor, Dr. Rubino. The Federal Circuit

has stated that "no similar condition of 'corroboration' is imposed on an inventor's notebook, or indeed any documentary or physical evidence, as a condition for its serving as evidence of reduction to practice," although an "unwitnessed notebook is insufficient on its own to support a claim of reduction to practice." Medichem, S.A. v. Rolabo, S.L., 437 F.3d 1157, 1169 (Fed. Cir. 2006); see also id. ("Once properly admitted into evidence, documentary and physical evidence is assigned probative value and collectively weighted to determine whether reduction to practice has been achieved."). Alvogen has not presented any countervailing evidence that calls into question the authenticity of the draft study report or the admissibility of the inventors' testimony.

Second, Alvogen argues that the inventors cannot antedate Huang unless "(1) the inventors appreciated that the species they reduced to practice included or pointed to the species disclosed in the prior art reference; or (2) the prior art species would have been an obvious variant of the species reduced to practice." Dkt. No. 164, at 4 (citing In re Clarke, 356 F.2d 987, 992–93 (CCPA 1966)). In Clarke, which was an appeal from an interference action before the Patent and Trademark Office ("PTO"), the applicant was seeking a patent on a genus of compounds and attempted to antedate an anticipatory reference that disclosed one species within that genus by demonstrating that the inventor had reduced a different species to practice.

The court rejected the applicant's argument. The court explained that in such a case, "antedating affidavits must contain facts showing a completion of 'the invention' commensurate with the extent the invention is shown in the reference, whether or not it be a showing of the identical disclosure of the reference." Id. at 992. That requirement was not satisfied in Clarke, the court held, because there was no evidence that either a person of ordinary skill in the art or the applicant would have considered that the prior art species "reasonably could be expected to have properties related to that found for the [applicant's] species, such that the [prior art] species

would be properly included within the invention." Id. at 993. The court therefore could not conclude from the evidence "that so much of the invention as encompasses the referenced species was in appellant's possession, and thereby reduced to practice prior to the effective date of the reference." Id.

Alvogen argues that this case is identical to Clarke. Alvogen contends that although the inventors discovered that Devane's formulation of extended release hydrocodone can be administered to hepatically impaired patients without adjusting the starting dose, the inventors did not appreciate, nor would it have been obvious, that the formulation disclosed in Huang would have the same property. In support of its position that the inventors did not appreciate that their discovery of the properties of the Devane formulation would apply to Huang's formulation, Alvogen cites testimony from two of the inventors that even as of the present day they do not know why Devane's formulation exhibits that unexpected result, as compared to other opioid products. See Dkt. No. 165-5, at 254:20–25 (deposition of Cynthia Robinson, "Q: Do you know what it is about the Zohydro formulation that resulted in the surprising result? . . . A: I honestly couldn't say."); Dkt. No. 165-6, at 167:24–168:5 (deposition of Andrew Hartman, "Q: . . . . Why do you believe the Zohydro product performed differently, in your view, than the other products that you—opioid products that you were referencing? . . . [A:] I don't know the answer to that question."); Dkt. No. 136-7, at 82:10–13 (deposition of Brooks Boyd, Rule 30(b)(6) designee for Zogenix, Inc., Pernix's predecessor: "Q: And are you aware of other—any other hydrocodone formulations that achieve the results of the hepatic impairment study? A: No.").

Although the Clarke decision is a half-century old, Clarke is still good law. See In re Mulder, 716 F.2d 1542, 1546 (Fed. Cir. 1983) (discussing and distinguishing Clarke); In re Schaub, 537 F.2d 509, 512 (CCPA 1976) (applying Clarke); Unified Patents Inc. v. Heslop, No.

IPR2016-01464, 2018 WL 801602, at *13 (PTAB Feb. 6, 2018) (citing Clarke in inter partes review proceeding); In the Matter of Certain Anti-Theft Deactivatable Resonant Tags & Components Thereof, Inv. No. 337-TA-347, USITC Pub. 2811, 1994 WL 931908 (Sept. 1, 1994) (citing Clarke). The PTO's Manual of Patent Examining Procedure ("MPEP") cites Clarke and instructs as follows:

> Proof of prior completion of a species different from the species of the reference or activity will be sufficient to overcome a reference indirectly under 37 CFR 1.131(a) if the species shown in the reference or activity would have been obvious in view of the species shown to have been made by the applicant. Alternatively, if the applicant cannot show possession of the species of the reference or activity in this manner, the applicant may be able to antedate the reference or activity indirectly by, for example, showing prior completion of one or more species, placing applicant in possession of the claimed genus prior to the reference's or activity's date. The test is whether the species completed by applicant prior to the reference date or the activity's date provided an adequate basis for inferring that the invention has generic applicability.

MPEP § 715.03 (9th ed., rev. Jan. 2018) (citations omitted).

Moreover, the rationale underlying Clarke is consistent with the reasoning of more recent Federal Circuit decisions. See Frazer v. Schlegel, 498 F.3d 1283, 1287 (Fed. Cir. 2007) ("[P]riority as to a genus may be indeed shown by prior invention of a single species . . . but the genus will not be patentable to an applicant unless he has generic support therefor" (quoting In re Zletz, 893 F.2d 319, 323 (Fed. Cir. 1989))); In re Rozmus, 928 F.2d 412, 1991 WL 17232, at *1 (Fed. Cir. 1991) ("In order to remove a reference, a Rule 131 declaration must show that prior to the effective date of the reference the applicant had reduced to practice so much of the claimed invention as the reference shows.").

Pernix responds that Clarke is inapplicable to the facts of this case, for several reasons. See Dkt. No. 185, at 1–2. First, Pernix suggests that Clarke should be limited to the interference context and applied only to "chemical Markush genus-species situations." Dkt. No. 185, at 1

(quoting Clarke, 356 F.2d at 990). However, Pernix gives no reasoned explanation why Clarke should be limited in that manner, nor does the Court perceive any. See, e.g. Alcon Research Ltd. v. Barr Labs., Inc., 745 F.3d 1180, 1190 (Fed. Cir. 2014) (in a Hatch-Waxman infringement action, applying Newman v. Quigg, 877 F.2d 1575 (Fed. Cir. 1989), a decision from an appeal from the U.S. Patent and Trademark Office).

Pernix next points to the fact that Alvogen expert Michael Mayersohn purportedly "admitted" that the claims do not recite a genus. Dkt. No. 187-1, at 133:24–134:4 ("Q. Do the asserted claims recite a genus? . . . A. No, I don't believe so."). Pernix's reliance on Dr. Mayersohn's testimony on this point is not persuasive. Dr. Mayersohn explained that "[t]he specifications cite a very specific narrow range of examples with overly broad claims. So the genus and the species associated with the genus, I believe, are not well defined." Id. at 133:18–22. More importantly, the fact that the claims encompass both Devane's and Huang's formulations is sufficient reason for Clarke to apply.

Finally, Pernix notes that Clarke instructs that "all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show." Dkt. No. 185, at 1 (quoting Clarke, 356 F.2d at 989). Under that standard, Pernix argues that Huang is not prior art because it does not show all of the following: a "patient having mild or moderate hepatic impairment"; "treating pain" in such a patient; administering to such a patient "a starting dose of an oral dosage unit . . . wherein the starting dose is not adjusted relative to a patient without hepatic impairment"; or any release profile data for hepatically impaired patients. Dkt. No. 185, at 2. However, Pernix has Clarke backwards: To antedate a reference, the patentee needs to show that the inventors possessed knowledge of the species contained in both the reference and the patent, not to show that the invention is broader than the reference. See

Clarke, 356 F.2d at 991 ("[I]t it is not the entire scope of the claims which is determinative of the issue here. Rather, it is how much the reference shows of the claimed invention that is crucial to the requirement of what the affidavit must show."); see also In re DaFano, 392 F.2d 280, 284 (CCPA 1968) ("[In Clarke, we] set forth, as a test for the adequacy of the affidavit, a standard of whether the showing would convince one of ordinary skill in the art to a reasonable certainty that the applicant possessed so much of the invention as to encompass the reference disclosure. . . . It is necessary that the species which were reduced to practice provide an adequate basis for inferring that the invention has generic applicability."). Pernix's argument that Huang does not disclose additional limitations in the patents-in-suit does not focus on the proper question under Clarke with respect to the factual issues of inherent anticipation or obviousness.

For these reasons, the Court finds that, in light of the analysis required by the decision in Clarke, there are disputes of fact that preclude a determination as to whether the inventors reduced the species disclosed in Huang to practice as of November 2, 2011, so as to preclude Huang from serving as prior art. Alvogen's motion for summary judgment of anticipation must therefore be denied with respect to Huang.

B. Anticipation by Devane

Alvogen argues that Devane inherently anticipates all of the asserted claims. Devane is a published patent application entitled "Multiparticulate Modified Release Composition." It is directed to a controlled release composition that provides both immediate and delayed release of the active ingredient or ingredients. Dkt. No. 122-3 ¶ 26. Devane teaches that its "modified release composition" can be used with hydrocodone to provide continuous analgesia for up to 24 hours. Id. ¶ 70. It provides an example of a hydrocodone bitartrate modified release

composition with six possible immediate release components and seven possible modified release components. Id. ¶¶ 99–102.

Devane also describes the results of an in vivo study using one of those formulations, and it provides the pharmacokinetic results from that study. Id. ¶¶ 103–05. The dosage formulation disclosed in Devane's in vivo study is identical to the dosage formulation disclosed in the patents-in-suit and contained in the product that has been commercialized by Pernix under the name Zohydro ER. Id. ¶¶ 104–05 (Tables 6 and 7, disclosing immediate and modified released components); '706 patent, col. 22, ll. 50–58 (describing the clinical study performed to determine the influence of hepatic impairment of controlled release hydrocodone prepared according to the formulations from Devane); Dkt. No. 163-3, at 3–8 (Pernix's responses to Alvogen's requests for admission).

To anticipate a patent claim, a single prior art reference must contain all of the limitations of the asserted claim, either explicitly or inherently. See In re Omeprazole Patent Litig., 483 F.3d 1364, 1378 (Fed. Cir. 2007). In order to establish inherent anticipation, any missing limitations must necessarily be present in the prior art, not merely probably or possibly present. See Trintec Indus., Inc. v. Top-U.S.A. Corp., 295 F.3d 1292, 1295 (Fed. Cir. 2002); Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268–69 (Fed. Cir. 1991). If the prior art reference "necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." Atlas Powder Co. v. Ireco, Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999) (quoting In re King, 801 F.2d 1324, 1326 (Fed. Cir. 1986)). In general, "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Id.

The parties do not dispute that Devane discloses using the same extended release hydrocodone formulation that is described in the patents-in-suit to treat pain. In addition, the parties agree that Devane discloses the pharmacokinetic profile of that hydrocodone formulation in healthy patients. Finally, the parties do not dispute that Devane is silent on the issue of treating patients with hepatic impairment.[5]

Each claim at issue recites a "method of treating pain in a patient having mild or moderate hepatic impairment," the method comprising "administering to the patient having mild or moderate hepatic impairment an oral dosage unit having hydrocodone bitartrate as the only active ingredient," and that the "dosage unit comprises an extended release formulation of hydrocodone bitartrate." Claim 1 of the '760 patent further provides that "the starting dose is not adjusted relative to a patient without hepatic impairment." Dependent claims 2, 3, 4, and 11 each add aspects of the release profile for the hydrocodone formulation. Similarly, claims 12, 17, and 19 of the '760 patent and claim 1 of the '499 patent recite aspects of the release profile of the hydrocodone formulation, such as that the dosage unit "does not increase average hydrocodone AUC_{0-inf} in subjects suffering from mild hepatic impairment relative to subjects not suffering from renal or hepatic impairment in an amount of more than 14%."

Federal Circuit case law is clear that the pharmacokinetic features of particular compounds are inherent properties of those compounds that "add[] nothing of patentable consequence" when claimed as limitations. See In re Kao, 639 F.3d 1057, 1070 (Fed. Cir. 2011); see also Santarus, Inc. v. Par Pharm., Inc., 694 F.3d 1344, 1354 (Fed. Cir. 2012) ("The initial blood serum concentration resulting from administering a PPI dosage is an inherent property of

[5] As Pernix notes, Devane is also silent as to the proper dosages for other special populations, such as pregnant women and nursing mothers, populations that are often specifically addressed in drug labels. Dkt. No. 141, at 13 n.6.

the formulation, and an obvious formulation cannot become nonobvious simply by administering it to a patient and claiming the resulting serum concentrations."); see also PAR Pharm., Inc. v. TWI Pharm., Inc., 773 F.3d 1186, 1195–96 (Fed. Cir. 2014) (inherency in an obviousness analysis may be found where the property is "necessarily present" or "the natural result of the combination of elements explicitly disclosed by the prior art"). See generally Gen. Elec. Co. v. Jewel Incandescent Lamp Co., 326 U.S. 242, 249 (1945) ("It is not invention to perceive that the product which others had discovered had qualities they failed to detect.").[6] Accordingly, Devane inherently anticipates the release profile limitations.

Devane recites a method "for the treatment of pain comprising administering a therapeutically effective amount" of a "multiparticulate modified release composition" containing hydrocodone as the active ingredient, in which the composition is delivered orally. Dkt. No. 122-3, cl. 81 (depending on claims 1 and 17). Devane is silent, however, as to the treatment or dosing of patients having mild or moderate hepatic impairment, and Pernix points to evidence in the record that the testing on which Devane was based was performed on healthy patients not including hepatically impaired individuals. See Dkt. No. 142-1, ¶¶ 67—77 (Dr. Gudin's assessment that the study underlying Devane did not include hepatically impaired patients); Dkt. No. 146-1, Ex. N (the report on the clinical study underlying Devane). Accordingly, the parties disagree about whether Devane inherently discloses either treating hepatically impaired individuals for pain, or administering an extended release hydrocodone composition to patients with mild or moderate hepatic impairment without adjusting the starting dose relative to patients without hepatic impairment.

[6] Of course, if a claim defines the claimed subject matter by its properties rather than, for example, by the chemical name of the compound, it will be the properties that define the scope of the claim. But the mere articulation of newly recognized properties does not in itself make a previously known compound novel.

The Federal Circuit has addressed cases in which a prior art reference describes a broad treatment method and the claimed invention is directed to a narrow subset of patients, and it has analyzed those types of cases as presenting genus-species issues. For example, in Prometheus Laboratories, Inc. v. Roxane Laboratories, Inc., 805 F.3d 1092 (Fed. Cir. 2015), the Federal Circuit affirmed a district court's finding of obviousness of a claim directed at treating irritable bowel syndrome ("IBS") in a subset of patients—"those who (1) are women (2) with IBS–D (3) who have experienced symptoms for at least six months and (4) who have had moderate pain"—in light of a prior art reference that disclosed the same treatment for IBS generally. Id. at 1098. The court explained:

> The genus-species distinction may have particular relevance in the field of personalized medicine, where, for example, a particular treatment may be effective with respect to one subset of patients and ineffective (and even harmful) to another subset of patients. Singling out a particular subset of patients for treatment (for example, patients with a particular gene) may reflect a new and useful invention that is patent eligible despite the existence of prior art or a prior art patent disclosing the treatment method to patients generally. An obviousness rejection likely would not be appropriate where the new patient subset displayed unexpected results.

Id. at 1099 (citation omitted). Similarly, in Abbvie Inc. v. Mathilda and Terence Kennedy Institute of Rheumatology Trust, 764 F.3d 1366 (Fed. Cir. 2014), the patent-in-suit claimed treating patients with "active disease," while the prior art taught the genus of treating patients "in need" of treatment. Id. at 1369–70. There, too, the Federal Circuit considered the treatment of a narrowly defined population of patients as a species of the broad genus consisting of the treatment of patients generally, and the court concluded that the species claims would have been obvious in light of the prior art reference regarding the applicable genus. See id. at 1378–80.

As a general matter, a prior art reference that discloses a genus "does not inherently disclose all species within that broad category." Metabolite Labs., Inc. v. Lab. Corp. of Am.

Holdings, 370 F.3d 1354, 1367 (Fed. Cir. 2004). In such a case, "the issue of anticipation turns on whether the genus was of such a defined and limited class that one of ordinary skill in the art could 'at once envisage' each member of the genus." Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC, 683 F.3d 1356, 1361 (Fed. Cir. 2012) (quoting Eli Lilly & Co. v. Zenith Goldline Pharm., Inc., 471 F.3d 1369, 1376 (Fed. Cir. 2006)). In order to find that a generic disclosure anticipates a species within that genus, the generic reference must identify the claimed species with "sufficient specificity"; that is, the reference must express "specific preferences" for one or more particular species or must disclose a genus that is sufficiently small such that the disclosure of the genus effectively describes the species. See Abbvie, 764 F.3d at 1379; Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1380 (Fed. Cir. 2001); Atofina v. Great Lakes Chem. Corp., 441 F.3d 991, 999 (Fed. Cir. 2006); In re Petering, 301 F.2d 676, 682–83 (CCPA 1976).

The question whether a generic reference identifies the claimed species with sufficient specificity is a factual issue. The standard for finding that a prior art genus anticipates an incorporated species is significantly more restrictive than the standard for determining whether a prior art genus renders obvious a species that is incorporated within it. See Sanofi-Synthelabo v. Apotex, Inc., 550 F.3d 1075, 1083–84 (Fed. Cir. 2008).

Alvogen has not met its burden on summary judgment to show that Devane's genus of treating patients for pain inherently anticipates the species of treating hepatically impaired patients for pain. In that regard, it is significant that there is evidence suggesting that the underlying clinical study described in Devane was limited to the treatment of healthy patients. Dkt. No. 141, at 10–11 (citing Dkt. No. 146-1, Ex. N). In addition to citing the study itself, Pernix points to testimony elicited from Alvogen's expert that if the study had included patients

with hepatic impairment, data regarding those patients would have been described in the study because such patients, like elderly or pediatric patients, are often considered "special population[s]." Dkt. No. 141, at 11; see Dkt. No. 146-1, Ex. D, at 112:10–18 (Alvogen's expert testifying that "if any of the patients had hepatic impairment, . . . it is highly likely that that would have been revealed in the Devane document").

Alvogen argues that the population of pain patients receiving treatment using Devane's formulation will "inevitably include[] patients with mild or moderate" hepatic impairment. Dkt. No. 119, at 14 (citing Dkt. No. 122-12, at 27:23–29:9). That argument, however, does not reflect what Devane inherently teaches, particularly in light of the evidence that the study underlying Devane's application did not include hepatically impaired patients. Drawing all reasonable inferences in Pernix's favor, Alvogen has not met its burden of showing that there is no dispute of fact as to whether Devane specifically discloses treating pain in patients with mild or moderate hepatic impairment.

This analysis is consistent with the Federal Circuit's decision in Perricone v. Medicis Pharmaceutical Corp., 432 F.3d 1368 (Fed. Cir. 2005), on which Alvogen heavily relies. In Perricone, the prior art reference taught a cosmetic composition for topical application; the reference disclosed a variety of ingredients that, when applied topically, have beneficial effects on the skin. Id. at 1376. The asserted independent claims of the patent in suit recited methods for: "treating skin sunburn comprising topically applying to the skin sunburn . . ."; "preventing sunburn damage to exposed skin surfaces, comprising topically applying to said skin surfaces . . ."; "the treatment of skin disorders which arise because of depleted or inhibited collagen synthesis which comprises topically applying to affected skin areas . . ."; "the treatment of skin damaged or aged by . . . which comprises topically applying to affected skin areas a

composition containing . . ."; and "the treatment of damaged or aging skin and epithelial tissue disorders . . . said treatment comprising topically applying to affected tissue areas the combination of . . . ." Id. at 1378 (alterations in original).

All three judges on the Perricone panel agreed that the prior art inherently anticipated the claims that "merely require[d] application of the composition to exposed skin surfaces." Id. at 1379; see also id. at 1381 (Bryson, J., concurring in part and dissenting in part). However, the panel majority distinguished the claims that were limited to applying lotion to sunburned skin, which was a narrower application that was not disclosed in the prior art reference. Id. at 1379 (majority opinion). Just as the prior art did not disclose applying lotion to sunburned skin, Devane may not inherently disclose treating pain in patients with mild or moderate hepatic impairment, at least in the absence of evidence to the contrary regarding the Devane reference.

Alvogen also argues that this case is identical to Aventis Pharmaceuticals, Inc. v. Barr Laboratories, Inc., 411 F. Supp. 2d 490 (D.N.J. 2006), aff'd, 208 F. App'x 842, 208 F. App'x 843 (Fed. Cir. 2006) (per curiam summary affirmances). The patent-in-suit in that case recited a "method of treating a histamine-mediated condition in a patient having impaired liver function due to disease or due to administration of a concomitant drug which inhibits normal liver metabolic function while avoiding cardiac events associated with the administration of terfenadine, said method comprising administering to said patient an effective antihistaminic amount of" fexofenadine. Id. at 519. The prior art patent claimed a "method of treating allergic reactions in a patient in need thereof which comprises administering to said patient an effective amount of" fexofenadine. Id. On a motion for a preliminary injunction, the district court in Aventis denied preliminary injunctive relief based in part on a finding that the defendants had "raised a substantial question of invalidity." Id. at 518. On an interlocutory appeal from that

denial, the Federal Circuit summarily affirmed without opinion. Aventis Pharm., Inc. v. Barr Labs., Inc., 208 F. App'x 843 (Fed. Cir. 2006).

Although there are several similarities between Aventis and the present case, the district court's decision in Aventis is not dispositive here, for several reasons. First, the Aventis court found, as a factual matter, and under the "reasonable likelihood of success" standard, that the "characteristic of treating hepatically impaired patients is necessarily present in the teaching" of the prior art reference that "discloses a method for treating all patients." Id. at 522. Second, the issue of inherent anticipation was raised in the context of a preliminary injunction, and thus the issue of anticipation was not conclusively decided at that time. The applicable standards for granting preliminary injunctive relief and granting summary judgment are, of course, quite different. Finally, the district court's decision in Aventis was issued in 2006, and the court therefore did not have the benefit of the Federal Circuit's subsequent decisions in cases such as Prometheus Laboratories and Abbvie.

For purposes of trial, the Court notes that Pernix's argument that inherent anticipation requires that the "missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill" is, at best, only partially true. Dkt. No. 141, at 19 (quoting Continental Can, 948 F.2d at 1269–69). The Federal Circuit has clarified that Continental Can does not require "that an inherent feature of a prior art reference must be perceived as such by a person of ordinary skill in the art before the critical date." Schering Corp. v. Geneva Pharm., Inc., 339 F.3d 1373, 1377 (Fed. Cir. 2003). Rather, when read in context, Continental Can held that "inherency, like anticipation itself, requires a determination of the meaning of the prior art." Id. A court therefore may "consult artisans of ordinary skill to ascertain their understanding about subject matter disclosed by the prior art,

including features inherent in the prior art" and may "resolve factual questions about the subject matter in the prior art by examining the reference through the eyes of a person of ordinary skill in the art, among other sources of evidence about the meaning of the prior art." Id. at 1377–78; see also, e.g., In re Omeprazole Patent Litigation, 483 F.3d 1364, 1373 (Fed. Cir. 2007) ("[I]nherency is not necessarily coterminous with knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art" (quoting In re Cruciferous Sprout Litig., 301 F.3d 1343, 1349 (Fed. Cir. 2002))); Abbott Labs v. Baxter Pharm. Prods., 471 F.3d 1363, 1367 (Fed. Cir. 2006) ("Our cases have consistently held that a reference may anticipate even when the relevant properties of the thing disclosed were not appreciated at the time."); SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1343 (Fed. Cir. 2005) ("[I]nherent anticipation does not require a person of ordinary skill in the art to recognize the inherent disclosure in the prior art at the time the prior art is created."); Toro Co. v. Deere & Co., 355 F.3d 1313, 1321 (Fed. Cir. 2004) ("Simply put, the fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.").[7]

For the reasons stated above, Alvogen's motion for summary judgment of invalidity by anticipation, Dkt. No. 115, is DENIED.

[7] Alvogen argues that genus-species case law does not apply to inherency because of the case law holding that inherent anticipation does not require recognition by a person of skill prior to the priority date. Dkt. No. 179, at 3–4. However, Alvogen conflates two separate parts of the anticipation analysis. A property—such as the pharmacokinetic profile in a patient with mild hepatic impairment compared to the profile in a patient without hepatic impairment—may be found to be inherent when it is "'necessarily present,' not merely probably or possibly present, in the prior art," even if that property was not previously recognized. Trintec Indus., Inc. v. Top-U.S.A. Corp., 295 F.3d 1292, 1295 (Fed. Cir. 2002). But a modification of a method of treatment is not a "necessarily present" property found in the prior art, and it must be analyzed accordingly. See, e.g., AstraZeneca, 633 F.3d at 1055.

IV. The Cross-Motions for Summary Judgment as to Patent Eligibility

The parties have filed cross-motions for summary judgment addressing whether the asserted claims of the '760 and '499 patents satisfy the requirements of the patent eligibility statute, 35 U.S.C. § 101. Dkt. Nos. 111, 114.

As articulated by the Supreme Court, the analysis of patent eligibility under section 101 entails two steps. Step one requires the Court to "determine whether the claims at issue are directed to a patent-ineligible concept" such as a natural law or an abstract idea. Alice Corp. Pty. v. CLS Bank Int'l, 134 S. Ct. 2347, 2355 (2014). If so, the Court proceeds to step two, which requires the Court "to consider the elements of each claim both individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." Id. (quoting Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66, 78–79 (2012)). In that step, the Court searches "for an 'inventive concept'—i.e., an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" Id. (alteration in original) (quoting Mayo, 566 U.S. at 72–73).

Alvogen argues that the asserted claims of the '760 and '499 patents are ineligible for patent protection under section 101 because they are "premised on the relationship between [hepatic impairment] and the bioavailability of hydrocodone in the body after administration of Devane's [extended release hydrocodone] prior art formulation—namely that the response of the human body to this formulation is similar in patients with and without mild or moderate [hepatic impairment]." Dkt. No. 112, at 11; see also Dkt. No. 145, at 3.

The claims asserted in this case are distinguishable from the claim examined by the Supreme Court in Mayo, a decision on which Alvogen heavily relies. In Mayo, the

representative claim recited a two-step method that involved administering a known drug and using routine processes to determine the level of a certain metabolite. The claim also included a wherein clause that identified the significance of metabolite level. Mayo, 566 U.S. at 74–75. The Supreme Court explained that the wherein clause "at most add[ed] a suggestion that [doctor] should take those [natural] laws into account when treating his patient . . . while trusting [the doctor] to use those laws appropriately where they are relevant to their decisionmaking." Id. at 78. The Court distinguished the claim at issue in Mayo from "a typical patent on a new drug or a new way of using an existing drug," on the ground that the claims before the Court "add[ed] nothing of significance to the natural laws themselves." Id. at 87; see also Vanda Pharm., 887 F.3d at 1134 ("Although the representative claim in Mayo recited administering a thiopurine drug to a patient, the claim as a whole was not directed to the application of a drug to treat a particular disease.").

Two recent decisions of the Federal Circuit are instructive in this regard. In Rapid Litigation Management Ltd. v. CellzDirect, Inc., 827 F.3d 1042 (Fed. Cir. 2016), the inventors of the patent at issue had discovered that hepatocytes, a type of liver cell, could survive multiple freeze-thaw cycles. Id. at 1050. The representative claim recited a "method of producing a desired preparation of multi-cryopreserved hepatocytes." Id. at 1046. Although the representative claim applied a natural property of hepatocytes, "that is not where [the inventors] stopped, nor is it what they patented." Id. at 1048. Rather, "'as the first party with knowledge of' the cells' ability, they were 'in an excellent position to claim applications of that knowledge.'" Id. at 1048 (quoting Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 596 (2013)). Instead of claiming "nothing more than observing or identifying the ineligible concept itself," the inventors "employed their natural discovery to create a new and

improved way of preserving hepatocyte cells for later use." Id.; see also id. at 1048 ("Through the recited steps, the patented invention achieves a better way of preserving hepatocytes.").

The CellzDirect court concluded that patents that "recite processes to achieve a desired outcome, e.g., methods of producing things, or methods of treating disease" are generally not patent-ineligible. Id. at 1048–49. If it were otherwise, "we would find patent-ineligible methods of, say, producing a new compound (as directed to the individual components' ability to combine to form the new compound), treating cancer with chemotherapy (as directed to cancer cells' inability to survive chemotherapy), or treating headaches with aspirin (as directed to the human body's natural response to aspirin)." Id. at 1049.

Similarly, in Vanda Pharmaceuticals, Inc. v. West-Ward Pharmaceuticals International Ltd., the Federal Circuit held that a method of treatment claim that adjusted dosage based on whether the patient had normal or lower enzyme activity was patent-eligible under section 101. 887 F.3d at 1121. The representative claim recited a "method for treating a patient with iloperidone, wherein the patient is suffering from schizophrenia." Id. The claim required two steps: first, determining the patient's metabolizer genotype "by (a) obtaining a biological sample and (b) performing a genotyping assay"; and second, "administering specific dose ranges of iloperidone depending on the patient's" genotype. Id. at 1134. The court held that the claims at issue in Vanda were "directed to a method of using iloperidone to treat schizophrenia" and not a natural law. Distinguishing Mayo, the court emphasized that the "inventors recognized the relationships between iloperidone, CYP2D6 metabolism, and QTc prolongation, but that is not what they claimed. They claimed an application of that relationship." Id. at 1135. Unlike the claim in Mayo, the court explained, "[t]hese are treatment steps" that are "directed to a specific

method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome." Id. at 1135–36.

The independent claims asserted in this case are indistinguishable from the representative claim discussed in Vanda. Claim 1 of the '760 patent recites a "method of treating pain in a patient having mild or moderate hepatic impairment," and teaches using an extended release formulation of hydrocodone bitartrate wherein the "starting dose is not adjusted relative to a patient without hepatic impairment." Claim 12 of the '760 patent and claim 1 of the '499 patent each recites a "method of treating pain in a patient having mild or moderate hepatic impairment," and teaches using a specific extended release formulation of hydrocodone bitartrate that has a particular release profile. Although the inventions recited in those claims were based upon a natural law—the physiological response to hydrocodone in individuals with or without mild or moderate hepatic impairment—the claims do more than merely report those physiological responses. Rather, like the claim discussed in Vanda, the claims asserted in this case describe a specific dosing regimen to treat a specific condition based on the patient's medical status.

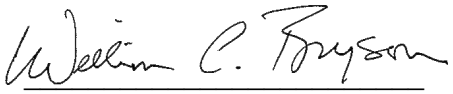
Alvogen contends that the opposite result is compelled by the decisions in Endo Pharmaceuticals Inc. v. Actavis Inc. ("Endo I"), No. 14-cv-1381, 2015 WL 5580488 (D. Del. Nov. 17, 2015), report and recommendation adopted by Endo Pharmaceuticals Inc. v. Actavis Inc. ("Endo II"), No. 14-cv-1381, 2015 WL 7253674 (D. Del. Sept. 23, 2015). In that case, a representative claim recited a "method for treating pain in a renally impaired patient" that required: (1) providing an oral controlled release dosage form of oxymorphone; (2) measuring the patient's creatinine clearance rate; and (3) administering a lower dosage, based on the creatinine rate, so as to not exceed a maximum total drug exposure over time. Endo I, 2015 WL 5580488, at *1–2.

The Endo opinions do not support Alvogen's position. First, as acknowledged in both decisions, the patentee effectively conceded that the claim was directed to a natural law. Id. at *6 ("Indeed, plaintiffs effectively concede the first step of the Mayo analysis."); Endo II, 2015 WL 7253674 at *3 ("As the Magistrate Judge points out, Plaintiffs essentially admitted in their briefing that the '737 patent claims a natural law as its invention."). Moreover, the representative claim in Endo is more akin to the claim in Mayo than to the claims at issue in CellzDirect, Vanda, and this case. As in Mayo, the claim at issue in Endo in effect simply stated the law of nature—i.e., renally impaired patients may be more sensitive to oxymorphone—"while adding the words 'apply it.'" Endo II, 2015 WL 7253674 at *3. Finally, to the extent there is any tension between the decisions in Endo and the subsequently issued Federal Circuit opinions in CellzDirect and Vanda, those later cases necessarily control.

Because the asserted claims are not directed to a patent-ineligible concept, Pernix's motion for summary judgment of no invalidity under section 101, Dkt. No. 114, is GRANTED, and Alvogen's motion for summary judgment of invalidity under section 101, Dkt. No. 111, is DENIED.

IT IS SO ORDERED.

SIGNED this 15th day of May, 2018.



WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE