United States Court of Appeals for the Federal Circuit

PURDUE PHARMA L.P., THE P.F. LABORATORIES, INC., PURDUE PHARMACEUTICALS L.P., RHODES TECHNOLOGIES,
Plaintiffs-Appellants

v.

EPIC PHARMA, LLC,
Defendant

2014-1294

Appeal from the United States District Court for the Southern District of New York in No. 1:13-cv-00683-SHS, Senior Judge Sidney H. Stein.

PURDUE PHARMA L.P., THE P.F. LABORATORIES, INC., PURDUE PHARMACEUTICALS L.P., RHODES TECHNOLOGIES,
Plaintiffs-Appellants

v.

MYLAN PHARMACEUTICALS INC., MYLAN INC.,
Defendants-Appellees

2014-1296

Appeal from the United States District Court for the Southern District of New York in No. 1:12-cv-02959-SHS, Senior Judge Sidney H. Stein.

PURDUE PHARMA L.P., THE P.F. LABORATORIES, INC., PURDUE PHARMACEUTICALS L.P., RHODES TECHNOLOGIES, GRUNENTHAL GMBH,
Plaintiffs-Appellants

v.

AMNEAL PHARMACEUTICALS, LLC,
Defendant-Appellee

2014-1306, -1307

Appeals from the United States District Court for the Southern District of New York in No. 1:11-cv-08153-SHS, Senior Judge Sidney H. Stein.

GRUNENTHAL GMBH, PURDUE PHARMA L.P., THE P.F. LABORATORIES, INC., PURDUE PHARMACEUTICALS L.P., RHODES TECHNOLOGIES,
Plaintiffs-Appellants

v.

TEVA PHARMACEUTICALS USA, INC.,
Defendant-Appellee

2014-1311, -1312, -1313, -1314

Appeals from the United States District Court for the Southern District of New York in Nos. 1:11-cv-02037-SHS, 1:12-cv-05083-SHS, Senior Judge Sidney H. Stein.

Decided: February 1, 2016

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BENJAMIN CONRAD BLOCK, Covington & Burling LLP, Washington, DC, for amicus curiae Center for Lawful Access and Abuse Deterrence.

Before PROST, *Chief Judge,* REYNA, *Circuit Judge*, and STARK, *Chief District Judge*.[*]

PROST, *Chief Judge*.

This appeal arises from consolidated Hatch-Waxman proceedings involving the reformulated version of the pain reliever OxyContin®. The Appellants, Purdue Pharma L.P., The P.F. Laboratories, Inc., Purdue Pharmaceuticals L.P., and Rhodes Technologies (collectively, "Purdue") and Grunenthal GmbH ("Grunenthal") asserted a number of claims from multiple different patents against the Appel-

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[*] Honorable Leonard P. Stark, Chief District Judge, United States District Court for the District of Delaware, sitting by designation.

lees, Amneal Pharmaceuticals, LLC ("Amneal"), Epic Pharma, LLC ("Epic"), Mylan Pharmaceuticals Inc. and Mylan Inc. (collectively, "Mylan"), and Teva Pharmaceuticals USA, Inc. ("Teva"), all of whom have filed Abbreviated New Drug Applications ("ANDAs") seeking to sell generic versions of OxyContin®. The United States District Court for the Southern District of New York held a three-week bench trial in the case against Teva, following which it held all of the asserted patent claims invalid. *In re OxyContin Antitrust Litig.*, 994 F. Supp. 2d 367, 377 (S.D.N.Y. 2014) ("*District Court Decision*"). The court then entered orders of dismissal in the three remaining cases against Amneal, Epic, and Mylan based on collateral estoppel. Purdue and Grunenthal appeal the final judgment in the Teva action, and Purdue also appeals the orders of dismissal in the three other cases. For the reasons stated below, we affirm the district court's rulings.

BACKGROUND

Oxycodone hydrochloride—the active pharmaceutical ingredient ("API") in OxyContin®—is an opioid analgesic used to treat moderate to severe pain. This consolidated appeal concerns four patents associated with the reformulated version of OxyContin®: U.S. Patent No. 7,674,799 ("'799 patent"), U.S. Patent No. 7,674,800 ("'800 patent"), U.S. Patent No. 7,683,072 ("'072 patent") (collectively, "the low-ABUK patents"), and U.S. Patent No. 8,114,383 patent ("'383 patent").

I. The Low-ABUK Patents

The low-ABUK patents recite an improved formulation of oxycodone hydrochloride. Those patents describe an oxycodone salt with extremely low levels of a particular impurity, 14-hydroxycodeinone ("14-hydroxy"), which belongs to a class of potentially dangerous compounds known as alpha, beta unsaturated ketones ("ABUKs"). The prior art method of synthesizing oxycodone hydro-

chloride involved three steps: first, thebaine, a derivative of the opium poppy, was oxidized to form 14-hydroxy; second, the 14-hydroxy was converted to oxycodone free base through hydrogenation; and third, the oxycodone free base was reacted with hydrochloric acid to form oxycodone hydrochloride. The end product created by that process, however, contained high levels of 14-hydroxy, on the order of 1500 parts per million ("ppm").

In January 2004, the U.S. Food and Drug Administration ("FDA") became concerned that 14-hydroxy was potentially toxic and thus mandated that oxycodone hydrochloride manufacturers either provide evidence that the 14-hydroxy levels in their formulations were safe or reduce the amount of 14-hydroxy to less than 10 ppm. Even before the FDA's mandate, however, Rhodes Technologies—a subsidiary of Purdue—had begun researching methods to reduce 14-hydroxy levels in its oxycodone API. The scientists initially hypothesized that the 14-hydroxy present in the final salt was leftover 14-hydroxy that had not been hydrogenated in the second step. Thus, they extended the hydrogenation reaction to completion, confirming that every molecule of 14-hydroxy converted to oxycodone free base at step two. But the scientists found that after step three—transforming the oxycodone free base into oxycodone hydrochloride—the 14-hydroxy had returned.

The scientists thus shifted their focus to step three. It was well known in the art that an impurity, 8,14–dihydroxy–7,8–dihydrocodeinone ("8,14-dihydroxy") was produced as a byproduct of the oxidation of thebaine (step one). More specifically, it was known that a particular isomer of 8,14-dihydroxy was formed: 8β, 14–dihydroxy–7,8–dihydrocodeinone ("8β"). Scientists did not know with certainty, however, whether 8α, 14–dihydroxy–7,8–dihydrocodeinone ("8α")—a diastereomer of 8β—was also produced during the oxidation step. Purdue scientists had previously noted the potential existence of 8α, but no scientific literature discussed that particular isomer.

Through experimentation, the scientists determined that 8α was indeed being produced at step one and, in fact, was transforming into 14-hydroxy during the acid-catalyzed dehydration at step three. To remove the 14-hydroxy from the oxycodone API, the scientists added another hydrogenation step at the end of step three to convert the remaining 14-hydroxy into oxycodone free base. By June 2003, Rhodes's laboratory could routinely produce oxycodone API with 14-hydroxy levels less than 10 ppm using the double-hydrogenation process. Purdue and Rhodes thus sought approval from the FDA and patent protection for their low-ABUK oxycodone product.

The low-ABUK patents continue from application No. 11/391,897, known as the "Chapman Application." The claims of the Chapman Application have previously been before us; we authored a non-precedential decision affirming the Board of Patent Appeals and Interferences' determination that the Chapman claims were obvious. *Chapman v. Casner*, 315 F. App'x 294, 295 (Fed. Cir. 2009) (Rader, CJ., dissenting). In that case, the Board declared an interference between the Chapman Application and U.S. Patent No. 7,153,966 ("Casner"). The relevant claims in the Chapman Application related to a method for making oxycodone API using a hydrogenation step to remove 14-hydroxy, but they did not require that some of the remaining 14-hydroxy be derived from the 8α isomer. *Id.* The Board compared Chapman's claims to the prior art and concluded that they were obvious. Chapman appealed directly to us, and we agreed with the Board. We reasoned that, because the claims did not specify the source of the 14-hydroxy, any prior art reference that disclosed conditions under which either 8α or 8β converted to 14-hydroxy would render the claim obvious. *Id.* at 297. We further noted that the prior art references did just that—they disclosed the conversion of 8β to 14-hydroxy under certain conditions. *Id.* Thus we affirmed the Board's decision to reject the Chapman claims as obvious. *Id.* at 297–98.

Purdue eventually amended the Chapman claims to include the claims now on appeal. Unlike the claims in the Chapman Application, the claims at issue here are product claims instead of process claims, and they explicitly recite 8α as the source of at least a portion of the minimal amounts of 14-hydroxy remaining in the oxycodone API. In 2010, the U.S. Patent and Trademark Office allowed the claims and issued the low-ABUK patents.

II. The '383 Patent

The '383 patent covers abuse-resistant formulations. Original OxyContin® was a popular opioid analgesic which delivered a large dose of oxycodone over a twelve-hour period. In the early 2000s, however, reports of widespread abuse of Original OxyContin® emerged, and the problem began to garner significant public attention. Original OxyContin® was susceptible to tampering because abusers could crush the tablets easily into powder, which could then be swallowed, snorted, or injected for an instant opioid "high." In 2001, Purdue and the FDA changed the label of Original OxyContin® to warn doctors about the potential for abusers to tamper with the dosage form.

Purdue thus investigated ways to reformulate OxyContin® to deter abuse. Purdue initially considered, among other ideas, creating a tablet that would be difficult to crush and difficult to inject, but those efforts were unsuccessful. In 2003, Purdue became aware of technology developed by Grunenthal that made tablets extremely hard (in order to prevent crushing) and formed a gel upon dissolution in water (in order to prevent injecting).

Grunenthal first began to research abuse resistant properties for its opioid product, tapentadol. In October 2002, Johnson & Johnson proposed a joint venture with Grunenthal, using Johnson & Johnson's osmotically controlled-release oral delivery system ("OROS") to deter abuse. The OROS technology consists of a tablet with an outer shell that limits the flow of the API from an inner

core through the use of a "push compartment" in the tablet. The hard outer shell is composed of high molecular weight polyethylene oxide ("PEO"), and the "push compartment" expands to force the API through a hole in the outer shell. But the tablet could still be easily crushed with a mortar and pestle, so it was not a workable solution. Dr. Johannes Bartholomaeus, who was the head of pharmaceutical development for Grunenthal at the time, tried to strengthen tapentadol's dosage form by making the entire tablet, instead of just the outer shell, resistant to crushing. Dr. Bartholomaeus thus designed a formulation that contained a matrix of API and PEO throughout the tablet. Moreover, Dr. Bartholomaeus's experimentation with PEO demonstrated that using both heat and pressure to form the tablet resulted in a stronger solid that resisted breaking by a hammer or by a mortar and pestle, and withstood a breaking strength test that exerted 500 N of force.

After a series of negotiations, Purdue obtained a license from Grunenthal to use the abuse deterrent technology of the '383 patent in its Reformulated OxyContin® product. Purdue submitted a New Drug Application to the FDA in November 2007, proposing a Reformulated OxyContin®, which the FDA approved in April 2010. By July 2012, Purdue noted reductions in the abuse of OxyContin® and provided that information to the FDA. On April 16, 2013, the FDA withdrew its approval for Original OxyContin® and stopped accepting ANDAs that proposed generic versions of it, reasoning that Reformulated OxyContin® was available to provide the same benefits with lower risks of abuse and misuse. On the same day, the FDA approved a new label that allowed Purdue to market Reformulated OxyContin® on the basis of its abuse deterrent properties.

III. Procedural History

In March 2011, Purdue sued Teva for infringement of the low-ABUK patents in response to Teva's filing of an

ANDA seeking FDA approval to market generic versions of Reformulated OxyContin®. Between November 2011 and January 2013, Purdue filed similar lawsuits against Epic, Mylan, and Amneal. In addition, in June 2012, Grunenthal and Purdue jointly sued Teva for infringement of the '383 patent. The two Teva cases were consolidated and joined with the Epic, Mylan, and Amneal cases, along with six actions involving other defendants, in multi-district litigation for pretrial purposes.

In September 2013, the district court held a three-week bench trial in the Teva cases.[1] The district court found that the asserted claims were infringed by Teva's proposed generic product, but it also held that all of the claims were invalid as anticipated by or obvious over the prior art. *District Court Decision*, 994 F. Supp. 2d at 377. Based on that decision, the district court issued an order for Purdue to show cause as to why the actions against Epic, Mylan, and Amneal should not be dismissed under the doctrine of collateral estoppel. Purdue stated that it intended to appeal the Teva decision but it agreed that the district court's decision regarding the invalidity of the low-ABUK patents precluded Purdue's claims for relief against the other defendants. Accordingly, the district court dismissed the three remaining actions based on collateral estoppel.

Purdue and Grunenthal appeal the final judgment in the Teva actions and Purdue also appeals the orders of dismissal in the three other cases. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

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[1] Before the district court, Purdue accused Teva of infringing claims 3 and 19 of the '799 patent, claims 30–34 and 76–79 of the '800 patent, claims 1, 4, and 5 of the '072 patent, and claims 1, 2, 5, 7, and 8 of the '383 patent.

DISCUSSION

A patent is invalid for anticipation under 35 U.S.C. § 102 if a single prior art reference discloses each and every limitation of the claimed invention. *Schering Corp. v. Geneva Pharm.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003). A single prior art reference may anticipate without disclosing a feature of the claimed invention if such feature is necessarily present, or inherent, in that reference. *Id.* Anticipation is a question of fact, which we review for clear error. *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1346 (Fed. Cir. 1999).

A patent is invalid for obviousness "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). Obviousness is a legal conclusion based on underlying facts. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). We review the underlying findings of fact for clear error, and we review de novo the court's ultimate legal conclusion of whether the claimed invention would have been obvious. *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 719 F.3d 1346, 1354 (Fed. Cir. 2013). Underlying factual inquiries include (i) the scope and content of the prior art; (ii) the differences between the prior art and the claims at issue; (iii) the level of ordinary skill in the field of the invention; and (iv) relevant secondary considerations. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 406 (2007); *Graham*, 383 U.S. at 17–18.

I. Invalidity of the Low-ABUK Patents

Purdue challenges the district court's conclusion that the asserted claims of the low-ABUK patents are invalid as obvious. Those claims recite an oxycodone API product

with low ABUK levels.[2] The district court found that the prior art taught that oxidation of thebaine produced 14-hydroxy and that it was well known in the art that 14-hydroxy could be removed using hydrogenation. *District Court Decision*, 994 F. Supp. 2d at 395–96. The court further determined that the discovery of 8α was not necessary to the claimed invention: a skilled artisan would recognize that hydrogenation could be used to remove the remaining 14-hydroxy, regardless of the source of the 14-hydroxy. *Id.* at 405–06. Moreover, the court concluded that the claim limitation requiring that the remaining 14-hydroxy is at least in part "derived from 8α[]" is a product-by-process limitation and thus immaterial in the obviousness determination. *Id.* at 405. Finally, the district court found that the secondary considerations did not demonstrate nonobviousness. *Id.* at 407. Purdue alleges clear error in a number of the court's findings, but none of its arguments are meritorious.

A. Discovery of 8α

First, Purdue contends that the court failed to properly credit the discovery of 8α as the core of the claimed inventions. It relies heavily on *Eibel Process Co. v. Minnesota & Ontario Paper Co.*, 261 U.S. 45, 68 (1923), for the proposition that "where an inventor discovers a non-

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[2] All of the asserted claims are product claims. The asserted claims of the '072 patent are directed to "an oxycodone hydrochloride active pharmaceutical ingredient" with low ABUK levels, *see, e.g.*, '072 patent col. 34 ll. 57–60, while the asserted claims of the '799 patent are directed to an "oral dosage form" of low-ABUK oxycodone hydrochloride, *see, e.g.*, '799 patent col. 35 ll. 8–15. The asserted claims of the '800 patent are product-by-process claims; they are directed to "[o]xycodone salt prepared according to [a] process" that yields low ABUK levels. *See, e.g.*, '800 patent col. 35 ll. 49–50.

obvious source of a problem and then applies a remedy in response, the invention is nonobvious and worthy of a patent—even if the remedy, standing alone, would generally appear to be known in the art." Purdue Br. 40. In *Eibel Process*, the invention was a machine that could make quality paper at high speeds. 261 U.S. at 54. At the time, paper-making machines could not operate at high speeds without producing wrinkled paper. *Id.* Eibel discovered that the unequal speeds of paper stock and a wire in the machine produced the wrinkled paper. Thus, he made a minor modification in the existing paper-making machines: he increased the pitch (angle) of the wire so that, through gravity, the paper stock would travel at substantially the same speed as the wire, and the paper would not wrinkle. *Id.* at 57–58, 64–65. The Supreme Court upheld the validity of Eibel's patent, reasoning that the discovery of the problem—unequal speeds of paper stock and the wire—was nonobvious, and thus the solution was as well. *Id.* at 68. Purdue contends that, similarly here, the discovery of the source of 14-hydroxy was not obvious, so the solution of hydrogenating the oxycodone salt must also be nonobvious.

Purdue's reliance on *Eibel Process* is misplaced. Even if determining the source of 14-hydroxy in the end product was not obvious, that problem did not need to be solved to arrive at the claimed invention; thus, *Eibel Process* does not apply. As discussed above, the claimed invention in *Eibel Process* was a machine that remedied the problem of wrinkled paper at high-speed printing. But, here, Purdue did not claim the remedy of the problem of remaining 14-hydroxy in the oxycodone API—performing a second hydrogenation step. Instead, it claimed the end product—an oxycodone API with low ABUK levels. And, as the district court found, identification of the source of the remaining 14-hydroxy as being 8α had no effect on the structure or nature of the low-ABUK oxycodone product. Because "[o]ne molecule of 14-hydroxy is the same as the next, whether derived from 8α or 8β," knowledge of 8α

"did not make hydrogenation more or less effective as a technique for converting 14-hydroxy to oxycodone." *District Court Decision*, 994 F. Supp. 2d at 405.

Purdue also argues that, without knowing that the 14-hydroxy was derived from 8α, a person of ordinary skill in the art would not know when to conduct the hydrogenation step or under what conditions to run the hydrogenation to create low-ABUK oxycodone. Purdue notes that the prior art references were directed to lowering 14-hydroxy levels in the oxycodone free base, not the API or salt. For example, U.S. Patent No. 6,177,567 ("Chiu reference") disclosed a method for preparing low-ABUK free base, but it did not teach how to convert the low-ABUK free base into low-ABUK salt. In fact, as Purdue and the district court noted, Chiu completed his method by adding acetic acid to the free base. In so doing, Chiu likely converted the latent 8α into 14-hydroxy in the final product because 8α reacts with the acid to form 14-hydroxy. But, again, Purdue claimed the end product; it did not claim a particular method for creating that product, such as the use of hydrogenation after the salting step. In fact, Teva's generic product would not infringe if that were the case because the Teva product is not made by hydrogenating the salt—instead the free base is purified through two hydrogenation cycles and then is treated with acid to create the oxycodone salt. Similarly, nothing in the asserted patents indicates that the hydrogenation process to remove 14-hydroxy derived from 8α must be conducted under different conditions from the process used to remove 14-hydroxy that is derived from 8β. The issue again comes down to whether it would be obvious to a person having ordinary skill in the art to use hydrogenation to remove the excess 14-hydroxy in the oxycodone API. One need not know that the 14-hydroxy was derived from 8α as opposed to 8β to answer that question.

B. "Derived from 8α[]" Limitation

Purdue next argues that, because the asserted claims require that the remaining 14-hydroxy in the oxycodone API is derived from 8α and because 8α was not previously known in the art as being the source of 14-hydroxy, the claims must be nonobvious. Indeed, Purdue points out that the reason it added that limitation was because of our decision in *Chapman* where we said the claims were obvious *because* the claims did not differentiate between the 8α and 8β. 315 F. App'x at 297. The district court rejected that argument because it found that the "derived from 8α[]" limitation was a process limitation and thus immaterial to the obviousness analysis.

Purdue says, first, the limitation is not a process limitation, and, second, even if it is, it should not be wholly disregarded. Again, Purdue's arguments fail.

The relevant claim language provides:

> An oral dosage form comprising . . . oxycodone hydrochloride active pharmaceutical ingredient having less than 25 ppm 14-hydroxy[], *wherein at least a portion of the 14-hydroxy[] is derived from 8α[]* during conversion of oxycodone free base to oxycodone hydrochloride[.]

See, e.g., '799 patent col. 34 l. 65 to col. 35 l. 4 (emphasis added). We agree with the district court that "derived from 8α[]" does not describe the structure of 14-hydroxy and thus is a process limitation. The patent specification describes methods for detecting and removing 14-hydroxy without regard to the source. For example, the written description defines 8,14-dihydroxy as 8α, 8β, or a mixture of the two and does not indicate any difference in the resulting 14-hydrodxy depending on the particular isomer from which it is derived. More specifically, there is no suggestion in the patents that the hydrogenation process changes depending on whether the 14-hydroxy is created by 8α or 8β. Indeed, even Purdue's expert testified that

"[t]he structure of the 14-hydroxy that is generated from 8α is the same structure that is generated from 8β." J.A. 4428. Because the source of the 14-hydroxy has no effect on its structure or its removal through hydrogenation, the limitation that it be "derived from 8α[]" cannot be a structural limitation.

We also conclude that, because "derived from 8α[]" is a process limitation, the district court did not err in disregarding the limitation in its obviousness analysis. We have clearly stated that "'[i]n determining validity of a product-by-process claim, the focus is on the product and not the process of making it.'" *Greenliant Sys., Inc. v. Xicor LLC*, 692 F.3d 1261, 1268 (Fed. Cir. 2012) (quoting *Amgen Inc. v. F. Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1369 (Fed. Cir. 2009)). "That is because of the . . . long-standing rule that an old product is not patentable even if it is made by a new process." *Id.*; *see also SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1317 (Fed. Cir. 2006) ("It has long been established that one cannot avoid anticipation by an earlier product disclosure by claiming . . . the product as produced by a particular process."); *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985) ("If the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.").

Purdue looks to the exception we carved out in *Amgen*: "if the process by which a product is made imparts 'structural and functional differences' distinguishing the claimed product from the prior art, then those differences 'are relevant as evidence of no anticipation' although they 'are not explicitly part of the claim.'" *Greenliant*, 692 F.3d at 1268 (quoting *Amgen*, 580 F.3d at 1340). As previously discussed, however, the fact that the 14-hydroxy is derived from 8α imparts no structural or functional differences in the low-ABUK hydrocodone API as compared to the prior art products. Thus, the court did

not err in disregarding the process limitation in its obviousness determination.

C. Secondary Considerations

Finally, Purdue contends that the court erroneously discounted the secondary considerations which it argues demonstrate nonobviousness. Purdue first points to Rhodes's commercial success; it says that Rhodes became Purdue's oxycodone API supplier by marketing the low-ABUK features of its product to Purdue, which resulted in almost $71 million in sales in 2010. As the district court found, however, Rhodes was not successful at marketing its low-ABUK oxycodone API to any significant customer other than Purdue, which is its corporate affiliate. The district court further found that Purdue invested in Rhodes not because of the low-ABUK features, but because it could get oxycodone API at a lower cost from its subsidiary than it could from an unaffiliated manufacturer during times of high demand. Purdue does not persuasively rebut these findings on appeal. Thus, the district court did not clearly err in concluding that there was no nexus between the low-ABUK product of the patents and the commercial success of Purdue or Rhodes.

Purdue next argues that the failure of others is shown by the experience of Teva's oxycodone API supplier, Noramco, Inc. ("Noramco"). Purdue claims Noramco was unable to obtain low ABUK levels until 2007, years after Purdue discovered 8α, and only then by infringing the low-ABUK patents. But, as the district court found, there is no evidence that Noramco tried but failed to create low-ABUK oxycodone API. Instead, the record showed that Noramco and the FDA agreed to a timetable for producing low-ABUK oxycodone API, that Noramco adhered to that timetable, and that Noramco continued to manufacture the higher ABUK products during that time. Purdue also argues that long-felt need was shown because, although the FDA only made low-ABUK oxycodone API a regulatory requirement in 2003—less than a year before Purdue

commercialized its low-ABUK product—the need for low-ABUK products was present long before. That does not, however, change the fact that there was no pressing need for companies to create a low-ABUK product before the FDA's mandate, as they were able to continue to sell their higher-ABUK products. Thus, the district court did not clearly err in finding that Purdue failed to prove the failure of others or long-felt but unaddressed need.

Finally, Purdue points to the fact that Noramco credited Purdue and Rhodes with the discovery of 8α and contends that such recognition shows praise from competitors. But recognition that Rhodes discovered that 8α is a byproduct of thebaine oxidation does not equal praise for the invention—the low-ABUK oxycodone API. Purdue also argues that industry praise is shown because Noramco copied its process for creating low-ABUK oxycodone, but provides no support whatsoever for that argument. Finally, Purdue contends that the court wholly ignored evidence showing that Purdue and Rhodes were surprised over their discovery and solution. But, again, there was no surprise as to the patented product. Even if it was unexpected that thebaine oxidation would create 8α, it was not surprising that, after the FDA mandate, manufacturers would create a low-ABUK oxycodone API or that they would do so using the known technique of hydrogenation.

We find Purdue's remaining arguments unpersuasive and conclude that the asserted claims of the low-ABUK patents are obvious. We thus affirm the district court's finding of invalidity as to those claims.

II. Invalidity of the '383 Patent

Purdue and Grunenthal also challenge the district court's conclusion that the asserted claims of the '383 patent are invalid as anticipated, or, in the alternative,

obvious.[3] The district court concluded that the asserted claims are anticipated by WO 97/49384, known as the McGinity reference, which later became U.S. Patent No. 6,488,963. *District Court Decision*, 994 F. Supp. 2d at 421–26. The McGinity reference discloses the use of hot-melt extrusion of high molecular weight PEO to create a controlled-release dosage form for pharmaceuticals. The district court found that McGinity disclosed opioid formulations and that it inherently disclosed tablets with a breaking strength in excess of 500 N, as required by the asserted claims. Alternatively, the district court concluded that even if the McGinity reference did not anticipate the '383 patent, "a person of ordinary skill in the art would have had sufficient knowledge and motivation to make the invention claimed by the '383 patent." *Id.* at 426.

On appeal, Grunenthal contends that the district court clearly erred in finding that McGinity discloses all of the limitations of the asserted claims and that the

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[3] Claim 1 is the only independent claim of the '383 patent and recites:

> A thermoformed dosage form comprising:
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> i) one or more active ingredients with abuse potential (A) selected from the group consisting of opiates and opioids,
>
> ii) optionally physiologically acceptable auxiliary substances (B),
>
> iii) at least 60% by weight of polyalkylene oxide (C) having a molecular weight of 1–15 million according to rheological measurements, and
>
> iv) optionally at least one wax (D)
>
> wherein said dosage form has a breaking strength of at least 500 N and wherein the active ingredient with abuse potential (A) is present in a controlled release matrix of component (C).

district court impermissibly combined discrete disclosures in McGinity to arrive at its anticipation determination. Grunenthal also asserts a number of grounds of error in the district court's obviousness determination.

A. McGinity's Disclosure of Opioid Formulations and Breaking Strength

McGinity discloses a variety of therapeutic compounds to be used in its formulations, including "analgesics such as aspirin, acetaminophen, d[i]flunisal and the like." J.A. 135074. Grunenthal argues that, because the only specifically mentioned drugs are non-opioids, McGinity does not describe formulations that contain opioids such as oxycodone. It invokes the canon of construction *ejusdem generis*—which provides that general terms are construed as referring to things of the same kind as those specifically mentioned—to argue that the terms "such as" and "and the like" should be understood as also referring to other non-opioids. But, as the district court found, the McGinity reference cannot be read so narrowly. The McGinity reference explicitly notes the use of its process with analgesics to treat pain, and the words "such as" and the residual clause "and the like" demonstrate that the application discloses a broader group of analgesics than just those listed. Moreover, the record showed that opioids are a major class of analgesics and that oxycodone was one of the most widely prescribed analgesics at the time. The district court also noted that the McGinity reference is directed to sustained-release dosage forms and credited expert testimony that the only analgesics on the market in a sustained-release form at the time were opioids.[4] The district court's assessment is persuasive and not clearly erroneous.[5]

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[4] Grunenthal says that the record evidence expressly contradicts this testimony, as it shows that there were, in fact, three analgesics on the market in a sustained-

Grunenthal next argues that McGinity does not inherently disclose the limitation that the dosage forms have a breaking strength of at least 500 N. According to the district court,

> The pivotal evidence [with respect to the breaking strength limitation] is a series of breaking strength tests that Dr. Fernando Muzzio performed in preparation for this litigation. Muzzio thermoformed thousands of tablets according to the McGinity Application disclosures. He used a variety of chemical compositions, extruder temperatures, screw speeds, and die diameters. He tested a vast number of the resulting tablets, and without exception they withstood forces greater than 500N. In fact, Muzzio often exerted forces in the thousands of Newtons and never had a tablet break.

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release form at the time and only two of them were opioids. But Grunenthal never made that argument before the district court—it did not cross-examine the expert on this point or otherwise take issue with the accuracy of the expert testimony. In any event, the fact that two of the three sustained-release drugs on that market at the time were opioids is persuasive evidence that a skilled artisan would understand McGinity as describing formulations that use opioids.

[5] Grunenthal also contends that McGinity does not disclose the limitation that the active ingredient has "abuse potential." '383 patent col. 22 l. 3. Because we find that the district court did not err in concluding that McGinity discloses the use of an opioid as an active ingredient, and because the record clearly demonstrates that opioids have abuse potential, we similarly find that the district court did not err in concluding that McGinity discloses formulations where the active ingredient has abuse potential.

District Court Decision, 994 F. Supp. 2d at 423. The district court credited Dr. Muzzio's testing and noted that, "[i]n contrast with [Dr. Muzzio's] persuasive experimental evidence, plaintiffs have not put forward any evidence that any tablet produced according to the McGinity Application can ever break when a force of 500N is applied to the tablet." *Id.* The district court thus concluded that the McGinity reference "inherently discloses a breaking strength greater than 500N, because the experimental results indicate unanimously, reliably, clearly, and convincingly that any tablet made according to the McGinity Application would exhibit this characteristic." *Id.* at 424.

Grunenthal asserts a number of grounds of error, many of which focus on the adequacy and reliability of Dr. Muzzio's testing. For example, Grunenthal argues that Dr. Muzzio did not provide API release data, photographs after breaking strength testing, or laboratory notebooks for his reproductions of the McGinity disclosures. But the district court rejected that argument, finding that "Muzzio has supplemented his own credibility with abundant documentary support in the form of raw data, photographs, and force curves" and concluded that Grunenthal's attacks "do not seriously lessen the weight the Court assigns to Muzzio's vast empirical results and credible opinion on the inherency of a 500N breaking strength." *Id.* Similarly, Grunenthal says that Dr. Muzzio did not perform a torque test on its reproductions, which would have shown if the extrusion was being accurately repeated. Again, however, the district court found that argument unpersuasive, concluding that "because torque is not an input or setting in the extrusion process, the lack of torque data does not affect the reliability of Muzzio's process as a replication of the McGinity Application's process." *Id.* The district court credited Dr. Muzzio with having "recreated the McGinity Application's process fairly, accurately, and with no material variation," and Grunenthal has shown no clear error in that finding.

Grunenthal also points to specific disclosures in McGinity which it argues show that the McGinity formulations do not necessarily have the required breaking strength. First, it notes that McGinity discloses tablets that can be scored—making them easy to break in half—or ground, which it contends is the antithesis of high breaking strength tablets. Next, Grunenthal argues that McGinity contemplates the use of heat *or* pressure to create the disclosed tablets, but notes that tablets with 500 N breaking strength can only be formed using *both* heat and pressure. Neither of those disclosures, however, changes the fact that every tablet made according to McGinity's disclosures and tested by Dr. Muzzio had a breaking strength of over 500 N. And, again, Grunenthal has not shown clear error in the district court's crediting of Dr. Muzzio's testing results, nor has it provided any independent testing to rebut Dr. Muzzio's findings.[6]

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[6] Moreover, Grunenthal incorrectly characterizes the McGinity disclosures. Grunenthal relies on one isolated sentence to support its argument that McGinity contemplates the use of heat *or* pressure in its process: "[A] hot-melt extrudable polymer is one that is . . . capable of deformation . . . under elevated heat or pressure." J.A. 135076. But that sentence merely defines the type of polymer used; it does not say that the extrusion process requires only heat or pressure and not both. In fact, in describing the actual hot-melt process, McGinity says it should be "conducted at an elevated temperature" and explains that the pharmaceutical mixture should be "passed through the heated area of the extruder at a temperature which will melt or soften the PEO." J.A. 135077. Indeed, Grunenthal's own expert testified that hot-melt extrusion requires achieving the "melt flow" temperature of ninety-eight degrees Celsius for high molecular weight PEO. J.A. 3845–46.

Grunenthal's last two arguments relate to testing that Dr. Muzzio did not perform. Grunenthal notes that Dr. Muzzio only tested formulations with the active ingredient disclosed in McGinity, chlorpheniramine maleate ("CPM"), which is an antihistamine, not an opioid. Thus, Grunenthal says that Dr. Muzzio's tests only proved that CPM formulations would have a breaking strength of 500 N or more, not that opioid formulations, as claimed in the '383 patent, would have such a breaking strength. But, Dr. Muzzio testified that *any* tablet made using at least fifty weight percent PEO and heated above the melting point of PEO would have a breaking strength above 500 N, regardless of the active ingredient used. J.A. 3462. The district court did not clearly err in crediting that testimony.

Next, Grunenthal argues that Dr. Muzzio did not perform any testing to confirm that the tablets he made according to the McGinity disclosures were controlled-release formulations. Grunenthal contends that without this testing, "there is no clear proof that Teva actually carried out the same process—and made the same tablets—disclosed in McGinity." Grunenthal Br. 38. That is incorrect. As stated above, the district court credited Dr. Muzzio with recreating the McGinity process "fairly, accurately, and with no material variation." *District Court Decision*, 994 F. Supp. 2d at 424. Grunenthal has not shown clear error in the district court's finding and cannot do so by claiming that Dr. Muzzio did not conduct an additional test to confirm what the district court already found—that he properly replicated the McGinity process. Grunenthal also says that, without testing the controlled-release properties of the tablets, Teva cannot prove that the limitation requiring "a controlled release matrix of [the PEO]" is disclosed by McGinity. That is also incorrect. Teva did not need to conduct any controlled-release testing because McGinity clearly discloses PEO formulations with controlled-release properties. For example, in the "Field of the Invention" section, McGinity

says, "The invention relates more specifically to formulations which have been prepared by hot melt extrusion of mixtures containing high molecular weight PEO and a therapeutic compound for use in controlled-release drug delivery." J.A. 135067. Thus, the district court did not clearly err in concluding that the controlled-release limitation was disclosed in McGinity.

B. Combination of McGinity Disclosures

Finally, Grunenthal argues that the district court erred by using distinct sections of McGinity and reassembling them into an embodiment to find that all of the limitations were present. *See Application of Arkley*, 455 F.2d 586, 587 (C.C.P.A. 1972) (noting that an anticipating reference "must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference"). For example, Grunenthal points out that the court selected only "analgesics" from the long list of pharmaceutical categories that could be used as the active ingredient, and then further picked oxycodone, which was not even disclosed, to find anticipation. Moreover, Grunenthal notes that McGinity teaches that the amount of PEO will vary depending on various factors and does not consistently disclose formulations with at least sixty weight percent PEO, as required by the claims. Thus, Grunenthal argues that the court impermissibly chose only those examples that included the claimed amount of PEO to find anticipation.

These arguments are without merit. The disclosures pointed to by the district court are all "directly related" and thus there is no impermissible picking and choosing. *Arkley*, 455 F.2d at 587. For example, in the section providing a detailed description of the preferred embodiment, McGinity says:

> [T]he invention provides a hot-melt extrudable controlled release pharmaceutical formulation comprising an effective amount of a therapeutic compound, high molecular weight [PEO] . . . , the [PEO]:therapeutic compound ratio being in the range from about 99.99:0.01 to about 80:20 % wt.

J.A. 135802. In that single disclosure, McGinity describes the controlled-release formulation and the use of over sixty weight percent PEO. It does not specifically say what therapeutic compound is used, but it provides a list of the types of therapeutic compounds contemplated. That list of compounds, although in a distinct section of the reference, is directly related to the disclosure reproduced above. Thus, the district court did not impermissibly combine distinct disclosures in McGinity to arrive at the claimed invention.

We conclude that the district court did not clearly err in finding that the McGinity reference discloses each and every limitation in the asserted claims of the '383 patent. We thus affirm the district court's anticipation determination and do not reach the question of obviousness.

III. Collateral Estoppel

In addition to appealing the judgments of invalidity, Purdue also appeals the dismissal of the Epic, Mylan, and Amneal actions with respect to the low-ABUK patents. On appeal from orders of dismissal due to collateral estoppel, "our role is limited to reviewing the district court's application of collateral estoppel, not the correctness of the [underlying] verdict[]." *Pharmacia & Upjohn Co. v. Mylan Pharm., Inc.*, 170 F.3d 1373, 1380 (Fed. Cir. 1999). Before the district court, Purdue conceded that collateral estoppel applied to the judgment of invalidity as to the low-ABUK patents in the Teva case, which precluded it from obtaining the relief sought in the remaining actions. Purdue also does not present any persuasive argument on appeal as to why collateral estoppel should

not apply. Thus, we affirm the district court's dismissal of the remaining actions as barred by collateral estoppel.

CONCLUSION

For the foregoing reasons, we affirm the district court's invalidity determinations as to the low-ABUK patents and the '383 patent and the district court's dismissal of the Epic, Mylan, and Amneal actions.

AFFIRMED