IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PURDUE PHARMA L.P., PURDUE PHARMACEUTICALS L.P., and RHODES TECHNOLOGIES, Plaintiffs, v. ACCORD HEALTHCARE INC., Defendant.	Civil Action No. 20-1362-RGA

TRIAL OPINION

Jack B. Blumenfeld, Rodger D. Smith II, Megan E. Dellinger, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, DE; John J. Normile, Gasper J. LaRosa, Kevin V. McCarthy, Adam M. Nicolais, JONES DAY, New York, NY; Pablo D. Hendler, POTOMAC LAW GROUP, New York, NY; Jennifer L. Swize, JONES DAY, Washington, DC,

Attorneys for Plaintiffs.

Benjamin J. Schladweiler, Renée Mosley Delcollo, GREENBERG TRAURIG, LLP, Wilmington, DE; Alejandro Menchaca, Ben J. Mahon, Bradley P. Loren, Ashley M. Ratycz, MCANDREWS, HELD & MALLOY, LTD., Chicago, IL,

Attorneys for Defendant.

April 11, 2023

ANDREWS, U.S. DISTRICT JUDGE:

Plaintiffs Purdue Pharma L.P., Purdue Pharmaceuticals L.P., and Rhodes Technologies brought this patent infringement action under 35 U.S.C. § 271(e)(2)(A) against Defendant Accord Healthcare. (D.I. 1 ¶ 2). I held a three-day bench trial from September 19 to September 21, 2022. The parties narrowed the issues to invalidity for obviousness of each of six asserted claims from five remaining patents.

The asserted patents fall into two groups, each of which shares a substantively identical specification. (D.I. 89-1 ¶¶ 10, 21). One group consists of U.S. Patent Nos. 9,763,933 ("the Mannion '933 patent"), 9,775,808 ("the '808 patent"), and 9,763,886 ("the '886 patent"). The parties refer to these patents as the "Tamper Resistant" or "Abuse-Deterrent Patents." I refer to them as the "Abuse-Deterrent Patents." The claims at issue are claim 3 of the Mannion '933 patent, claim 3 of the '808 patent, and claim 6 of the '886 patent.

The second group consists of U.S. Patent Nos. 9,073,933 ("the '933 patent") and 9,522,919 ("the '919 patent"). The parties (and I) refer to these as the "Low ABUK Patents." The claims of the "Low ABUK Patents" at issue are claims 3 and 11 of the '933 patent and claim 21 of the '919 patent.

For the following reasons, I find all six of the asserted claims invalid for obviousness under 35 U.S.C. § 103.

I. BACKGROUND

Purdue holds New Drug Application ("NDA") No. 022272 for OxyContin (oxycodone hydrochloride). OxyContin is an extended-release analgesic. (D.I. 89-1 ¶ 32). The Abuse-Deterrent Patents relate to an abuse-deterrent reformulation of OxyContin that make it hard enough to resist crushing and viscous enough to deter intravenous users. (D.I. 106 at 3, 5). The

reformulation was approved in 2010, and the Food and Drug Administration ("FDA") approved an abuse-deterrent label for the reformulation in 2013, following postmarketing studies. (D.I. 107 ¶ 20). I will refer to the pre-reformulation version of OxyContin as "Original OxyContin."

The Low-ABUK Patents relate to compositions of oxycodone containing 8α-14-dihydroxy-7,8-dihydrocodeinone ("8α") and having particularly low levels of the impurity 14-hydroxycodeinone ("14-hydroxy"). (*Id.* ¶¶ 48-49). 14-hydroxy is an alpha beta unsaturated ketone ("ABUK"), a class of compounds thought to be genotoxic. The evolution of the scientific understanding of these compounds' genotoxicity is a factual issue in this case. (D.I. 100 ¶ 158).

Accord submitted an Abbreviated New Drug Application ("ANDA") No. 213564 for approval to market a generic version of OxyContin. Plaintiffs then initiated this lawsuit. (D.I. 1 ¶¶ 1-2). The Mannion '933, '808, '933, and '919 patents are all listed in the FDA's Orange Book for OxyContin. The '886 patent is not. (*Id.* ¶ 1).

II. LEGAL STANDARD

A patent claim is invalid as obvious under 35 U.S.C. § 103 "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103; *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406-07 (2007). "As patents are presumed valid, a defendant bears the burden of proving invalidity by clear and convincing evidence." *Shire, LLC v. Amneal Pharms., LLC*, 802 F.3d 1301, 1306 (Fed. Cir. 2015) (citations omitted). "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against

this background, the obviousness or nonobviousness of the subject matter is determined." *KSR*, 550 U.S. at 406 (internal citation and quotation marks omitted).

A court is required to consider secondary considerations, or objective indicia of nonobviousness, before reaching an obviousness determination, as a "check against hindsight bias." *See In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1078-79 (Fed. Cir. 2012). "Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17–18 (1966).

III. THE ABUSE-DETERRENT PATENTS

A. The Asserted Claims

The claims at issue are claim 3 of the Mannion '933 patent, claim 3 of the '808 patent, and claim 6 of the '886 patent. Claim 3 of the Mannion '933 patent is a product-by-process claim that depends on claim 1. Claims 1 and 3 read,

> 1. A pharmaceutical composition comprising:
> at least one active agent;
> at least one high molecular weight polyethylene oxide (PEO) having an approximate molecule weight of from 1 million to 15 million;
> optionally at least one additive;
> optionally at least one film coating; and
> optionally at least one low molecular weight PEO having an approximate molecular weight of less than 1,000,000; wherein
> (a) the active agent and high molecular weight PEO are combined in a solid oral extended release dosage form that is (i) compression shaped, (ii) air cured by heated air, without compression, for at least about 5 minutes at a temperature above the softening temperature of the high molecular weight PEO, (iii) cooled, and (iv) hardened;
> (b) the high molecular weight PEO comprises at least about 30% (by weight) of the dosage form;
> (c) the molecular weight of each PEO is based on rheological measurements; and
> (d) the total weight of the dosage form is calculated by excluding the combined weight of said film coatings.

. . .

3. A pharmaceutical composition according to claim 1, wherein the curing temperature is from about 70° C. to about 85° C. and the curing time is from about 10 minutes to about 10 hours.

(Mannion '933 patent at 158:61-159:16, 159:20-23).

Claim 3 of the '808 patent is a product-by-process claim that depends on claim 1. The two claims read,

1. A pharmaceutical composition comprising:
at least one active agent comprising oxycodone or a pharmaceutically acceptable salt thereof;
at least one high molecular weight polyethylene oxide (PEO) having an approximate molecule weight of from 1 million to 15 million;
at least one additive and a film coating; and
optionally at least one low molecular weight PEO having an approximate molecular weight of less than 1,000,000; wherein
(a) the active agent and high molecular weight PEO are combined in a solid oral extended release dosage form that is (i) compression shaped, (ii) air cured by heated air, without compression, for at least about 5 minutes at a temperature above the softening temperature of the high molecular weight PEO, (iii) cooled, and (iv) hardened;
(b) the high molecular weight PEO comprises at least about 30% (by weight) of the dosage form;
(c) the molecular weight of each PEO is based on rheological measurements; and
(d) the total weight of the dosage form is calculated by excluding the combined weight of said film coatings.

. . .

3. A pharmaceutical composition according to claim 1, wherein the curing temperature is from about 70° C. to about 85° C. and the curing time is from about 10 minutes to about 10 hours.

('808 patent at 159:37-57, 159:61-64).

Claim 6 of the '886 patent is a method claim, which depends on claims 5, 3, 2, and 1. The claims read,

1. A method of producing a plurality of solid oral extended release pharmaceutical dosage forms comprising the steps of:
mixing at least one active agent, at least one high molecular weight polyethylene oxide (PEO) having an approximate molecular weight of from 1 million to 15 million, to provide a PEO composition;

compressing the PEO composition to provide a plurality of shaped matrix compositions;
curing the shaped matrix compositions by exposure to heated air at a curing temperature that is at least the softening temperature of the high molecular weight PEO for a curing time of at least about 5 minutes, to provide a plurality of cured matrix compositions;
cooling the cured matrix compositions;
optionally combining any of the matrix compositions with at least one additive, before or after curing; and
optionally providing the cured matrix compositions with at least one film coating, after curing and cooling; wherein
(a) the molecular weight of each PEO is based on rheological measurements;
(b) the high molecular weight PEO comprises at least about 30% (by weight) of each dosage form;
(c) the total weight of each dosage form is calculated by excluding the combined weight of said film coatings.
(d) each cured matrix composition comprises a solid oral pharmaceutical dosage form that provides an extended release of at least one active agent.
2. A method according to claim 1, wherein the curing temperature is at least about 60° C. and the curing time is at least 10 minutes.
3. A method according to claim 2, wherein the high molecular weight PEO has an approximate molecular weight of from 1 million to 8 million.
. . .
5. A method according to claim 3, wherein the high molecular weight PEO comprises at least about 50% (by weight) of each dosage form.
6. A method according to claim 5, wherein the curing temperature is from about 65° C. to about 90° C. and the curing time is from about 10 minutes to about 10 hours.

('886 patent at 171:35-172:22, 172:26-32).

B. Findings of Fact

1. Both Original OxyContin and the reformulation that the Abuse-Deterrent Patents concern are extended-release matrix tablets. (Tr. at 204:16-21;[1] '886 Patent at 171:42-50). Matrix tablets contain an active ingredient embedded in a polymer matrix. (Tr. at 202:23-203:9)

2. Polyethylene oxide (PEO) is among the most commonly used matrix polymers. (Tr. at 204:6-8).

3. With respect to the Abuse-Deterrent Patents, a person of ordinary skill in the art ("POSA") has an advanced degree and substantial experience drawn from the fields of medicine, chemical engineering, polymers, pharmaceutical sciences, pharmaceutics, pharmacokinetics, and pharmacology. (D.I. 89-1 at ¶ 134).

[1] The transcript is available at D.I. 102-105. It is consecutively paginated.

4. The Abuse-Deterrent Patents are directed to compositions and methods of producing abuse-deterrent pharmaceutical formulations. (D.I. 89-1 ¶¶ 21-22).

5. For purposes of this action, the priority date of the patents is August 25, 2006. (D.I. 89-1 ¶¶ 24, 27, 30).

6. Abuse by crushing was a known issue with OxyContin. (DTX-008).

7. United States Patent No. 6,488,963 to McGinity ("McGinity") is prior art to the Abuse-Deterrent Patents under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 120).

8. A POSA would have understood that, because McGinity's tablets were made from melted PEO, they had increased breaking strength that provided resistance to crushing. (Tr. at 220:17-26).

9. McGinity teaches that its formulations can be used on "analgesics" (DTX-009 at 6:10), which a POSA would understand includes oxycodone. (Tr. at 220:7-16).

10. McGinity teaches melting PEO in a hot-melt extruder to create hardened tablets. (DTX-009 at 8:8-28). At the time of the invention, hot melt extruders, though known, were not common. (Tr. at 219:3-13). They could be used at contract manufacturers. (Tr. at 257:17-19).

11. U.S. Patent Publication No. 2005/0031546 ("Bartholomaus") is prior art to the Abuse-Deterrent Patents under 35 U.S.C. § 102(b). (DTX-010; D.I. 89-1 ¶ 123).

12. Bartholomaus teaches pressing PEO tablets in a "heating cabinet." (DTX-010 at [0117]). A POSA would understand that the purpose of the heating was to melt the PEO. (Tr. at 227:5-13).

13. The method disclosed in the examples in Bartholomaus was not scalable. (Tr. at 226:7-26, 332:5-24).

14. Bartholomaus contemplates pressing tablets and heating them as separate steps. (Tr. at 227:20-228:4; DTX-010 at [0067]).

15. Zezhi J. Shao et al., *Effects of Formulation Variables and Post-compression Curing on Drug Release from a New Sustained-Release Matrix Material: Polyvinylacetate-Povidone*, 6 Pharm. Dev. and Tech. 2, 257 (2001) ("Shao") is prior art to the Tamper Resistant Patents under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 126). Shao discloses matrix tablets made with the polymer Kollidon-SR (polyvinylacetate-povidone). (DTX-011 at 0001).

16. Nashiru Billa et al., *Diclofenac Release from Eudragit-Containing Matrices and Effects of Thermal Treatment*, 24 Drug Dev. and Indus. Pharm. 1, 45-50 (1998) ("Billa") is prior art to the Tamper Resistant Patents under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 127). Billa discloses matrix tablets made with the polymer

EUDRAGIT (ethyl acrylate-methyl methacrylate copolymer). (DTX-012 at 0002).

17. Marcelo O. Omelczuk & James W. McGinity, *The Influence of Thermal Treatment on the Physical-Mechanical Properties of Tablets Containing Poly(DL-Lactic Acid)*, 10 Pharm. Rsch. 4, 542 (1992) ("Omelczuk;" together with Billa and Shao, the "Oven Art") is prior art to the Tamper Resistant Patents under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 128). Omelczuk discloses matrix tablets made with the polymer PLA (poly(DL-lactic acid)). (DTX-014 at 0001).

18. The Oven Art teaches heating various non-PEO polymers in ovens (Tr. at 229:20-25, 231:11-22, 232:1-11), though not to their melting points. (Tr. at 286:5-14, 287:6-8).

19. Shao concluded that the curing process increased the hardness of the tablets. (DTX-011 at 0005; Tr. at 230:9-20).

20. Both Bartholomaus and the Oven Art disclose cooling and hardening the tablet. (Tr. at 240:8-11).

C. Conclusions of Law

As a preliminary matter, the parties treat the three asserted Abuse-Deterrent claims as though they rise and fall together. Neither party contends that their arguments or my analysis should apply differently to the product-by-process than to the method claims. Therefore, I too will treat the three claims together. For the following reasons, I conclude that each of the three claims is invalid for obviousness under 35 U.S.C. § 103.

Defendant relies on five pieces of prior art in arguing for the obviousness of the Abuse-Deterrent Patents. Bartholomaus and McGinity broadly teach PEO matrix tablets formed with simultaneous compression and heating. The three Oven Art references broadly teach curing non-PEO matrix tablets in ovens after compression. The parties generally agree on two ways in which the Abuse-Deterrent Patents depart from the prior art. First, the prior art that used PEO (Bartholomaus and McGinity) taught simultaneous compression and heating (D.I. 99 at 5; D.I. 106 at 7), while the prior art that taught sequential compression and heating (the Oven Art) used polymers other than PEO. (D.I. 99 at 10-11; D.I. 106 at 13). The parties disagree about whether a

POSA would have been motivated to make PEO tablets with sequential compression and heating, and whether there would have been a reasonable expectation of success in doing so. Second, no prior art used the same combinations of curing time and temperature ranges as those disclosed in the Abuse-Deterrent Patents. (D.I. 99 at 6; D.I. 106 at 13). The parties disagree about whether routine experimentation by a POSA would have yielded the times and temperatures disclosed in the patents. I focus in turn on each difference between the asserted claims and the prior art, though some of the parties' arguments are common to both.

1. Sequential Compression and Heating

The first gap between the Abuse-Deterrent Patents and the prior art can be bridged by combining the PEO tablets of Bartholomaus and McGinity with the heating techniques taught in the Oven Art. With all elements of the claim present in the prior art, "[a] party seeking to invalidate a patent on the basis of obviousness must 'demonstrate by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.'" *Kinetic Concept, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1360 (Fed. Cir. 2012) (quoting *Procter & Gamble Co. v. Teva Pharm, USA, Inc.*, 566 F.3d 989, 1014 (Fed. Cir. 2009)).

a. Motivation to Combine

In arguing for a POSA's motivation to combine the prior art, Defendant asserts that a POSA would look to Bartholomaus and McGinity in the first place because abuse by crushing was a known problem. (D.I. 99 at 7-8). A POSA would then seek to modify Bartholomaus and McGinity because the processes disclosed in those references would not have been suitable for large-scale production. (*Id.* at 13). For example, Defendant's expert, Dr. Leah Appel, testified

that the Bartholomaus method applies heat by placing a tablet press in a heated chamber, but scaling this to produce many tablets at once would require a large space heated to a high temperature—and it is unclear how one would operate a tablet press in those conditions. (Tr. at 226:1-18). Dr. Appel also testified that the hot melt extruders used in McGinity were "niche" at the time of invention—they were available at some facilities, but access to one was not a given. (*Id.* at 219:3-13). Researchers might have to contract with other companies in order to use one. (*Id.* at 258:8-16). Dr. Appel testified that ovens, by contrast, were a common and readily accessible tool for heating tablets. (*Id.* at 219:14-19). Defendant argues that a POSA would therefore naturally turn to ovens in either scaling up Bartholomaus or adapting McGinity to more commonly available equipment. The Oven Art would have provided guidance for a POSA on how to cure matrix tablets in an oven, leading to the claimed invention.[2]

Plaintiffs respond with several critiques of Dr. Appel's analysis. First, Plaintiffs argue that a POSA presented with Bartholomaus and McGinity would not have a motivation to modify those references, because each of those references discloses an effective crush-resistant tablet. (D.I. 106 at 10). As to McGinity, Plaintiffs also challenge the idea that hot-melt extruders were niche, arguing that they were available at certain facilities that could be contracted with. (*Id.* at 8). Second, Plaintiffs assert that even if a POSA sought to modify Bartholomaus and McGinity,

[2] Defendant also argues—in a footnote—for collateral estoppel on the factual issue of whether simultaneous and sequential heating and compression are equivalent. (D.I. 99 at 14 n.7). In prior litigation, Plaintiffs successfully argued that a sequential heating process infringed, under the doctrine of equivalents, a patent that disclosed simultaneous heating. *See In re Oxycontin Antitrust Litig.*, 994 F. Supp. 2d 367, 419 (S.D.N.Y. 2014). Plaintiffs respond that this case involved different patents and products. (D.I. 106 at 9). The application of collateral estoppel here was barely briefed. I think it is extremely unlikely that collateral estoppel applies. Whether or not it does, I do not think a factual determination that simultaneous and sequential processes are equivalent is necessary for a finding of obviousness. Therefore, I do not address the application of collateral estoppel and disregard the factual findings that Defendant offers in footnotes.

the POSA would not have a motivation to combine Bartholomaus and McGinity with the Oven Art in particular, because the Oven Art did not use PEO and did not teach heating matrix tablets to their polymers' melting points. (*Id.* at 13). Third, Plaintiffs argue that a POSA would never have looked to Bartholomaus and McGinity in the first place and would instead have sought to add an antagonist. (*Id.* at 15). Plaintiffs' expert, Dr. Bley, testified that the prior art reference Mansbach "teaches that antagonists are the way to go and particularly for opioid analgesics . . . if there's an antagonist available, that's the preferred path." (Tr. at 425:23-25; PTX-131 at S19). Dr. Bley also testified that he himself, as a POSA in the field at the relevant time, did not pursue crush resistant tablets, characterizing Dr. Appel's analysis as "hindsight-driven." (*Id.* at 398:16-399:14).[3]

On the first issue of whether a POSA would want to modify Bartholomaus and McGinity, the parties agree that the processes taught by those references successfully produced hardened tablets. (D.I. 99 at 11; D.I. 106 at 10). They disagree on how this success relates to the Abuse-Deterrent Patents. Defendant argues that the processes' viability would make them a good starting point for a POSA trying to develop hardened tablets, while Plaintiffs contend that the successful processes would be a POSA's ending point. Plaintiffs' position fails to address the crux of Defendant's argument. Defendant is arguing that while the processes were successful for "one-off tablets" (Tr. at 228:20-229:7), a POSA would have sought a process that could be scaled up. Plaintiffs do not make a plausible argument that a POSA would not want to develop a scalable process. Plaintiffs also do not make a plausible argument that a POSA would have

[3] Plaintiffs also argue, in a single paragraph, that the problem of crushable tablets is not a sufficient "known problem" to support a motivation to modify the prior art. (D.I. 106 at 17). I do not think this is the case, and the briefing on this argument was so summary that I will not address it further.

options other than modifying Bartholomaus and McGinity if they wanted to produce hardened tablets at scale.[4] I also do not think the option to contract with third-party research or manufacturing facilities—in the case of McGinity's hot-melt extruders—would negate the motivation to adapt the method to ovens.

A POSA's "[m]otivation to combine may be found in many different places and forms." *Par Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1197 (Fed. Cir. 2014) (quoting *Allergan, Inc. v. Sandoz, Inc.*, 726 F.3d 1286, 1292 (Fed. Cir. 2013)). "[I]t often may be the case that market demand, rather than scientific literature, will drive design trends." *KSR*, 550 U.S. at 419. I think that a desire to manufacture hardened tablets at scale and with minimal switching costs is a motivation to modify the prior art. Finding otherwise would run the risk of "[g]ranting patent protection to advances that would occur in the ordinary course without real innovation," which *KSR* cautioned against. *Id.* Therefore, while it is true that Bartholomaus and McGinity's processes resulted in hardened tablets, I find that a POSA would not stop at their teachings.

Plaintiffs also contend regarding the motivation to modify Bartholomaus and McGinity that "the claims are not limited to commercial manufacturing." (D.I. 106 at 8). However, it is not necessary for commercial manufacturing to be claimed for it to serve as a motivation to combine. In *Alcon Research, Ltd. v. Apotex, Inc.*, the Federal Circuit found that known "antihistaminic efficacy" would be a valid motivation to combine certain allergy treatment prior art references. 687 F.3d 1362, 1368-69 (Fed. Cir. 2012). However, the patent at issue claimed the treatment for its ability to "stabiliz[e] conjunctival mast cells"—a different allergy treatment mechanism. *Id.* at 1363-64. I also note that whether the inventors of the Abuse-Deterrent Patents themselves were

[4] I note that the question of a POSA's options for producing hardened tablets at scale is distinct from the issue of whether a POSA would want to pursue hardened tablets at all, which I discuss below.

motivated a desire to produce at a commercial scale is immaterial. The Federal Circuit has "repeatedly held that the motivation to modify a prior art reference to arrive at the claimed invention need not be the same motivation that the patentee had." *Id.* at 1368.

Overall, I find that Defendant presented clear and convincing evidence of a POSA's motivation to modify Bartholomaus and McGinity. I am convinced by Dr. Appel's testimony that a POSA would seek a commercially viable process for producing hardened tablets.

Second, Plaintiffs argue that even with a motivation to modify Bartholomaus and McGinity, a POSA would not combine them with the Oven Art in particular. I find that Dr. Appel presented clear and convincing testimony that ovens were commonly available and used to heat tablets. Plaintiffs' witnesses did not provide any testimony to the contrary. Plaintiffs did not attempt to show, for example, that a POSA would not have access to ovens, or that other equipment would be a more natural choice than ovens for heating tablets.

I do not think Defendant's theory of obviousness is hampered by the fact that ovens had only been used to heat polymers other than PEO. The Oven Art taught the use of ovens to heat matrix tablets made from several different polymers. (DTX-011 at 0001; DTX-012 at 0002; DTX-014 at 0001). Shao specifically taught that the heat curing made its tablets harder. (DTX-011 at 0005). It is not much of a leap to infer that ovens would also be useful for applying heat to harden the matrix tablets disclosed by Bartholomaus and McGinity. At the very least, in the absence of testimony about other heating tools, employing a commonly available tool to apply heat to tablets is obvious to try. *See KSR*, 550 U.S. at 421. While the Oven Art does not teach heating tablets to their melting points, Bartholomaus and McGinity both teach hardening PEO by heating it to its melting point. (DTX-009 at 8:8-28; DTX-010 at [0117]). Dr. Appel credibly

testified that a POSA combining these references would seek the same result in an oven. (Tr. at 233:6-13).

I turn to Plaintiffs' third argument, that a POSA would not be motivated to combine Bartholomaus and McGinity with the Oven Art because adding an antagonist would have been a more obvious path. (D.I. 106 at 17). Plaintiffs offer evidence that OxyContin had approved antagonists at the time of the invention (Tr. at 419:8-420:8), and the prior art explicitly taught using an antagonist for abuse deterrence (Tr. at 417:25-419:5). Plaintiffs also offer evidence that both Dr. Bley and Purdue itself first pursued paths other than physical abuse deterrence. (Tr. at 422:3-25, 304:18-305:4). However, a path does not need to be the most obvious or preferred path in order to be obvious. "[C]ase law does not require that a particular combination must be the preferred, or the most desirable, combination described in the prior art in order to provide motivation for the current invention." *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004) (quoting *In re Beattie*, 974 F.2d 1309, 1311 (Fed. Cir. 1992)).

Dr. Bley's testimony about his own research may support the viability of the antagonist route, but it does not undermine the viability of the hardness route. Plaintiffs do not, as far as I can tell, argue that the prior art taught *away* from hardened opioid formulations for abuse deterrence—they simply argue that the prior art taught an alternative. I likewise find that the Mansbach reference on which Plaintiffs rely encourages the use of an antagonist, but does not teach away from using physical abuse deterrence. The passage that Dr. Bley discussed at trial, (Tr. 425:3-25), says, "For drugs of abuse without an approved antagonist, countermeasures against physical tampering may represent the best means to reduce the risk of oral or parenteral abuse." (PTX-131 at S19). While this passage certainly suggests that a POSA should pursue physical abuse deterrence for drugs without an approved antagonist, it says nothing about the

inverse of that statement—that a POSA should *not* use such methods for drugs *with* an approved antagonist. Therefore, I do not find that the prior art discourages physical abuse deterrence and I am not persuaded by Plaintiffs' third argument.

Overall, through Dr. Appel's testimony, I find Defendant has presented clear and convincing evidence of a motivation to combine Bartholomaus and McGinity with the Oven Art.

b. Reasonable Expectation of Success

Having found a motivation to combine the prior art references, I consider whether a POSA would have had a "reasonable expectation of success" in "achiev[ing] the claimed invention." *Kinetic Concept*, 688 F.3d at 1360. Defendant notes that a POSA would need to balance opposing considerations in arriving at the claimed invention, ensuring that the PEO would harden, the active ingredient would not degrade, and the method would be practical. (D.I. 99 at 17). Defendant asserts that a POSA would reasonably expect there to be an optimal time and temperature that balances these considerations, discoverable through routine experimentation.[5] (*Id.* at 16-17). In general support of its obviousness argument, Defendant also notes that Bartholomaus "teaches that its formulations can be made using compression followed by heating." *Id.* at 10. Specifically, Defendant points to passages of Bartholomaus that refer to "subsequent exposure to heat." (DTX-010 at [0065], [0067]). In fact, Bartholomaus notes, "In direct tableting with subsequent exposure to heat, the formed tablets are briefly heated at least to the softening temperature . . . and cooled again." (*Id.* at [0067]).

[5] This issue relates to both of the differences between the claims and the prior art noted previously. I discuss whether the experimentation would be routine when discussing the second difference of time and temperature ranges. For the purposes of reasonable expectation of success, I only ask whether a POSA could reasonably expect to make hardened tablets by combining Bartholomaus and McGinity at the claimed times and temperatures.

Plaintiffs argue that there could not have been a reasonable expectation of success in arriving at the claimed invention. Plaintiffs criticize Dr. Appel's testimony as conclusory (D.I. 106 at 18) and the passages about subsequent exposure to heat from Bartholomaus as "generic." (*Id.* at 8-9). Plaintiffs point to testimony by Dr. Richard Mannion, a named inventor on each of the Abuse-Deterrent Patents, that he had reasons to doubt that the method would work. (*Id.* at 19). Specifically, Dr. Mannion testified that heating the tablets without compression might cause them to change shape or stick together. (Tr. at 320:1-18).[6] Plaintiffs also note that Dr. Appel's trial demonstrative does not suggest the same time and temperature ranges disclosed in the patent. They argue that this indicates that a POSA could not have reasonably expected success. (D.I. 106 at 19-20).

"Obviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988). I think there is a reasonable expectation of success in producing a hardened tablet from sequential compression and then heating of PEO. I am persuaded by Dr. Appel's testimony that a POSA would understand that applying heat to melt PEO would cause it to harden. I think a POSA could reasonably expect similar success by simply changing the heating tool.

I also find that Bartholomaus's discussion of subsequent exposure to heat contributes to a reasonable expectation of success—a POSA would expect, upon reading Bartholomaus, to be able to achieve similar results with other heating methods. The statement in Bartholomaus is

---

[6] Dr. Mannion also testified more generally about challenges associated with PEO tablets, including achieving the same extended release profile as original OxyContin (Tr. at 308:16-25) and abuse by hot water extraction. (Tr. at 310:12-311:7). I do not treat this testimony as part of the reasonable expectation of success analysis because it does not relate to claimed aspects of the invention. The patents do not claim a particular extended release profile, nor do they claim tablets that cannot have their contents extracted with hot water. I do address this testimony as part of the secondary consideration of skepticism, *infra* p. 24.

generic, as Plaintiffs contend, but I find it nevertheless sufficient to support a POSA's expectations. Plaintiffs argue that the sentence in question "makes no sense" because the phrase "cooled again" suggests some undisclosed "prior heating step." (D.I. 106 at 8). I disagree. Just as one might say, "I threw a boomerang, and it came back again," having only thrown the boomerang once, saying that tablets have been "heated . . . and cooled again" seems to be a commonplace, if somewhat vernacular, construction in English.

I do not think that Dr. Mannion's testimony about his own expectations outweighs Dr. Appel's testimony about a POSA's. It is possible that heating tablets without simultaneously compressing them could change their properties, causing some of the problems Dr. Mannion listed. It is also possible that applying heat with an oven rather than with the equipment used by Bartholomaus or McGinity would simply not work. Neither of these possibilities seem likely given Dr. Appel's credible testimony. I appreciate that the prior art does not support a guarantee of success—but the law does not require a guarantee. I was not persuaded, based on Dr. Mannion's testimony about his concerns as an individual fact witness, that a POSA could not still reasonably expect the process to produce hardened tablets.

Plaintiffs' argument about Dr. Appel's trial demonstrative seems irrelevant. I think the demonstrative was clearly intended as an example of how generally to find optimal ranges through experimentation. It was not intended to be indicative of how a POSA would approach the specific task of combining Bartholomaus and McGinity with the Oven Art. Further, there is no need to show that a POSA would know the precise temperatures and times in the patent before trying the method—only that a POSA might reasonably expect to achieve success in that range. *See Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1381 (Fed. Cir. 2021) (noting that obviousness does not require a showing that "a skilled artisan would have

precisely predicted" the claimed dosage of a drug, merely a showing of "a reasonable expectation of success in achieving the specific invention claimed"). Here, common sense, as well as the Oven Art, would suggest that heating times in ovens might be longer than, for example, the times in Bartholomaus, which heated through direct contact. Unlike in *Teva v. Corcept*, nothing in the prior art taught against the times and temperatures in the Abuse-Deterrent Patents. *See id.* at 1379-80.

In sum, I find there was clear and convincing evidence that a POSA would reasonably expect to produce hardened tablets by heating PEO tablets to their melting points in an oven. Further, I find a POSA might reasonably expect the optimal heating times for its combined process to align with those in the patent.

2. Time and Temperature Ranges

I turn now to the second difference between the prior art and the claims at issue: the curing times and temperatures disclosed in the patents. Of the three asserted claims, two claim curing temperatures of 70° C to 85° C, while the third claims 65° C to 90° C. (Mannion '933 patent at 159:21-22; '808 patent at 159:62-63; '886 patent at 172:30). All three claim heating times from ten minutes to ten hours. (Mannion '933 patent at 159:22-23; '808 patent at 159:63-64; '886 patent at 172:31). The times taught in Shao overlap with the time ranges in the patents, but Shao does not use PEO. (DTX-011 at 0002). The temperatures in Bartholomaus and Omelczuk are consistent with those in the asserted claims, but Bartholomaus teaches shorter and Omelczuk longer heating times. (DTX-010 at [0117]; DTX-014 at 0002). Because McGinity teaches melting the PEO, its temperatures are also consistent with those in the patent. (DTX-009 at 13:1-13).

Defendant argues that the times and temperatures in the patent are the product of routine experimentation. Thus, even though the exact ranges and combinations claimed are not present in the prior art, they can be found obvious. Dr. Appel testified regarding how a POSA would conduct these routine experiments to find an optimal range. (Tr. at 232:21-235:2). Plaintiffs respond that more than routine experimentation is required because of the large range of possible times and temperatures.

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges [of a result effective variable] by routine experimentation." *In re Applied Materials, Inc.*, 692 F.3d 1289, 1295 (Fed. Cir. 2012) (quoting *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955)). Plaintiffs do not challenge the idea that time and temperature are result-effective—that is, that they "would . . . have been recognized by one of ordinary skill to affect a particular result." *Id.* at 1296.

I am persuaded by Dr. Appel's testimony that testing the curing procedure for various periods of time is simple and routine. Her testimony aligns with common sense. Plaintiffs have not offered any contrary evidence that arriving at a range of ten minutes to ten hours would be beyond the routine skill and creativity of a POSA.

On the whole, I am persuaded that Defendant has presented clear and convincing evidence the patents are obvious over the prior art of Bartholomaus, McGinity, and the Oven Art. The two primary differences between the patent and the prior art can be overcome by combining the prior art references and engaging in routine experimentation. Defendant offered clear and convincing evidence that a POSA would be motivated to combine the references and would have had a reasonable expectation of success in doing so. Next, I turn to secondary considerations of nonobviousness.

3. Secondary Considerations

Plaintiffs have offered evidence of four secondary considerations of nonobviousness: unexpected results, commercial success, skepticism, and failure of others. A patentee is not required to present evidence of secondary considerations. *See Prometheus Lab'ys., Inc. v. Roxane Lab'ys., Inc.*, 805 F.3d 1092, 1101-02 (Fed. Cir. 2015). There must be enough evidence, however, for a finding that a given secondary consideration exists by a preponderance of the evidence. *See Apple Inc. v. Samsung Elecs. Co., Ltd.*, 839 F.3d 1034, 1053 (Fed. Cir. 2016) (en banc). If there is, then the probative value of each secondary consideration will be considered in light of the evidence produced. That does not mean, though, that the burden of persuasion on the ultimate question of obviousness transfers to the proponent of the secondary consideration. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1359 (Fed. Cir. 2007). That burden stays always with the patent challenger. *Id.* at 1359-60.

a. Unexpected Results

"In considering unexpected results, courts ask whether 'the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected.'" *Forest Lab'ys., LLC v. Sigmapharm Lab'ys., LLC*, 918 F.3d 928, 937 (Fed. Cir. 2019) (quoting *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995)). These results support a conclusion of nonobviousness where "[t]he unexpected properties of the claimed formulation, even if inherent in that formulation, differ in kind from the prior art." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1307 (Fed. Cir. 2015) ("*Allergan v. Sandoz II*"). "[E]vidence of unexpected results and other secondary considerations will not necessarily overcome a strong prima facie showing of obviousness." *Sud-Chemie, Inc. v. Multisorb Techs.*, 554 F.3d 1001, 1009 (Fed. Cir. 2009).

Plaintiffs argue that the decrease in tablet density caused by their novel manufacturing process enhanced the abuse-deterrent properties of the tablet. Plaintiffs contend that even though the decrease in density is not claimed, its unexpectedness may still support nonobviousness under *Allergan v. Sandoz II*. (D.I. 106 at 20). Plaintiffs' fact witness Dr. Mannion testified that the Abuse-Deterrent Patents' specifications describe determining a tablet's density because a more porous tablet would be "potentially, more resistant to abuse." (Tr. at 326:2-11). Plaintiffs' expert Dr. Bley likewise testified that a more porous tablet could gel more quickly if it were crushed, making it more difficult to abuse by injection or inhalation. (*Id.* at 403:24-407:7). Plaintiffs also note that the patent examiner cited the surprising decrease in density as a reason for allowing the claims. (D.I. 89-1 ¶ 140).

Defendant does not seem to dispute that the decrease in density was unexpected. Dr. Appel agreed that curing a tablet usually results in an increase in density. (Tr. at 264:4-25). However, Defendant argues that the decrease in density does not contribute to abuse deterrence and is therefore irrelevant to obviousness. (D.I. 109 at 8). Dr. Appel provided testimony that in other contexts, a decreased density in a gel could lead to faster drug release, and that it was unclear that the decrease in density from the patented process had any significant impact. (Tr. at 675:1-676:1).

While I find that Plaintiffs have established by a preponderance of the evidence the existence of unexpected results, I do not find that the nature of these results is sufficient to undermine Defendant's clear and convincing evidence of obviousness. Specifically, I am not persuaded that Plaintiffs have established by a preponderance of the evidence that the decrease in density constituted a "superior property or advantage." *Forest Lab'ys*, 918 F.3d at 937. The testimony on the impact of a decrease in tablet density was too speculative for me to credit Dr.

Bley's opinions above Dr. Appel's—at most, they seem to be in equipoise. Further, even if Plaintiffs had proven that the decrease in density was beneficial to abuse-deterrence, any increased gelling benefit the decrease in density might offer would not alone undermine the clear and convincing evidence that the invention's claimed properties are obvious.

b. Commercial Success

"Commercial success is relevant because the law presumes an idea would successfully have been brought to market sooner, in response to market forces, had the idea been obvious to persons skilled in the art. Thus, the law deems evidence of (1) commercial success, and (2) some causal relation or 'nexus' between an invention and commercial success of a product embodying that invention, probative of whether an invention was nonobvious." *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1376 (Fed. Cir. 2005). When others are "legally barred from commercially testing" the ideas of the claimed invention, "[f]inancial success is not significantly probative of that question." *Id.* at 1377. Even when commercial embodiments of the invention enjoy commercial success, the "failure to link that commercial success to the features of [the] invention that were not disclosed in [the prior art] undermines the probative force of the evidence." *Asyst Techs., Inc. v. Emtrack, Inc.*, 544 F.3d 1310, 1316 (Fed. Cir. 2008).

Plaintiffs' expert, Mr. Arun Sharma, testified that OxyContin was and has continued to be the most commercially successful extended-release opioid in the United States. (Tr. at 359:23-25, 368:11-15). Plaintiffs argue that OxyContin's dominance of the extended-release opioid market is due to its combination of "Original OxyContin's medical advantages to patients, along with the additional public-health benefits of being abuse deterrent." (D.I. 106 at 21-22). Plaintiffs contend that because of the FDA and the public's desire for abuse-deterrent properties, "[a]bsent [the abuse-deterrent] features, there would be no OxyContin and no commercial success at all."

(*Id.* at 22). They also argue, citing only to other district court cases, that Accord's choice to file an ANDA for OxyContin, rather than for another opioid, and rather than developing their own formulation, is "strong evidence of commercial success." (*Id.* at 21).

Defendant argues that Plaintiffs have shown no nexus between OxyContin's commercial success and the asserted claims. (D.I. 109 at 8-9). Defendant notes that Mr. Sharma admitted on cross-examination that he did not specifically consider the claimed features of OxyContin. (Tr. at 382:15-383:5). Defendant's expert, Mr. Ivan Hofmann, also noted that the new formulation replaced the original formulation, with all sales transferred to the new formulation. (*Id.* at 653:3-9).

Based on the testimony of Plaintiffs' and Defendant's experts, I cannot conclude that reformulated OxyContin's commercial success was the result of anything other than Purdue's existing monopoly. Plaintiffs' argument that Original OxyContin would have been withdrawn absent the innovations of the Abuse-Deterrent Patents cannot support a finding of nonobviousness—the argument speaks only to the importance of abuse deterrence, not to its obviousness. I also note that there was no demonstrated increase in the success of OxyContin relative to other opioids when the patented features were introduced. While the abuse-deterrent reformulation clearly did not drive customers away from OxyContin, a lack of commercial failure is not the same as commercial success.

I am also completely unpersuaded by the argument that Accord's choice to file an ANDA for OxyContin in particular could be evidence of OxyContin's commercial success or nonobviousness. The argument requires numerous unfounded assumptions. Further, the argument implies that it ought to be artificially more difficult to challenge a patent on obviousness grounds through ANDA litigation than through other channels.

In all, I do not find that Plaintiffs have proven commercial success due to the claimed features of the invention by a preponderance of the evidence.

c. Skepticism

"Evidence of industry skepticism weighs in favor of non-obviousness. If industry participants or skilled artisans are skeptical about whether or how a problem could be solved or the workability of the claimed solution, it favors non-obviousness." *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1335 (Fed. Cir. 2016).

Plaintiffs offer two examples of skepticism, by Dr. Mannion and by the FDA. Specifically, as I discussed above, Dr. Mannion was skeptical that heating PEO tablets after compression would work. He was concerned they might not hold shape (Tr. at 320:1-18), might not achieve the original extended release profile (*id.* at 308:16-25), and might be abused by hot water extraction (*id.* at 310:12-311:7). The FDA, meanwhile, required postmarketing studies before approving abuse-deterrent labeling. (D.I. 106 at 23). Defendant responds that neither of these instances of skepticism represents the kind of "industry skepticism" used in an obviousness analysis. (D.I. 109 at 8).

I agree with Defendant. Dr. Mannion's own testimony, as a named inventor, would seem to carry limited weight. He does not serve as a stand-in for a POSA, or for the industry. Likewise, the FDA, which is not in the industry, displayed an amount of skepticism commensurate with the fact that this was the first extended-release opioid to receive abuse-deterrent labelling. It seems natural that the FDA, as a regulatory body, would require real world studies before being satisfied that a hard tablet was indeed abuse-deterrent. Therefore, I do not find that Plaintiffs have proven industry skepticism by a preponderance of the evidence.

d. Failure of Others

The failure of others may serve to "negat[e] an expectation of success." *In re Cyclobenzaprine*, 676 F.3d at 1081. "The purpose of evidence of failure of others is to show 'indirectly the presence of a significant defect in the prior art, while serving as a simulated laboratory test of the obviousness of the solution to a skilled artisan.'" *Id.* at 1082 (quoting *Symbol Techs., Inc. v. Opticon, Inc.*, 953 F.2d 1569, 1578-79 (Fed. Cir. 1991)). However, for the failure of others to be probative, it should be the case that "these prior attempts failed because the devices lacked the claimed features." *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1313 (Fed. Cir. 2006).

Plaintiffs note two failures of others: Accord's own attempts to develop an abuse-deterrent oxycodone formulation by acquiring Develco, and Grunenthal's crush resistant technology, which was used in the withdrawn opioid product, Opana ER. (D.I. 106 at 23-24). Defendant responds that its efforts with Develco failed due to difficulties with scaling and production. (Tr. at 674:12-14). It also notes that Opana ER used a different active ingredient, and that it is unclear why Opana ER was withdrawn. (Tr. at 673:7-22).

First, if anything, the production failures of Develco seem to weigh in favor of the production-scale-based motivation to combine that I found above, rather than in favor of the nonobviousness of the patents. Second, I agree with the Defendant that the record is not clear on why Opana was removed from the market. Plaintiffs did not establish by a preponderance of the evidence that Opana's removal was related to its lack of "the claimed features." *Ormco*, 463 F.3d at 1313.[7] Even if Opana was withdrawn because its different manufacturing process made it

[7] I note also that the claims do not specify any particular level of abuse deterrence or ability to withstand crushing forces. I address Plaintiffs' argument that Opana was removed because it was

insufficiently abuse-deterrent, I am not sure that indicates a failure by Grunenthal. Specifically, Grunenthal seemed satisfied with the results of its manufacturing process, as evidenced by the fact that a product made with its technology was released to market. The record does not indicate that Grunenthal tried and failed to make a more abuse-deterrent or otherwise superior product. Thus, this seems to be at most an issue of Grunenthal's standards, and not of a POSA's ability to invent the claimed product. I do not find that these failures—if they are failures—weigh in favor of nonobviousness.

IV. THE LOW-ABUK PATENTS

A. The Asserted Claims

The claims at issue are claims 3 and 11 of the '933 patent and claim 21 of the '919 patent. Claim 3 of the '933 patent and claim 21 of the '919 patent claim pharmaceutical compositions, while claim 11 of the '933 patent is a method claim for preparing such compositions. Claim 3 of the '933 patent depends on claim 1. The two claims read,

> 1. An oxycodone hydrochloride composition, which comprises at least 95% oxycodone hydrochloride, 8α,14-dihydroxy-7,8-dihydrocodeinone, and less than 25 ppm of 14-hydroxycodeinone.
> . . .
> 3. The oxycodone hydrochloride composition of claim 1, having less than 10 ppm of 14-hydroxycodeinone.

('933 patent at 34:27-30, 33-34). Claim 11 of the '933 patent depends on claim 10. Those claims read,

> 10. A process for preparing an oxycodone hydrochloride composition having less than 25 ppm 14-hydroxycodeinone, comprising removing 8α,14-dihydroxy-7,8-dihydrocodeinone from an oxycodone base composition and converting the oxycodone base composition to an oxycodone hydrochloride composition having less than 25 ppm 14-hydroxycodeinone.

---

not sufficiently abuse deterrent, but I am not sure the argument is relevant to the nonobviousness of anything actually claimed by the patents.

11. The process of claim 10, comprising combining hydrochloric acid and the oxycodone base composition in a solvent to form a solution, and isolating the oxycodone hydrochloride composition having less than 25 ppm 14-hydroxycodeinone from the solution.

('933 patent at 34:52-63).

Claim 21 of the '919 patent depends on claim 18. The claims read,

18. A pharmaceutically acceptable formulation comprising oxycodone HCl, 8α,14-dihydroxy-7,8-dihydrocodeinone, and less than 100 ppm of 14-hydroxycodeinone, wherein the ratio of 8α,14-dihydroxy-7,8-dihydrocodeinone to oxycodone HCl is 0.04% or less as measured by HPLC.

. . .

21. The pharmaceutically acceptable formulation of claim 18, comprising less than 15 ppm of 14-hydroxycodeinone.

('919 patent at 36:7-11, 16-17).

B. Findings of Fact

1. The earliest effective filing date of the Low ABUK patents is March 30, 2004. (D.I. 89-1 ¶¶ 13, 16). The Low ABUK patents are entitled to an invention date of June 11, 2003, which is the first time Plaintiffs reduced the complete invention to practice. (Tr. at 510:19-514:8; PTX-641 at 57; *see also* PTX-371).

2. A POSA for the purposes of the asserted claims of the Low ABUK patents is an organic chemist with experience in synthetic and analytical chemistry. Such a person would have knowledge of the publicly-disclosed chemical reactions relevant to the field, how to search the relevant literature, and how to accomplish such chemical reactions. (D.I. 89-1 ¶ 95).

3. Roland Kraßnig et al., *Optimization of the Synthesis of Oxycodone and 5-Methyloxycodone*, 329 Archiv der Pharmazie. 6, 325 (1996) ("Krassnig") is prior art to the asserted patents under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 61; DTX-019). Krassnig teaches that the naturally occurring compound thebaine can be oxidized to form 14-hydroxy, which can be hydrogenated into oxycodone. (DTX-019).

4. U.S. Patent No. 6,177,567 ("Chiu") is prior art to the asserted patents under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 67; DTX-022). Chiu teaches both measuring the 14-hydroxy content of a composition to determine the completeness of hydrogenation with high performance liquid chromatography ("HPLC") and extending hydrogenation if the 14-hydroxy content is higher than desired. (DTX-022 at 15:60-16:4).

5. V. S. Ramanathan et al., *Dihydrocodeine, Dihydrocodeinone, 14-Hydroxydihydrocodeinone & Their Derivatives*, 2 Indian J. Tech. 10, 350 (1964)

("Ramanathan") is prior art under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 72; DTX-023). Ramanathan teaches that the salt 14-hydroxy hydrochloride can be hydrogenated into oxycodone hydrochloride. (Tr. 67:20-69:10).

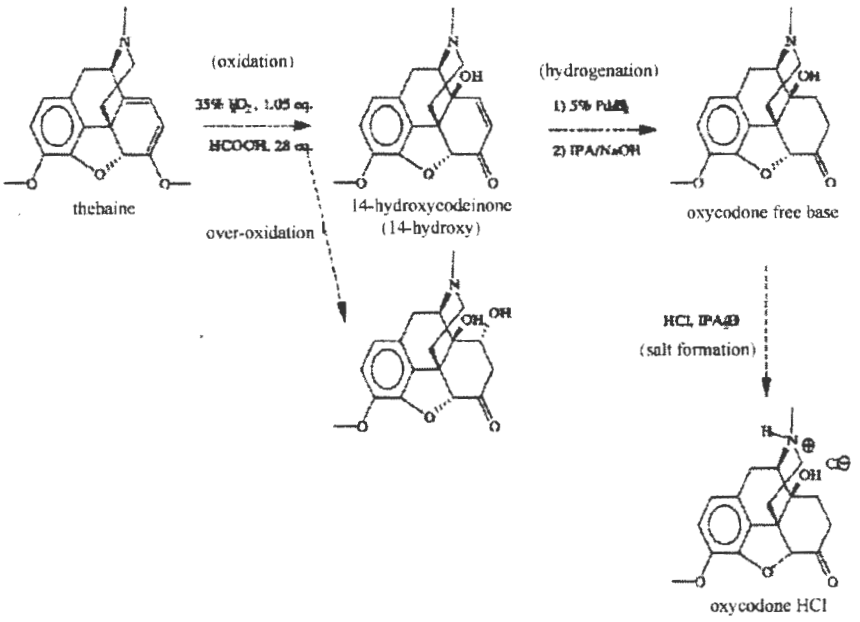
6. Bohumil Proksa, *10-Hydroxythebaine*, 332 Archiv der Pharmazie 10, 369 (1999) ("Proksa") is prior art under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 77; DTX-020). Proksa discloses byproducts from the oxidation of thebaine, including 8β and other uncharacterized compounds. (DTX-020; Tr. at 38:16-39:14, 46:22-47:13).

7. U.S. Patent No. 6,864,370 ("Lin") has a priority date of June 5, 2003. (DTX-024). It is prior art. Lin teaches the synthesis of oxycodone hydrochloride in high yields and purities. *Id.*

8. Ulrich Weiss, *Derivatives of Morphine. II. Demethylation of 14-hydroxycodeinone. 14-Hydroxymorphinone and 8,14-Dihydroxydihydromorphinone*, 22 J. Organic Chemistry 11, 1505 (1957) ("Weiss") is prior art to the asserted patents under 35 U.S.C. § 102(b). (D.I. 89-1 ¶ 81; DTX-021). Weiss discloses that 8β can form from the hydration of 14-hydroxy, and can undergo acid-catalyzed dehydration to form 14-hydroxy in the presence of hydrochloric acid. (DTX-021; Tr. at 50:17-51:7).

9. Ikuo Iijima et al., *The Oxidation of Thebaine with m-Chloroperbenzoic Acid. Studies in the (+)-Morphinan Series. III*, 60 Helvetica Chimica Acta 7, 2135 (1977) ("Iijima") is prior art under 35 U.S.C. § 102(b). (PTX-310). Iijima discloses the ring-opening of an epoxide as a possible mechanism for the formation of 8β. (PTX-310; Tr. at 53:1-55:10).

10. Prior art oxycodone hydrochloride synthesis involved three major reactions: (1) the oxidation of thebaine to form 14-hydroxy (the "oxidation step");(2) the hydrogenation of 14-hydroxy to form oxycodone free base (the "hydrogenation step"); and (3) the addition of hydrochloric acid to the oxycodone free base composition to form oxycodone hydrochloride (the "salt formation step"). (D.I. 89-1 ¶ 98; JTX-004 at Figure 1; JTX-005 at Figure 1; Tr. at 34:7-35:8).



11. The intermediate product 14-hydroxy is an "alpha beta unsaturated ketone" or "ABUK," a class of compounds understood at the time of the invention to be highly reactive and potentially genotoxic. (D.I. 89-1 ¶ 113; Tr. at 59:23-60:9, 465:3-18). By 2000, named inventor Dr. Robert Kupper was concerned that ABUKs, which had certain structural features similar to other, genotoxic compounds, might also be genotoxic, based on his prior experience. (Tr. at 463:24-25, 465:3-18).

12. A POSA would understand that not all the intermediate 14-hydroxy would necessarily be turned into oxycodone during the hydrogenation step. (Tr. at 74:4-74:15). 14-hydroxy remaining after the hydrogenation step would be turned into 14-hydroxy hydrochloride by the salt formation process. (Tr. 69:21-70:5).

13. At least by September 3, 2002, the FDA began requesting that opioid manufacturers either reduce the levels of ABUKs in opioid products to under 10 ppm or provide testing demonstrating that they were not genotoxic. (PTX-560 at P4107528; Tr. at 493:15-494:7). This information went to multiple opioid manufacturers. (Tr. at 493:15-494:7). The FDA also made clear that "the issue is general and will affect all products containing opioid derivatives." (PTX-560 at P4107528).

14. A POSA seeking to modify the three-step prior art oxycodone synthesis process to achieve lower 14-hydroxy levels in the final oxycodone composition would have had two options. First, a POSA could have used the teachings of Ramanathan to hydrogenate the composition again after the salt formation step, which would turn any of the 14-hydroxy hydrochloride into oxycodone hydrochloride. (Tr. at 70:6-71:8). Second, since 14-hydroxy is an intermediate product, a POSA could have tried to intervene during or after hydrogenation to ensure that no 14-hydroxy

would remain in the composition prior to the salt formation step. (Tr. at 74:4-75:4).

15. The first path would not be desirable, because it would be costly, likely reduce yield, and possibly introduce impurities. (Tr. at 73:16-74:3, 587:3-18). A POSA would prefer to solve the problem at an earlier stage. (Tr. at 73:23-25).

16. Taking the second path would cause 14-hydroxy to reappear during the salt formation. A POSA motivated to lower 14-hydroxy levels would attempt to determine why 14-hydroxy was reappearing. (Tr. at 74:4-75:19).

17. 8β,14-dihydroxy-7,8-dihydrocodeinone ("8β") was known in the prior art to form as a byproduct during the oxidation step. (D.I. 89-1 ¶ 78; DTX-020; DTX-021; Tr. at 46:22-47:13).

18. 8α is a stereoisomer of 8β. (D.I. 98, Ex. 1 ¶ 102). 8α had always been present in oxycodone compositions but had not been described prior to the Low-ABUK Patents. (Tr. at 94:19-95:4).

19. A POSA would have contemplated a limited number of reaction mechanisms to explain the presence of 8β. (Tr. at 47:24-48:19, 50:1-50:16, 176:14-177:3). Two likely candidates, which were described in the prior art, would be the ring-opening of an epoxide (Tr. at 47:24-49:25; PTX-310), and the hydration of 14-hydroxy (Tr. at 50:1-51:7; DTX-032). A POSA considering either possibility would also predict the presence of 8α. (Tr. at 51:11-52:25; Tr. 53:1-54:16).

20. A POSA would understand that both 8β and 8α could undergo dehydration reactions to form 14-hydroxy, (Tr. at 76:25-81:25), and that the conditions of the salt formation step would cause such reactions. (Tr. at 101:15-19).

21. A POSA would understand that 8α would dehydrate under milder conditions and more rapidly than 8β, forming more 14-hydroxy more easily. (Tr. at 84:10-19).

22. A POSA would have the knowledge and experience to hypothesize that either 8α, 8β, or both were most likely responsible for the reappearance of 14-hydroxy. (Tr. at 76:16-24, 81:10-25). A POSA would be able to test and confirm this hypothesis through routine experimentation. (Tr. at 77:29-85:2).

23. A POSA seeking to lower 14-hydroxy levels would seek to convert 8α and 8β into 14-hydroxy through dehydration prior to the completion of hydrogenation, so that the resulting 14-hydroxy would then be converted into oxycodone by the hydrogenation. (Tr. at 76:16-77:24, 87:16-88:1). A POSA would have the knowledge and experience to understand from Weiss and Ramanathan how to dehydrate 8β and 8α into 14-hydroxy. (Tr. at 50:6-16, 88:2-11). Dehydration that targeted 8β would automatically convert 8α as well. (Tr. at 100:17-101:3).

24. A POSA would recognize that forcing the dehydration of 8α and 8β either before or during the hydrogenation would be effective. (Tr. at 88:12-89:6). A POSA

would have understood from Chiu that the hydrogenation could be performed in acidic conditions to allow the dehydration of 8α and 8β to occur simultaneously. (Tr. at 89:7-12).

C. Conclusions of Law

1. Invention Date of the Low ABUK Patents

The parties dispute whether the Lin reference, dated June 5, 2003, is prior art to the Low-ABUK Patents. They do not dispute that the Low-ABUK Patents were reduced to practice on June 11, 2003. This would ordinarily make Lin prior art, but "[p]re-AIA section 102(g) allows a patent owner to antedate a reference by proving earlier conception and reasonable diligence in reducing to practice." *Perfect Surgical Techniques, Inc. v. Olympus Am., Inc.*, 841 F.3d 1004, 1007 (Fed. Cir. 2016). "Whether a patent antedates a reference is a question of law based on subsidiary findings of fact." *Id.* at 1009. "An idea is sufficiently definite for conception 'when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue.'" *Creative Compounds, LLC v. Starmark Lab'ys.*, 651 F.3d 1303, 1312 (Fed. Cir. 2011) (quoting *Burroughs Wellcome Co. v. Barr Lab'ys.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994)).

The patent holder has the burden of producing evidence to support an earlier conception. *Mahurkar v. C.R. Bard, Inc.*, 79 F.3d 1572, 1576-77 (Fed. Cir. 1996). Where "a party seeks to prove conception via the oral testimony of a[n] . . . inventor, the party must proffer evidence corroborating that testimony." *Shu-Hui Chen v. Bouchard*, 347 F.3d 1299, 1309 (Fed. Cir. 2003). Specifically, "the inventor must provide independent corroborating evidence in addition to his own statements and documents." *Brown v. Barbacid*, 276 F.3d 1327, 1335 (Fed. Cir. 2002) (cleaned up). The sufficiency of the evidence of earlier conception is determined under the "rule of reason." *Mahurkar*, 79 F.3d at 1577. The "rule of reason" requires "examin[ing] all pertinent

evidence to determine the credibility of the inventor's story." *Brown*, 276 F.3d at 1335 (internal quotations omitted).

Plaintiffs offer testimony by named inventors Mr. Lonn Rider and Dr. Robert Kupper to meet their burden of production. (D.I. 106 at 30-31). They also offer Mr. Rider's lab notebooks and internal communications about the efforts to lower 14-hydroxy levels. (*Id.*). Plaintiffs argue, based on this evidence, that conception of the invention occurred no later than February 6, 2003, the date on which Mr. Rider wrote a memo to his supervisor about his efforts to lower 14-hydroxy levels. (D.I. 107 ¶ 63). Plaintiffs assert that the inventors were diligent after the February 6 conception, and certainly between the operative period of June 5-11, which allows the asserted patents to antedate Lin. (D.I. 106 at 30).

Defendant does not dispute that the Low ABUK Patents are entitled to a priority date of at least as early as June 11, 2003, when the invention was reduced to practice. (D.I. 100 ¶ 53). Defendant provides little argument against the antedating other than to say Plaintiffs are not entitled to a February 2003 invention date. (*Id.*)

Despite Defendant's conclusory response, I do not think that Mr. Rider's and Dr. Kupper's testimony, to the extent that they are corroborated by various documents, satisfy Plaintiffs' burden of production for conception. Dr. Kupper merely testified that as of November 2002, he thought "either 8α or 8β" was likely responsible for 14-hydroxy in the final product. (Tr. at 481:3-482:16). His testimony was corroborated by an internal report, but I do not find that it demonstrates conception of every feature of the claimed invention. (PTX-356). Dr. Kupper did not testify regarding the February 6 memo.

Mr. Rider testified more definitively that as of February he had concluded "[t]hat 8α was the source of the 14-hydroxycodeinone." (Tr. at 504:11-14). Plaintiffs offered Mr. Rider's

verified laboratory notebook and auxiliary data as corroboration. (PTX-352; PTX-354). However, Mr. Rider did not testify as to the interpretation or contents of his notes or the auxiliary data. Meanwhile, his February 6, 2003, memo to his supervisor said that "it [was] difficult to be certain" that 8α was responsible for the challenges in reducing 14-hydroxy, and that it "warrant[ed] further investigation." (PTX-352 at P4193989). The memo does not seem to corroborate Mr. Rider's testimony. It describes "a general goal or research plan" rather than "a specific, settled idea, a particular solution to the problem at hand." *Burroughs Wellcome*, 40 F.3d at 1228.

I conclude that Plaintiffs have not met their burden of producing sufficient, corroborated evidence that the Low-ABUK Patents were conceived of on February 6, 2003. Plaintiffs further did not present evidence of conception on any other date between February 6 and June 11. Therefore, the priority date of the patents remains the uncontested date of reduction to practice, June 11, 2003, and the Lin reference is prior art.

2. Obviousness of the Low-ABUK Patents

The asserted claims of the Low-ABUK Patents differ from each other in scope and content. Claim 3 of the '933 patent requires a composition of at least 95% oxycodone HCl, 8α, and levels below 10 ppm of 14-hydroxy. ('933 patent at 34:27-39, 33-34). Claim 21 of the '919 patent adds the requirement that the ratio of 8α to oxycodone HCl be 0.04% or less, but allows up 15 ppm 14-hydroxy. ('919 patent at 36:7-11, 16-17). Claim 19 of the '933 patent is a method claim. It requires that the final product have less than 25 ppm of 14-hydroxy and be made by a particular process that includes removing 8α from an oxycodone base before salt formation and employing hydrochloric acid in the salt formation step. ('933 patent at 34:52-63).

Broadly, the parties' disputes fall into two categories: the obviousness of low levels of 14-hydroxy and the obviousness of the inventors' discovery of 8α.[8] I address the 14-hydroxy and 8α arguments in turn, noting where they are interrelated.[9]

First, I discuss whether a POSA would have been motivated to achieve low levels of 14-hydroxy by modifying the prior art. "For a patent to be obvious, 'some kind of motivation must be shown . . . so that the jury can understand why a person of ordinary skill would have thought of either combining two or more references or modifying one to achieve the patented method.'" *Shire*, 802 F.3d at 1306 (quoting *Innogenetics, N.V. v. Abbott Lab'ys.*, 512 F.3d 1363, 1374 (Fed. Cir. 2008)). Then, I consider whether a POSA would have been able to do so by combining the teachings of the prior art and engaging in routine experimentation.

Second, I discuss whether the discovery of 8α renders the purified compositions patentable. I consider whether the various 8α limitations were inherently disclosed in the prior art. I also consider whether a POSA would have identified 8α as a matter of course while attempting to lower levels of 14-hydroxy, and whether explicit identification of 8α was necessary to arriving at the rest of the claimed inventions.

For the reasons below, I find the three asserted claims of the Low-ABUK Patents invalid for obviousness under 35 U.S.C. § 103

a. 14-Hydroxy

---

[8] Neither party presents any argument that the 10, 15, and 25 ppm requirements should be analyzed separately. Thus, I consider only the obviousness of levels of 14-hydroxy below 10 ppm, since the other thresholds would seem to follow. The parties likewise do not argue that other claim limitations, such as turning oxycodone free base into a hydrochloride salt or using hydrochloric acid to form a hydrochloride salt, are missing from the prior art or render the invention nonobvious.

[9] Defendant continues to refer to factual findings from *In re OxyContin* in footnotes. (*See, e.g.*, D.I. 99 at 26 n.11). I continue to disregard these findings for the same reasons described in *supra* n.1.

i. Motivation to Lower 14-Hydroxy

Defendant argues that a POSA would have been motivated to modify the prior art as of September 12, 2002, based on a communication from the FDA sent to multiple opioid manufacturers about future ABUK restrictions. (D.I. 99 at 23-24; PTX-560). Plaintiffs as a preliminary matter contend that Defendant waived its argument that the September FDA communication provided a motivation to modify, because Defendant "never identified that date or a purported evidentiary basis for it during fact or expert discovery, and it contradicts Accord's issues in the Pretrial Order." (D.I. 106 at 33). Plaintiffs assert that Accord changed its position about the timing of the motivation to combine because Plaintiffs successfully proved an earlier invention date (June 11, 2003) at trial. (*Id.* at 34). Defendant responds that it has always stated that the FDA provided the motivation and that Plaintiffs suffered no prejudice from Defendant's not specifically naming September 12, 2002, since testimony and evidence offered by Plaintiffs alluded to FDA communications about ABUKs as early as January 2003, which was still before June 11. (D.I. 109 at 11 & n.5).[10]

I do not find that Defendant waived the argument to a September 2002 motivation to combine. As far as I can tell, Defendant did not identify any specific date for a motivation to modify in the Pretrial Order, so failure to identify September 12 does not seem like a problem. Defendant did identify the FDA as the source of the motivation, which is consistent with its current argument. (D.I. 89-3 ¶ 74). While Defendant referred to "2003 and 2004" as the time period over which the FDA "became concerned," (*id.* at ¶ 11), I do not think this vague language

[10] Defendant also claims in a footnote that Plaintiffs only started arguing for the June priority date after Defendant submitted its Proposed Findings of Fact. (D.I. 109 at 11 n.5). It is not clear to me whether this is the case, though I note that Plaintiffs did not identify June 11 as a possible invention date in their statement of issues of fact. (*See* D.I. 89-2). I do not think it matters. If it is the case, it would only support my finding of no waiver.

rules out the possibility that murmurings about ABUKs in the industry began in late 2002 or early 2003—especially when evidence and testimony by Plaintiffs' witness support that idea. In the single case cited by Plaintiffs, a party did not express any intent to raise the issue of an earlier priority date until post-trial briefing. *UCB, Inc. v. Watson Lab'ys*, 2017 WL 11646645 at *40 (D. Del. Nov. 14, 2017). Here, the POSA's motivation was always at issue—as Plaintiffs acknowledge. (D.I. 89-2 ¶ 32).

Defendant's argument for a September 2002 motivation to combine relies on testimony by Plaintiffs' witness, Dr. Kupper. Dr. Kupper testified regarding an internal Rhodes email on September 12, 2002, which he agreed indicated that the "FDA was concerned about ABUK impurities." (Tr. at 493:20-22). The email stated that the FDA wanted Purdue to reduce morphinone, another ABUK, to levels of "less than 10 parts per million (ppm), or 0.001%" in the opioid product Palladone. (PTX-560 at P4107528). The email mentioned that the "issue is general and will affect all products containing opioid derivatives." (*Id.*). Dr. Kupper testified that he understood from the email that other manufacturers had also been told they would have to lower ABUK levels. (Tr. at 494:5-7). Defendant's expert, Dr. Stephen Martin, testified that "[C]ompounds related to [ABUKs] were long known . . . to be genotoxic. So there would always be some kind of concern about reactivity of this functional group." (Tr. at 60:6-60:9).

Plaintiffs argue that because the FDA did not specifically require ABUK levels below 10 ppm until December 2003, a POSA would not have been motivated to achieve such levels until December 2003 at the earliest. (D.I. 106 at 34-35). As for the 2002 communication, Plaintiffs argue that a subsequent internal email indicated that Purdue was proceeding under the assumption that existing approved products would not be affected. (D.I. 106 at 34; D.I. 107 ¶ 82). Plaintiffs also note that the 2002 communication related to "lowering the amount of a

different ABUK (morphinone) in a different unapproved product (Palladone) that had a different active ingredient (hydromorphone)." (D.I. 106 at 34; PTX-560 at P4107528). Plaintiffs argue that Purdue initially objected to the stringent requirement by proposing a more relaxed requirement of 0.05% (500 ppm) and stating it would attempt to test whether ABUKs were genotoxic. (D.I. 106 at 34; PTX-560 at P4107529).

FDA communications can "introduce[] a market force incentivizing" a particular invention. *Endo Pharms., Inc. v. Actavis LLC*, 922 F.3d 1365, 1376 (Fed. Cir. 2019). Indeed, a requirement that a product meet a particular threshold is likely to be a strong market force, since failure to meet that requirement would exclude the product from the market completely, rather than merely making it less competitive. As I also noted in my discussion of the Abuse-Deterrent Patents, *supra* p.12, "it often may be the case that market demand, rather than scientific literature, will drive design trends." *KSR*, 550 U.S. at 419. Thus, an FDA letter creating market forces may serve as a motivation to combine.

Defendant's evidence is clear and convincing. I think an awareness that the FDA might impose low-ABUK requirements would immediately motivate a POSA to seek a way to lower the levels of ABUKs in a pharmaceutical product. Even if the requirements were in the future, I think a POSA would be motivated to get ahead of the requirements. Further, the knowledge that the FDA was considering a threshold of 10 ppm would motivate a POSA to try to achieve that level in particular. It is true that the 2002 FDA email concerns a different product, but the email also clearly says, "While this was a Palladone-specific teleconference, the FDA informed us that this issue is general and will affect all products containing opioid derivatives." (PTX-560 at P4107528). Indeed, when the email was forwarded to Dr. Kupper, it was with an allusion to that sentence and its "implications." (*Id.*). Dr. Kupper further admitted on cross examination that he

"understood from [the email] that the FDA had communicated that same information to other manufacturers" (Tr. at 494:5-7), demonstrating that a POSA, and not just a Purdue or Rhodes employee, would have been motivated.

I am not persuaded by Plaintiffs' observation about Purdue's understanding that any future requirements would not affect approved products. The inquiry is not what Purdue understood from the communication but what a POSA would have understood. I also do not find Purdue's attempt to negotiate with the FDA on the strictness of the requirements to weigh against a POSA's motivation to modify the prior art. Purdue's response suggesting a 500 ppm threshold and proposing continued testing to determine toxicity suggests to me only that Purdue sought to keep its options for solving the problem open. Pursuing all available options seems like the prudent response for a company facing new regulations on a highly profitable class of products. In the absence of FDA acceptance of a higher threshold, I would still expect a POSA to prepare for the possibility of a lower threshold of 10 ppm. Likewise, the possibility of testing ABUKs for toxicity as an alternative option would not reduce a POSA's motivation to pursue other solutions.

Although not the focus of Defendant's argument, testimony at trial also indicated that an understanding or suspicion that ABUKs were toxic existed even before September 2002. Dr. Martin testified that a POSA would potentially be concerned about ABUKs anyway given their structure. (Tr. at 59:23-60:18). Dr. Kupper mentioned that he first became concerned about ABUKs based on their molecular structure. (Tr. at 464:24-465:15). Certainly, a statement by Dr. Kupper, an inventor on the patent, is not on its own probative of a POSA's motivation to modify the prior art. However, Dr. Kupper's concerns were consistent with Dr. Martin's expert testimony. I am not convinced that concerns about potential toxicity on their own would

motivate a POSA to incur the cost of developing a purified product. I do, however, think that such concerns in the field would serve to make the possibility of future FDA requirements a credible, and perhaps even expected, threat, thus making the motivation to combine all the stronger.

On the whole, I find that Defendant presented clear and convincing evidence that a POSA would have been motivated to modify the prior art process of synthesizing oxycodone to achieve ABUK levels below 10 ppm.

ii. Routine Experimentation

I now turn to whether, provided with this motivation, a POSA could reasonably have expected to arrive at the asserted claims through routine experimentation. Defendant asserts that a POSA would have two clear starting points: either adding a final hydrogenation step to remove 14-hydroxy hydrochloride or attempting to remove 14-hydroxy at an earlier stage. (D.I. 99 at 26, 30). Dr. Martin testified that pursuing the latter path would lead a POSA to try to ensure that all 8α and 8β in the composition dehydrated into 14-hydroxy before the hydrogenation step was complete. (*Id.* at 30). Defendant argues that because achieving the claimed invention from either starting point would require only routine techniques, a POSA would have a reasonable expectation of success. (D.I. 109 at 12).

Plaintiffs respond that a POSA would not have a reasonable expectation of success through the first option of adding a final hydrogenation step. (D.I. 106 at 36). Plaintiffs' expert witness, Dr. James Wuest, testified that a POSA would know that adding a hydrogenation step would reduce yield and potentially introduce impurities. (Tr. at 587:6-18). Plaintiffs argue that a POSA pursuing the second option of earlier removal of 14-hydroxy would be quickly stymied by a lack of knowledge of 8α. (D.I. 106 at 37-38). Specifically, they argue that a POSA would not

be led to ensure the dehydration of 8α and 8β because a POSA would not know that 8α was the source of the problem and would not think that 8β could be. Without such knowledge, Plaintiffs contend, the POSA could not have a reasonable expectation of success at lowering 14-hydroxy levels by ensuring the dehydration of 8α and 8β. (*Id.*).

"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp." *KSR*, 550 U.S. at 421. Thus, evidence of obviousness may be sufficient when "it indicates that the possible options skilled artisans would have encountered were 'finite,' 'small,' or 'easily traversed,' and that skilled artisans would have had a reason to select the route that produced the claimed invention." *In re Cyclobenzaprine*, 676 F.3d at 1072 (quoting *Ortho-McNeil Pharm., Inc. v. Mylan Lab'ys., Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008)). An invention is obvious over prior art if "the order and detail of the steps, if not already known, would have been discovered by routine experimentation while implementing known principles." *Merck Sharp & Dohme Corp. v. Hospira, Inc.*, 874 F.3d 724, 730 (Fed. Cir. 2017). The obviousnesss inquiry "not only permits, but *requires*, consideration of common knowledge and common sense." *Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013) (quoting *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1367 (Fed. Cir. 2006)).

I was persuaded by Dr. Martin's testimony that a POSA seeking to reduce 14-hydroxy levels would have a finite, small, and easily identified set of options. Dr. Wuest never testified, and Plaintiffs never argued, that a POSA would have had other options for reducing 14-hydroxy or that a POSA would not have known where to start. Based on both Dr. Wuest's and Dr. Martin's testimony, however, I am skeptical that a POSA would have pursued adding an extra

hydrogenation step to directly convert 14-hydroxy hydrochloride into oxycodone hydrochloride. Both testified that doing so would be expensive and potentially introduce other impurities. Plaintiffs argue that this cuts against Defendant's theory of obviousness. I disagree. If anything, a POSA's disinclination for adding an extra hydrogenation step would only further narrow the set of feasible options.

I find that Defendant has presented clear and convincing argument that a POSA would try to intervene at an earlier stage of the oxycodone synthesis to ensure that all 14-hydroxy was converted to oxycodone prior to salt formation. I am also persuaded that a POSA would have the knowledge and skill to do so successfully. 14-hydroxy was a known intermediate product. It seems well within a POSA's skill to more completely eliminate a known byproduct with a known method of conversion. It is true that this path would not immediately succeed—as the inventors themselves found, 14-hydroxy would reappear. However, Dr. Martin clearly testified that such a roadblock would be within the skill of a POSA to address.

Dr. Martin clearly and convincingly outlined that a POSA would have been trained to propose reaction mechanisms to explain the results of their experiments. (Tr. at 47:17-48:5). Dr. Wuest agreed that he trained students to propose reaction mechanisms. (Tr. at 602:16-603:2). Dr. Martin further testified, and Dr. Wuest agreed, that the possible reaction mechanisms at issue in this case would have been familiar to a POSA. (Tr. at 48:6-50:16, 603:3-8, 605:2-8, 608:23-609:6). Dr. Martin explained how a POSA would "analyze the reaction mixture," a procedure he characterized as routine, to test the limited number of possibilities in order to determine the source of the 14-hydroxy problem. (Tr. at 77:25-78:17, 79:17-81:9). As I discuss further below, Dr. Martin explained that solving a problem that the POSA now understood would be well within the POSA's skill. (Tr. at 87:16-89:12).

Plaintiffs do not offer any path along which a POSA would be led astray. Dr. Wuest only testified that no prior art reference was on its own a perfect fit and asserted that a POSA would face "obstacles." (Tr. at 600:13-14). As far as I can tell, Plaintiffs' reasoning leads to the conclusion that a POSA would simply have given up in the face of 14-hydroxy's reappearance. However, given my finding that a POSA would have been motivated to solve the issue of 14-hydroxy, I think a POSA would have "good reason to pursue the known options within his or her technical grasp" and to modify the prior art in readily apparent ways. *KSR*, 550 U.S. at 421. Therefore, I find Dr. Martin's testimony as to what a POSA would have done more credible. Further, because only routine techniques and commonly possessed training would be required, I find that the POSA would have had a reasonable expectation of success.

Plaintiffs also make something akin to a "failure of others" argument to "negat[e] an expectation of success."[11] *In re Cyclobenzaprine*, 676 F.3d at 1081. Plaintiffs presented evidence that oxycodone HCl manufacturer Noramco received a communication from the FDA in December 2003 requiring lower levels of 14-hydroxy. (DTX-115 at 0002). In response, Noramco characterized the task as "a technical and scientific challenge." (*Id.*). Plaintiffs introduced deposition testimony from earlier litigation indicating that Noramco did not finish developing its low-ABUK oxycodone until 2007, despite the project starting in 2003. (Tr. at 548:17-20). Defendant responds that Plaintiffs' evidence "shows Noramco was merely cautious." (D.I. 109 at 19).

[11] Although "failure of others" is usually a secondary consideration of nonobviousness, *Graham*, 383 U.S. at 17-18, Plaintiffs do not present this evidence as an independent secondary consideration. Instead, they characterize Noramco's failure as evidence that a POSA would not have had a reasonable expectation of success. (D.I. 106 at 39-40; Tr. at 754:19-24). Some cases have treated failure of others in this way. *See Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1354 (Fed. Cir. 2003).

I agree with Defendant. I do not find the Noramco evidence sufficient to contradict Dr. Martin's testimony that a POSA would have had a reasonable expectation of success. Noramco's characterizing the task as a challenge, like Purdue's earlier suggestion of a higher ABUK content threshold, seems like the expected and prudent behavior of a company facing a likelihood of stricter regulations. Noramco's desire to keep its options open seems reasonable and expected. The fact that Noramco took years to develop low-ABUK oxycodone is far from probative. The record, including the video deposition testimony by Noramco employees, is simply not clear on whether the time-consuming aspects of development had anything to do with the claimed invention. I do not find that Dr. Martin's testimony is contradicted by a single, incomplete anecdote that Noramco protested the requirements and took a long time to develop the product.

b. 8α

I now turn to the issue of whether the disclosure of 8α, either as an independent claim limitation not disclosed in the prior art, or as a necessary step to reaching the 14-hydroxy limitations, renders the patent nonobvious. Because I find that the discovery of 8α itself would have been routine for a POSA, I do not find that the explicit disclosure of 8α renders the claims patentable.

Defendant argues that although no claim limitations relating to 8α are in the prior art, 8α was inherently present in prior art oxycodone compositions. (D.I. 99 at 27). Defendant argues further that identifying 8α was itself a routine endeavor, and that a POSA could have arrived at the claimed inventions without discovering 8α at all. (D.I. 99 at 36, 38).

Plaintiffs respond that 8α is not merely an inherent property of oxycodone formulations but rather a "foundational discovery" in achieving low-ABUK oxycodone. (D.I. 106 at 32). Plaintiffs assert that the 8α limitations consequently "cannot be viewed in isolation from the

remainder of the claims." (*Id.*). They reason that the explicit disclosure of 8α renders the invention patentable, even if 8α can be found inherently in the prior art. (*Id.* at 30). Plaintiffs also note the field's "longstanding examination of oxycodone and its impurities," suggesting that if 8α were obvious it would already have been discovered. Plaintiffs further repeatedly note that 8α's level of reactivity is "surprising." (*See, e.g., id.* at 30). They argue that a POSA could not have known how reactive 8α would be, and without that knowledge, could not have realized that 8α needed to be removed in the way the inventors did. (*Id.* at 32).

"[I]nherency may supply a missing claim limitation in an obviousness analysis." *Par Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1194-95 (Fed. Cir. 2014). However, it "may not be established by probabilities or possibilities." *Id.* (quoting *In re Oelrich*, 666 F.2d 578, 581 (C.C.P.A. 1981)). A limitation "necessarily must be present" to be inherent. *Par Pharm.*, 773 F.3d at 1196. It is true that when "[t]he unexpected properties of the claimed formulation . . . differ in kind from the prior art," the formulation may be nonobvious. *Allergan v. Sandoz*, 796 F.3d at 1307. However, "merely recit[ing] the unknown properties of an otherwise obvious formulation" is not sufficient. *Id.*

Because each of the asserted claims has different 8α-related limitations, I consider the claims one by one.

Claim 3 of the '933 patent requires only that 8α be present in the composition. Plaintiffs do not dispute that 8α was present in prior art compositions. (*See* D.I. 106 at 27-28). Therefore, combined with my findings about 14-hydroxy above, I find that Defendant presented clear and convincing evidence that Claim 3 is obvious. Plaintiffs object to the idea that finding 8α inherently present in the prior art is sufficient to establish a conclusion of obviousness because "it was only after the inventors identified 8α and its surprising properties that they were able to

achieve the high purity and low levels of 14-hydroxy as claimed." (D.I. 106 at 32-33). However, I am persuaded by Defendant's evidence that the identification of 8α itself was merely routine. As a factual matter, I find that a POSA would have had the knowledge and skill not only to identify 8α and determine its role but also to achieve low-ABUK levels without even identifying 8α. Further, claim 3 in particular does not contain any reference to the role or purpose of 8α in the composition. The patent does not claim the fact that 8α converts to 14-hydroxy. Plaintiffs cite to no law that indicates I should consider claim 3 to encompass that discovery. They simply repeatedly state that the claim "cannot be viewed in isolation." (*Id.* at 25, 32).

Plaintiffs say that Defendant's theory that a POSA would inevitably discover 8α is "premise[d] . . . on the teachings of the patent." (*Id.* at 38). However, Plaintiffs' argument is equally tautological—since Plaintiffs never identified how a POSA could have been led astray, Plaintiffs' argument seems to simply be that a POSA would not have discovered 8α because 8α was nonobvious. For the purposes of determining that a POSA would have the knowledge and skill to discover 8α, I look to testimony provided by both sides' experts. The experts' testimony persuades me that a POSA would have quickly postulated and easily confirmed the existence of 8α. Plaintiffs once again would have a POSA give up rather than engage in routine experimentation, even in the face of external motivation.

Plaintiffs' protests that "[t]here is no evidence that anyone was trying to reduce the level of 8β to achieve low 14-hydroxy" miss the point. (D.I. 107 ¶ 87). As discussed previously, the motivation to achieve low 14-hydroxy came from the FDA in 2002, so one would not expect evidence that anyone was trying to reduce the level of 8β before then. There is no evidence in the record of what anyone other than the inventors was actually doing after 2002, so a lack of evidence that anyone was trying to reduce 8β is unremarkable. To the extent that Plaintiffs use

this observation to argue that a POSA would have known 8β could not possibly be the source of the problem (D.I. 106 at 38), I think that a POSA with such a belief would only be led more inevitably toward identifying 8α as a source of 14-hydroxy. As with the choice between an extra hydrogenation step and an earlier intervention, the improbability of one explanation for 14-hydroxy's reappearance would only serve to further narrow a POSA's limited set of viable options. I conclude that a POSA would seek to dehydrate 8α and 8β based on the credible testimony of Dr. Martin, not based on any evidence or lack thereof of what a particular pharmaceutical manufacturer tried.

I likewise do not find Plaintiffs' arguments about the prior art studies of impurities persuasive, since those studies did not purport to be exhaustive. Proksa, for example, explicitly notes that it only identified two of the impurities detected in the synthesis of oxycodone. (DTX-020 at 0001). Dr. Martin testified that a POSA would know how to analyze a mixture and identify its component compounds using HPLC, mass spectrometry, or NMR spectrometry. (Tr. at 79:17-81:9). Plaintiffs presented no evidence that 8α would not be identifiable with these routine techniques if a POSA bothered to try. Likewise, there was no evidence presented to suggest that anyone, POSA or otherwise, tried and failed to identify 8α.

8α's surprising reactivity also does not change the balance.[12] Both experts testified that a POSA would have expected 8α to be more reactive than 8β. (Tr. at 84:10-19, 575:5-24). The degree to which 8α was more reactive may have been surprising, but even if 8α were only as reactive a POSA would have expected, Dr. Martin's testimony convincingly indicates that a

[12] Surprising or unexpected results, like failure of others, are ordinarily secondary considerations of nonobviousness. *Sud-Chemie*, 554 F.3d at 1009. However, Plaintiffs do not present them as such. Again, I address the argument that Plaintiffs actually make: that because 8α's surprising reactivity was what kept 14-hydroxy levels high, a POSA would not have thought to look to 8α as the problem.

POSA would still have gone down the path that led to the invention. Said another way, 8α's surprising reactivity made it a surprisingly important component of the solution to lowering 14-hydroxy, but a POSA would have recognized it as a component of the solution even without the reactivity.

Claim 21 of the '919 patent additionally imposes a purity requirement that "the ratio of 8α,14-dihydroxy-7,8-dihydrocodeinone to oxycodone HCl is 0.04% or less as measured by HPLC." ('919 Patent at 36:16-17). Defendant argues that equally low levels were inherently disclosed in Lin. (D.I. 99 at 28-29). Defendant also argues that even if not disclosed in Lin, the low levels would still have been obvious. (D.I. 106 at 19). Plaintiffs note that the parties stipulated, "The prior art does not disclose, expressly or inherently, a composition wherein the ratio of 8α to oxycodone is 0.04% or less as measured by HPLC." (D.I. 89-1 ¶ 102). Plaintiffs also argue that Defendant cannot rely on Lin since doing so requires assumptions and is "pure speculation." (D.I. 106 at 32).

I think that the stipulation in the parties' Joint Statement of Uncontested Facts is conclusive on the issue of whether the limitation was inherently disclosed by Lin or any other reference—I must take as a fact that no prior art reference disclosed 8α levels below 0.04%. However, I still find that the limitation on the levels of 8α is obvious. As Plaintiffs themselves argue, "the amount of 14-hydroxy depends on the levels of 8α, and the levels of 8α, 14-hydroxy, and other unintended side-reaction impurities can affect oxycodone purity." (D.I. 106 at 25). In fact, Dr. Martin testified that a POSA, having found that any 8α in the composition could be converted to 14-hydroxy during salt formation, would seek to reduce the ratio of 8α to oxycodone to well below 0.04%. This would be necessary to ensure the low 14-hydroxy levels that the FDA was seeking. (Tr. at 99:19-100:7). Dr. Martin also testified that a POSA would be

able to monitor the levels of 8α in order to reduce the ratio of 8α to oxycodone. (*Id.* at 100:8-16). Dr. Wuest did provide any testimony to suggest that a POSA would not be able to do so. Therefore, I find that the limit on the level of 8α relative to oxycodone would likewise be obvious to POSA conducting routine experimentation.

Finally, claim 11 of the '933 patent requires "removing [8α] from an oxycodone base composition." ('933 Patent 34:54-55). Defendant argues that 8α is always removed during the salt formation step, because it is always converted to 14-hydroxy. (D.I. 99 at 29). Plaintiffs argue briefly that a POSA who did not intend to reduce levels of 8β would not have "removed" 8α but generally do not separately address claim 11. (D.I. 106 at 38).

The parties unfortunately do not address each other's arguments on removal head on, with Defendant arguing that 8α is always removed by the salt formation itself and Plaintiffs suggesting that removal of 8α could only occur if a POSA decided to remove 8β. However, I do not think this dispute matters. Whether or not 8α was removed in the prior art, its removal in the invention itself is still the result of applying routine techniques to what a highly skilled POSA would have seen as a simple problem—albeit one that nobody had previously given any thought to. Given that I have found that a POSA would have been able to routinely identify 8α or 8β as the source of extra 14-hydroxy, I find that removing 8α, either directly or by removing 8β, is also obvious.

I do not think Defendant's theory is hindsight-driven. This is not a case where a POSA would have to repeatedly choose correctly in a branching maze of paths forward. Instead, Defendant presented clear and convincing evidence that all a POSA would have had to do was repeatedly choose the only path forward, rather than giving up. Plaintiffs' expert did not provide plausible evidence to the contrary.

The parties do not offer any argument about secondary considerations of nonobviousness for any of the Low-ABUK patents.

V. CONCLUSION

For the foregoing reasons, I find claim 3 of the Mannion '933 patent, claim 3 of the '808 patent, claim 6 of the '886 patent, claims 3 and 11 of the '933 patent, and claim 21 of the '919 patent invalid for obviousness under 35 U.S.C. § 103.

The parties shall submit a final judgment consistent with this memorandum opinion within one week.