IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

PAR PHARMACEUTICAL, INC. and ALKERMES PHARMA IRELAND LTD	:	
v.	:	Civil No. CCB-11-2466
TWi PHARMACEUTICALS, INC.	:	

MEMORANDUM

Plaintiffs Par Pharmaceutical, Inc. and Alkermes Pharma Ireland, Limited (collectively, "Par") filed this action against TWi Pharmaceuticals, Inc. ("TWi") alleging infringement of U.S. Patent No. 7,101,576 ("'576 patent").[1] After a five-day bench trial, the court issued a memorandum concluding that "the '576 patent was obvious, and thus invalid." (Post-Tr. Mem. 1, ECF No. 212.) Par appealed to the Federal Circuit, which vacated the court's judgment of invalidity, and remanded the case for further analysis. The court held a hearing to consider the parties' remand arguments on invalidity. Based on the arguments presented then and in the parties' remand briefs, and after reviewing the trial record, the court now makes additional findings of fact and conclusions of law under Federal Rule of Civil Procedure 52(a). In sum, the court concludes that TWi has shown by clear and convincing evidence that the asserted claims in the '576 patent are invalid on two separate grounds: they are obvious, and they are not enabled.

BACKGROUND

The following has occurred since the court issued its post-trial memorandum on February 21, 2014.[2] On March 18, 2014, Par appealed the court's judgment in TWi's favor. (ECF No. 219.) On August 12, 2014, the court granted Par's motion for an injunction pending appeal.

[1] The patent relates to nanoparticulate formulations of megestrol acetate used to treat anorexia, cachexia, and unexplained weight loss in patients with HIV and AIDS.

[2] The court assumes familiarity with the facts of this case, which are described in the court's prior post-trial memorandum. (*See* Post-Tr. Mem. 1-4.)

(ECF Nos. 257-58.) On September 10, 2014, TWi filed a notice of appeal concerning the injunction.

On December 3, 2014, the Federal Circuit issued an opinion vacating the court's judgment that the '576 patent was invalid as obvious and remanding because, in its view, the court "incorrectly applied [Federal Circuit] law on inherency in the context of obviousness." *Par Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1188 (Fed. Cir. 2014).

The Federal Circuit's opinion began by outlining its standard for inherency. It stated that, while "inherency may supply a missing claim limitation[,] . . . the use of inherency . . . must be carefully circumscribed in the context of obviousness." *Id.* at 1194-95 (citations omitted). It then described the "high standard" parties must meet to show that a claim limitation is inherent in the prior art: "the limitation at issue necessarily must be present, or the natural result of the combination of elements explicitly disclosed by the prior art." *Id.* at 1196.

The Federal Circuit concluded that the court "did not require that TWi present evidence sufficient to prove inherency under this standard." *Id.* TWi had presented evidence that a reduction in particle size would improve bioavailability, and TWi had elicited testimony from its expert, Dr. Beach, that "an improvement in bioavailability 'necessarily results in a decrease in any food effect[.]'" *Id.* (citing Post-Tr. Mem. 13). On the basis of those two facts, the court concluded, "thus any food effect will inherently be reduced." (Post-Tr. Mem. 26.) But the Federal Circuit concluded that the court had "ignore[d] the claim limitations at issue." *Par Pharm.*, 773 F.3d at 1196. "There [we]re simply no findings of fact addressing th[e] question" of whether TWi had "present[ed] evidence sufficient to demonstrate that the *claimed* food effect limitations necessarily are present in the prior art combinations"—that is, whether "a reduction in particle size naturally results" in (1) "'no substantial difference in C_{max}' between the fed and

fasted states" (as in claim 1), and (2) a "'difference in C_{max}' between the fed and fasted states [that is] within an enumerated percentage difference" (as in claim 4). *Id.* (emphasis in original) (citations omitted).

The Federal Circuit accepted this court's analysis in all other respects. Specifically, the Federal Circuit held that the court did not err in: (1) concluding that TWi failed to prove "that a food effect for micronized megestrol was known in the art[,]" *id.* at 1194 (citing Post-Tr. Mem. 6-10); (2) considering "motivations beyond the food effect[,]" *id.* at 1197; (3) finding that "the viscosity and interpatient variability problems with micronized megestrol" were valid "alternate motivations[,]" *id.*; (4) finding sufficient "motivation to combine megestrol with nanoparticle technology[,]" *id.* at 1198; (5) finding a "reasonable likelihood of success in combining megestrol with nanoparticle technology[,]" *id.*; (6) concluding that "Graham d[id] not teach away from combining megestrol with the NanoCrystal technology[,]" *id.* at 1198-99; and (7) "its analysis of the objective indicia of nonobviousness[,]" *id.* at 1199.

The Federal Circuit's mandate issued on February 13, 2015. (ECF Nos. 267-68.) That same day, Par filed a motion for a temporary restraining order and injunction pending entry of final judgment on remand, (ECF No. 269), which the court granted as to the injunction, (ECF Nos. 279-80). After the parties filed briefs, the court held a hearing on June 12, 2015.

ANALYSIS

Because the parties dispute the scope of the issues on remand, the court addresses that question first before turning to the merits of TWi's invalidity arguments.

I. Scope of Issues on Remand

At the end of its opinion, the Federal Circuit concluded:

> [a]lthough we agree with the district court's analysis and conclusions on motivation to combine, reasonable expectation of success, and objective indicia of

> nonobviousness, we vacate the district court's judgment that the '576 patent is obvious, and remand for further analysis of the food effect limitation consistent with our precedent on inherency. The district court should also consider TWi's other grounds for invalidity, such as enablement, if necessary.

Par Pharm., 773 F.3d at 1200-01.

The Federal Circuit's instructions are clear. On obviousness, only the inherency analysis with respect to the food effect limitations is subject to further evaluation; motivation to combine, reasonable expectation of success, and the secondary considerations are not. The court is also free to consider TWi's other invalidity arguments. That is the full scope of the issues on remand; all the other issues decided on appeal "are deemed incorporated within the [Federal Circuit's] mandate and thus are precluded from further adjudication." *Engel Indus., Inc. v. Lockformer Co.*, 166 F.3d 1379, 1383 (Fed. Cir. 1999).

Despite these clear instructions, Par argues that two additional issues fall within this limited scope. Neither argument is persuasive.

First, Par argues that TWi "improperly attempts to narrow the broad motivation to combine nanoparticle technology and megestrol . . . found by this Court" to a particular particle size range. (Par Remand Br. 4, ECF No. 288 (citation omitted).) Par acknowledges that the court found there was a "general motivation" to combine megestrol acetate with nanoparticle technology, but it argues the court did not find "a *specific* motivation" to do so using the particle size range TWi now asserts inherently meets the claimed food effect limitations, and that a finding of such specificity was required for TWi to prove that those limitations were inherent in the prior art. (*Id.* at 4-5 (emphasis in original).)

This argument is unconvincing. Par conflates the inherency analysis with the motivation-to-combine analysis. The latter requires only that "a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and . . .

would have had a reasonable expectation of success in doing so." *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1360 (Fed. Cir. 2012) (citation and quotation marks omitted). The court has already made findings on motivation to combine, (*see* Post-Tr. Mem. 27-32), and reasonable expectation of success, (*see id.* at 34-35) neither of which the Federal Circuit disturbed, (*see Par Pharm.*, 773 F.3d at 1197-98).

Second, Par argues TWi needed to provide "evidence of inherency" on dependent claims 7, 12-15, 19, and 26-29 because those claims include "fasted state bioavailability (C_{max}) limitations" that are "food effect limitations" within the scope of the Federal Circuit's remand. (Par Remand Br. 10-11.) Accordingly, Par argues that TWi needed to show that the fasted-state bioavailability limitations in these dependent claims—i.e., "fasted-state C_{max} of greater than 700 ng/ml, 400 ng/ml or 300 ng/ml"—were inherent. (*Id.* at 11.)

This argument is also unconvincing. The Federal Circuit gave no indication that the dependent claims were within the scope of the remand. Indeed, the dependent claims do not even involve "food effect" limitations. A food effect is measured by calculating the *difference* between two pharmacokinetic values: the C_{max} found in the fed state, and the C_{max} found in the fasted state. (*See* '576 patent, DTX-001, at col. 8 ll. 54-63 (noting that whether a megestrol composition "eliminate[s] the effect of food on the pharmacokinetics of megestrol" involves comparing the pharmacokinetics of the composition "administered in the fed versus the fasted state").) The limitations in the dependent claims require no such comparison, and instead require only a single fasted-state C_{max} value. (*See, e.g.*, '576 patent col. 44 ll. 25-28 ("The method of claim 1, wherein a mean C_{max} of about 300 ng/ml to about 2000 ng/ml is obtained after a single administration . . . in a fasted state.").) The dependent claims will not be considered anew here.

II. Invalidity

On remand, the parties address TWi's three invalidity arguments: (1) the asserted claims are (still) invalid as obvious; (2) the asserted claims are not sufficiently enabled; and (3) the '576 patent claims unpatentable subject matter. The court concludes that the asserted claims are invalid on two grounds: they are obvious, and they are not sufficiently enabled.[3]

A. Obviousness

The court previously concluded that the prior art disclosed all of the limitations of the asserted claims of the '576 patent except the food effect limitations. (*See* Post-Tr. Mem. 24-25.) Accordingly, the court now considers whether the trial record shows that those food effect limitations are inherent in the prior art. To prove that a claim limitation is inherent in the prior art, TWi must show by clear and convincing evidence that "the limitation at issue [is] necessarily . . . present, or the natural result of the combination of elements explicitly disclosed by the prior art." *Par Pharm.*, 773 F.3d at 1196.[4] Based on the trial record, the court concludes that TWi has met its burden on inherency with respect to each of the claimed food effect limitations at issue.

There is a threshold question: to what degree must the food effect necessarily be reduced to meet the claimed food effect limitations? TWi appropriately focuses on the narrowest claimed C_{max} difference because, if the narrowest difference is met, any broader differences are necessarily met, too. Here, the narrowest C_{max} difference is in claim 5, which requires a difference that is "less than about 60%." ('576 patent col. 43 ll. 42-43.)[5] Thus, if a food effect reduction of that magnitude is inherent in the prior art, then the "less than about 100%" difference in claim 4 and the "no substantial difference" in claim 1 are also inherent.[6]

[3] Accordingly, the court need not, and does not, address TWi's patentable subject matter argument.
[4] At the hearing, neither party argued the "necessarily present" language differed from the "natural result" language.
[5] Claim 1 requires that the food effect be reduced such that "no substantial difference" exists between the fed and fasted states. Because Par has taken the position that a 100% difference could constitute "no substantial difference," (Summ. J. Hearing, at 74:14-19, ECF No. 143), and the court agreed, (*see* Summ. J. Mem. 7-10, ECF No. 140), claim 1's limitation does not displace claim 5's as the limitation requiring the greatest reduction in food effect.
[6] At the hearing, TWi also noted—and Par did not dispute—that 60% was the value the parties were targeting.

TWi has clearly and convincingly proven that a food effect reduction to a difference of "less than about 60%" is inherent in the prior art. The prior art discloses that a skilled artisan, in creating a nanosized formulation of Megace OS, would have used particle sizes in the 100-400 nm range. (*See, e.g.*, U.S. Patent No. 5,399,363, DTX-003, at col. 5 ll. 1-5 ("In particularly preferred embodiments of the invention, the effective average particle size is less than about 400 nm. In some embodiments . . . , the effective average particle size is less than about 300 nm."); European Patent No. 0577215B1, DTX-011, at p. 11 l. 52-p. 12 l. 14 ("A process for obtaining a composition comprising nanoparticles . . . wherein . . . at least 90% of the particles hav[e] an average particle size of less than 400 nm . . . ."); 2001 Elan NanoCrystal Brochure, DTX-013, at PAR-MEG945726 ("NanoCrystal® particles . . . are . . . in the size range of 100 nm to 400 nm . . . .").)

And TWi has proven that megestrol nanoparticles within that size range would *necessarily* reduce the food effect so that the C_{max} difference would be well under "less than about 60%." Specifically, TWi points to substantial evidence and expert testimony to prove that the claimed food effect reductions are inherent in multiple formulations of megestrol produced in the 100-400 nm range. Most significantly, there is example 9 of the '576 patent, which discloses three different formulations using particle sizes in the 223-237 nm range that show fed-fasted differences of 7.3%, 9.2%, and 13.7%, ('576 patent col. 38 l. 53-col. 41 l. 54)—differences well within the claimed food effect limitations. Second, there is Par's Megace ES—with particle sizes in the 270-290 nm range—which, as an embodiment of the asserted claims, also satisfies the food effect limitations. (*See* PTX-006, at ANC-MEG-0000131 (indicating that Megace ES's particle size distribution is 270-290 nm); Trial Tr. Day 5 Vol. 1, at 8:2-24, ECF No. 190 (describing how PTX-006 shows Megace ES's particle size distribution).) Third, there is Par's

stipulation that TWi's accused ANDA product, with particle sizes in the 230-330 nm range, meets the asserted claims. (*See* Stipulation Regarding Infringement ¶ 4, ECF No. 173 (stipulating that "TWi's ANDA Product . . . would actively induce and/or contribute to the infringement of [various] claims . . . of the '576 patent"); PTX-016, at ANC-MEG-0000874.)[7] Supporting these formulations is the expert testimony of Dr. Beach, who explained the causal relationship between nanosizing and food effect reductions. (*See, e.g.*, Trial Tr. Day 3 Vol. 1, at 17:3-25, ECF No. 188 (describing how applying "oral NanoCrystal technology" leads to "improved bioavailability," and "with improved bioavailability[,] [o]ne would get reduction in fed and fasted variability").)[8] This evidence, taken together, clearly and convincingly proves that the claimed food effect limitations are inherent in the prior art.

Par's primary counterargument is that mere examples of megestrol formulations within the claimed particle size range that meet the food effect limitations cannot, alone, prove an inherent property.[9] Moreover, Par believes it presented counterexamples at trial of "formulations using the nanoparticle technology in the prior art [that] did not solve the food effect problem," (Par TRO Reply 7), which suggests the food effect limitations are not inherent in nanosizing, and are rather the result of a combination of variables. Central to Par's argument is example 2 of the '576 patent, which shows two nanoparticulate megestrol formulations exhibiting C_{max} differences of 70.9% and 84.0%. ('576 patent col. 26 l. 59-col. 30 l. 18.)

[7] Par argues that the above examples are "not even three separate examples." (Par Remand Br. 9.) Even if TWi's ANDA product is substantially similar to Par's Megace ES, the trial record reflects that they are not identical in every respect. (*See, e.g.*, PTX-006, at ANC-MEG-0000129 ("TWi's drug product was formulated to have *similar* [attributes] as the reference listed drug, Megace® ES." (emphasis added)).)

[8] Par argues that Dr. Beach's testimony is not conclusive on the inherency question. The court agrees that he sometimes spoke in generalities. (*See, e.g.*, Trial Tr. Day 3 Vol. 1, at 15:19-21 ("As we go up in particle size from that to micron particle size and larger, we get very large particles and decreased bioavailability.").) Thus, his testimony might not independently satisfy TWi's inherency burden. His testimony nonetheless strengthens TWi's case by explaining the scientific relationships underlying the formulations TWi has already cited—relationships and formulations that Par does not contest.

[9] Par specifically argues TWi must show that a food effect reduction would "necessarily result from *any* combination of megestrol and nanoparticle technology." (Par TRO Reply 6, ECF No. 277 (emphasis added).)

Par's counterargument fails in several respects. At the outset, Par has not pointed to any authority requiring TWi to show that the claimed food effect limitations are inherent in *every* formulation claimed by the '576 patent. In the obviousness context, examples are enough. *See In re Cuozzo Speed Techs., LLC*, --- F.3d ---, No. 2014-1301, 2015 WL 4097949, at *10 (Fed. Cir. July 8, 2015) ("It is a long-established rule that claims which are broad enough to read on obvious subject matter are un-patentable even though they also read on nonobvious subject matter." (citation and quotation marks omitted)). Here, TWi has not only presented several examples of formulations that exhibit the claimed food effect limitations, but also provided expert testimony confirming the scientific principles underlying that result.

Par also has failed to present sufficient evidence to either (1) rebut TWi's examples, or (2) prove that there are formulations within the relevant particle size range that do not exhibit the claimed food effect reductions. Example 2 of the '576 patent does not refute TWi's inherency case because the study in that example used "[t]welve male beagles" as test subjects instead of humans. ('576 patent col. 26 l. 63; *see also* DTX-126, at ALK_M007136 (email from Dr. Bosch questioning "how [Par will] use the [dog study] data given that dogs have a shorter intestinal transit time than humans" and anticipating "differences in the dogs that wouldn't show up in humans").) And while Par implies that other counterexample formulations might exist, it does not actually come forward with any. Although TWi bears the burden of persuasion, Par has failed to rebut TWi's inherency case. *See Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 719 F.3d 1346, 1353 (Fed. Cir. 2013) ("[T]he presumption of validity does not relieve the patentee of any responsibility to set forth evidence in opposition to a challenger's prima facie case which, if left unrebutted, would be sufficient to establish obviousness.").

In sum, TWi has shown by clear and convincing evidence that the food effect limitations

are inherent in the prior art. Accordingly, the asserted claims of the '576 patent are invalid as obvious.

B. Lack of Enablement

The asserted claims of the '576 patent also are invalid for lack of enablement. For a claim to be enabled, a patent's specification must "contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same . . . ." 35 U.S.C. § 112. "Claims are not enabled when, at the effective filing date of the patent, one of ordinary skill in the art could not practice their full scope without undue experimentation." *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013) (citing *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1380-81 (Fed. Cir. 2012)). In determining whether a disclosure requires undue experimentation, courts consider the *Wands* factors,[10] which "while illustrative[,] are not mandatory." *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1336 (Fed. Cir. 2013) (quoting *Wands*, 858 F.2d at 736-37).

"[W]hen a range is claimed, there must be reasonable enablement of the scope of the range." *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1244 (Fed. Cir. 2003); *see also Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 999 (Fed. Cir. 2008) ("The full scope of the claimed invention must be enabled."). The court asks whether, with the specification "as an initial guide, the hypothetical skilled artisan's knowledge of the surrounding art and ability to modestly experiment would have been sufficient to enable him to make and use" the full scope of the claimed invention. *AK Steel*, 344 F.3d at 1244. This does not necessarily require that the

[10] These factors are: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

specification "describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art." *Id.* (citations omitted).

The court concludes that TWi has met its burden of proving, by clear and convincing evidence, that Par's asserted claims are invalid for lack of enablement. Simply put, TWi has proven that a skilled artisan using the '576 patent's specification as a guide would not be able to make and use, without undue experimentation, multiple portions of the claimed particle size range (i.e., "less than about 2000 nm"). Specifically, TWi provided expert testimony at trial explaining why formulations of the claimed invention that use particle sizes below 100 nm and above 750 nm cannot achieve the claimed food effect limitations. Particle sizes below 100 nm "reaggregate and begin to act again as large particles." (Trial Tr. Day 3 Vol. 1, at 15:22-25, 40:7-9.) And using particle sizes above 750 nm results in "decreased bioavailability." (*Id.* at 15:19-21, 40:9-11). Both phenomena preclude achievement of the claimed food effect reductions for roughly two-thirds of the '576 patent's claimed particle size range. Bolstering TWi's case is the fact that only a narrow subrange (i.e., 121-129 nm) of the claimed particle size range was actually successfully tested for the purposes of the '576 patent. (*See* '576 patent tbl. 11.) Additionally, the upper end of the claimed range is much closer to the particle size range of the prior art (i.e., 3,000 nm) that clearly did not achieve the claimed food effect reductions. (*See* Trial Tr. Day 3 Vol. 2, at 63:16-18, ECF No. 193 (noting that "basically all" of the prior art used "micronized particle size[s] . . . between 3 and 10 microns").) In short, the record reflects that essentially no amount of experimentation would have allowed a skilled artisan to achieve broad portions of the claimed particle size range because scientific phenomena made that practically

impossible. Accordingly, TWi has shown, by clear and convincing evidence, that the claims at issue are not enabled, and are therefore invalid.

Par responds with several arguments, but none have merit.

First, Par argues that TWi presented no evidence on the *Wands* factors. At the outset, the Federal Circuit does not require that every *Wands* factor must be considered and met in every case. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991) ("[I]t is not necessary that a court review all the *Wands* factors to find a disclosure enabling. They are illustrative, not mandatory."). In any event, the trial record clearly shows Dr. Beach addressed the *Wands* factors, even if he did not explicitly invoke the word "Wands." (*See, e.g.*, Trial Tr. Day 3 Vol. 1, at 38:12-16 (affirming he knew "that there are several factors to consider in determining whether there is undue experimentation"); *id.* at 39:1-2 (testifying that "the scope of this invention is not commensurate with the scope of the claims"); *id.* at 41:19-20 (testifying that "there's no human data about treating someone suffering from cachexia or AIDS").)

Second, Par argues that TWi's "framing of the enablement inquiry in this case . . . is incorrect." (Par Remand Br. 16.) Par believes TWi is attempting to apply a standard under which "the specification must provide a working example of every claimed particle size combined with the claimed food effect reductions[.]" (*Id.* (citing *United States v. Telectronics, Inc.*, 857 F.2d 778, 786 (Fed. Cir. 1988)).) In slightly different words, Par argues that "the specification need not describe 'every conceivable embodiment of the invention' to be enabled." (*Id.* at 17 (quoting *Telectronics*, 857 F.2d at 786).)

Par misconstrues TWi's argument. TWi does not argue that the specification must include working examples of every *embodiment* of the claimed invention (something that is not required). Rather, TWi argues the specification has not enabled every value in a *claimed range*

(something that is required). Indeed, Federal Circuit case law strongly supports TWi's position that the 576 patent's specification must enable the entire claimed range. Two cases—*Magsil* and *Alcon Research*—are particularly instructive.

In *Magsil*, the plaintiff asserted infringement of a "device . . . comprising . . . an electric insulator . . . wherein applying a small magnitude of electromagnetic energy to [it] . . . cause[d] *a change in the resistance by at least 10% at room temperature*." 687 F.3d at 1379 (emphasis in original). The district court construed the asserted claims to cover "resistance changes beyond 120% and up to infinity." *Id.* at 1381. Yet the asserted patent's specification taught "that the inventors' best efforts achieved a maximum change in resistance of only 11.8% at room temperature"—just barely above the bottom limit of the plaintiff's claimed range. *Id.* Accordingly, the district court concluded the asserted claims were not enabled. *Id.* The Federal Circuit affirmed, holding that the accused infringer had "shown with clear and convincing evidence that one skilled in the art could not have taken the disclosure in the specification regarding 'change in the resistance by at least 10% at room temperature' and achieved a change in resistance in the full scope of that term without undue experimentation." *Id.* The patent's specification only enabled a "small subset of the claimed range." *Id.* at 1384. It "only disclose[d] enough information to achieve an 11.8% resistive change." *Id.* at 1383. Moreover, it disclosed no "working examples" of "resistive changes of 20%, 120%, 604%, or 1000%." *Id.* at 1382. The Federal Circuit ignored, as irrelevant, the following: the aspirations held by inventors at time of filing, *id.* at 1383 ("The specification discloses that artisans *hoped* to achieve values of around 24%, but had not done so." (emphasis added)); the arguments made during prosecution that 100% resistive change was "possible," *id.* at 1383; and that inventors in the field had recently achieved 600% resistive change, *id.* at 1384.

In *Alcon Research*, the patentee asserted infringement of various claims that contained drug concentration ranges, including one as wide as from 0.0001% to 5%. 687 F.3d at 1364-65. In arguing the validity of this claim, the patentee conceded it had not enabled the portion of the claimed range below a 0.001% concentration, but argued that the claim should be construed so that only the enabled portions of the range were covered. *Id.* at 1367-68. The Federal Circuit rejected this argument, stating that "[t]his is not how patent law works." *Id.* at 1368. A patentee claiming a concentration range could not "simply disavow the invalid portion and keep the valid portion of the claim." *Id.* Rather, "[i]f everything up to 0.001% w/v is admittedly not enabled, then the entire claim is invalid." *Id.*

The present case is like *Magsil* and *Alcon Research*.[11] Here, as in both cases, Par has claimed a very broad range, but the specification does not show how to make the entire range (at least without undue experimentation). In addition, TWi has presented expert testimony explaining the scientific phenomena that make it potentially impossible to enable significant portions of the claimed range—and Par has not sufficiently rebutted that testimony.[12] Further, *Alcon Research* squarely disposes of any argument that the claims should be narrowed to cover

[11] An unpublished case that also supports TWi is *TSI Inc. v. Azbil BioVigilant Inc.*, Civ. No. 12-00083-PHX-DGC, 2014 WL 1604860 (D. Ariz. Apr. 22, 2014). The court relied on *MagSil* to hold that a patent did not enable a claim covering "a laser having the wavelength from 320 nm to 500 nm" when the patent itself "acknowledge[d] that laser diodes were not available at wavelengths below 400 nm at the time it was filed." *Id.* at *3 (citations omitted).

[12] In this respect, the present case is distinguishable from *Telectronics*, on which Par heavily relies. There, the asserted claim covered a system involving an electrode and a current level selected from "a predetermined microampere range . . . ." 857 F.2d at 780. The district court held that the claim was not enabled for *non*-stainless steel electrodes, in part because the specification provided insufficient guidance on how to select a current level within the claimed range. *See id.* at 785.

The Federal Circuit reversed the district court's non-enablement conclusion. *Id.* at 786. The Federal Circuit noted that it was "undisputed that the patent disclosures [we]re enabling with respect to *stainless steel* electrodes, with the range of current for such electrode set out in the specification." *Id.* at 785 (emphasis added). The specification further disclosed that that range could be obtained through a "dose response test." *Id.* Thus, a skilled artisan, equipped with the disclosed stainless steel embodiment, and the disclosed method to select a current level, could practice "other permutations of the invention . . . without undue experimentation." *Id.* at 786. The Federal Circuit added that "[t]he only impediments [we]re the time and cost" of the dose response test. *Id.*

Here, unlike in *Telectronics*, the specification does not provide any sort of guidance as to how to achieve effective formulations along the entire particle size range. Moreover, the experimental impediments go beyond time and cost and include overcoming scientific principles.

only the enabled ranges.[13] Finally, while Par offers the aspirations and possibilities existing at the time of filing, those facts, as *Magsil* makes clear, do not support a finding of enablement.

Third, Par argues that it presented affirmative evidence showing that the entire claimed range *was* enabled. Par combines the testimony of two of its experts to support this argument. Dr. Berkland testified that the '576 patent teaches how to make the range of nanoparticle sizes claimed in the patent. (*See* Trial Tr. Day 5 Vol. 1, at 18:13-18 (noting that a skilled artisan "could learn how to make a stable oral nanoparticulate suspension with a D50 of 2000 or less").) And Dr. Fleckenstein testified that formulations with a food effect ranging from 8-55% existed. (*See* Trial Tr. Day 4 Vol. 1, at 25:24-26:10 (noting "various Par studies" showing C_{max} differences "rang[ing] between 8 and 55 percent").)

But Dr. Berkland and Dr. Fleckenstein establish two independent propositions that have no bearing on the ultimate legal question: whether the specification enables a *union* of the two—that is, does the '576 patent teach how to make formulations across the claimed particle size range that *simultaneously* have the claimed food effects? Neither expert answered this question. Dr. Berkland speculated that "through routine experimentation, [skilled artisans] *could* test to see if [a formulation] had the claimed attributes," (Trial Tr. Day 5 Vol. 1, at 18:19-22 (emphasis added)), but he did not testify that a formulation using particle sizes greater than 750 nm would exhibit the claimed food effect limitations. Dr. Fleckenstein's testimony regarding the food effect range was deficient because it was untethered to particle size. (*See* Trial Tr. Day 4 Vol. 1, at 93:4-15 (agreeing that, "in rendering [his] opinions regarding enablement" of the food effect reductions, he "didn't do an analysis of the particle size").) Moreover, Par misconstrues Dr. Fleckenstein's testimony to stand for more than what he actually said. Regarding the '576

[13] *Magsil* also provides support. There, the Federal Circuit pointed out that "[t]he open claim language chosen by the inventors d[id] not grant them any forgiveness on the scope of required enablement." 687 F.3d at 1383. In short, a patentee is free to claim broadly, but risks being unable to "fully enable its broad claim scope." *Id.* at 1384.

patent's claimed *dose* range (i.e., "of about 40 mg to about 800 mg"), Dr. Fleckenstein testified that human testing had enabled "practically the entire range of the claim." (*Id.* at 26:11-22.) Par cites that testimony to suggest that the entire claimed *particle size* range (i.e., "of less than about 2000 nm") was enabled. But as already noted, he "didn't offer opinions on particle size." (*Id.* at 91:5.)

In sum, TWi has made a clear and convincing showing that over two-thirds of Par's claimed particle size range is not enabled. And Par has not sufficiently rebutted TWi's showing. Accordingly, the asserted claims of the '576 patent are invalid for lack of enablement.

CONCLUSION

For the above reasons, the court concludes that TWi has shown by clear and convincing evidence that the asserted claims of the '576 patent are (1) invalid as obvious and (2) invalid for lack of enablement.

A separate Order follows.

July 27, 2015
Date

/s/
Catherine C. Blake
United States District Judge