UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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INFOSINT, S.A.,

Plaintiff,

-against- 06 Civ. 2869 (LAK)

H. LUNDBECK A/S, et al.,

Defendants.

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MEMORANDUM OPINION

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LEWIS A. KAPLAN, *District Judge.*

This is an action for infringement of a patent for the synthesis of a chemical compound used by defendants in their manufacture of the antidepressant drug citalopram. The case was tried to a jury, which found that defendants had infringed the patent and awarded plaintiff fifteen million dollars in damages. The matter is before the Court on defendants' post-verdict motion for judgment as a matter of law that plaintiff's patent is invalid as obvious.

Background

Plaintiff Infosint, S.A. ("Infosint") owns the patent here at issue, U.S. Patent No. 6,458,973 (the "'973 Patent"), which claims an improved process for making the compound 5-carboxyphthalide, which is used as an intermediate in the synthesis of citalopram and another antidepressant drug, escitalopram.[1]

In general terms, the claimed process involves adding terephthalic acid to fuming sulfuric acid containing at least twenty percent sulfur trioxide, SO_3. Fuming sulfuric acid, also known as oleum,[2] is a mixture of sulfuric acid, H_2SO_4, and sulfur trioxide. Next, formaldehyde or a formaldehyde precursor is added to the mixture, which is heated at 120-145º C. The resulting 5-carboxyphthalide then is isolated from the solution.[3]

Defendants, H. Lundbeck A/S and subsidiary Lundbeck, Inc. (collectively "Lundbeck"), as well as Forest Laboratories, Inc., and Forest Pharmaceuticals, Inc. (collectively "Forest"), manufacture, market, and sell citalopram and escitalopram.[4] Lundbeck synthesizes 5-carboxyphthalide and manufactures citalopram and escitalopram at facilities located outside of the United States. Forest markets and sells these pharmaceuticals in the United States under the trademarks Celexa and Lexapro, respectively.[5]

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1 *Infosint, S.A. v. H. Lundbeck A/S*, 612 F. Supp. 2d 405, 408 (S.D.N.Y. 2009).

2 DTX 1 at col. 2:19.

3 *Id.* at col. 2:26-44; col. 2:49-4:17.

4 Ans. at 2-3.

5 *Infosint*, 612 F. Supp. 2d at 409.

The Dispute

Infosint claimed that Lundbeck used 5-carboxyphthalide made according to the process described in the '973 Patent as an intermediate in its production of citalopram and escitalopram, that Forest infringed by importing into and offering for sale in the United States citalopram and escitalopram products, and that Lundbeck induced Forest to do so.

Defendants contended that the '973 Patent does not cover the processes used by Lundbeck to make citalopram or escitalopram. They contended also that the patent is invalid on the ground that the claimed process was anticipated by the prior art and obvious to one of ordinary skill in art at the time it was invented.

The case was tried to a jury for three weeks in September and October 2009.

The Verdict

At the close of the evidence, defendants moved for judgment as a matter of law "on the invalidity defenses" pursuant to Federal Rule of Civil Procedure 50(a).[6] The Court reserved decision[7] and allowed the case to go to the jury. On October 15, 2009, the jury returned a verdict for Infosint. It found that the claimed process was neither anticipated nor obvious. It found also that defendants had infringed the '973 Patent and awarded Infosint what it deemed to be a reasonable

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[6] Trial Tr. 1063:24-1064:3.

[7] *Id.* at 1064:4. Federal Rule of Civil Procedure 50(b) provides that "[i]f the court does not grant a motion for judgment as a matter of law made under Rule 50(a), the court is considered to have submitted the action to the jury subject to the court's later deciding the legal questions raised by the motion." FED. R. CIV. P. 50(b). "Thus, even [when] the trial court expressly has denied the motion, it is considered to have reserved decision on it." 9B CHARLES ALAN WRIGHT & ARTHUR R. MILLER, FEDERAL PRACTICE AND PROCEDURE § 2522 [hereinafter WRIGHT & MILLER].

royalty, *viz*. $15 million.[8] Defendants now move for judgment as a matter of law that the '973 Patent is invalid as obvious.

Discussion

A. Legal Standard

A motion for judgment as a matter of law will be granted "only when, considering the evidence in the light most favorable to the non-moving party and drawing all reasonable evidentiary inferences in that party's favor, there was 'no legally sufficient evidentiary basis for a reasonable jury to find' in favor of the non-moving party."[9] In deciding the motion, a court "cannot assess the weight of conflicting evidence, pass on the credibility of the witnesses, or substitute its judgment for that of the jury."[10]

The ultimate judgment of obviousness is a legal determination.[11] "The moving party is entitled to [judgment as a matter of law] when the court is convinced: (1) that reasonable persons could not in light of th[e] evidence have found the facts necessary to support the jury's verdict; *or*

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8 *Id.* at 1165:15-1167:2.

9 *Nimely v. City of New York*, 414 F.3d 381, 389-390 (2d Cir. 2005) (quoting FED. R. CIV. P. 50(a)); *Kerman v. City of New York*, 374 F.3d 93, 118 (2d Cir. 2004) ("[T]he standard for judgment as a matter of law is the same as the standard for summary judgment."); *see also Muniauction, Inc. v. Thompson Corp.*, 532 F.3d 1318, 1324 (Fed. Cir. 2008) ("The [grant or] denial of a JMOL motion is a procedural issue not unique to patent law, which we review under the law of the regional circuit where the appeal from the district court normally would lie.") (citation omitted).

10 *Tolbert v. Queens Coll.,* 242 F.3d 58, 70 (2d Cir. 2001) (quoting *Smith v. Lightning Bolt Prods., Inc*., 861 F.2d 363, 367 (2d Cir.1988)).

11 *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 427, 127 S. Ct. 1727, 1745 (2007).

(2) that the facts properly found cannot in law support that verdict. . . . Thus the trial judge engages in a two step process . . . : (1) determine what facts are supported by substantial evidence; and (2) determine whether those facts support the legal conclusion necessarily drawn by the jury enroute [*sic*] to its verdict."[12]

B. Analysis

Defendants contend that Claim 24 of the '973 Patent is obvious as a matter of law on the ground that each of its limitations was disclosed by prior art. Infosint responds that defendants do not meet their burden of demonstrating obviousness because there was substantial evidence that the prior art taught away from the claimed process.

The '973 Patent claims in relevant part:

> "1. A process for the preparation of 5-carboxyphthalide . . . which comprises adding formaldehyde and terephthalic acid . . . to fuming sulfuric acid containing at least 20% of SO_3, heating the mixture at 120-145° C. and isolating the 5-carboxyphthalide thus obtained.
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> * * *
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> "21. A process for the synthesis of citalopram, in which a process for the synthesis of 5-carboxyphthalide according to claim 1 is contained.
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> * * *
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> "23. A process for the preparation of 5-carboxyphthalide . . . which comprises adding formaldehyde (or a formaldehyde precursor) and terephthalic acid . . . to fuming sulfuric acid containing at least 20% of SO_3, heating the mixture at 120-145° C. and isolating the 5-

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12 *R.R. Dynamics, Inc. v. A. Stucki Co.*, 727 F.2d 1506, 1513 (Fed. Cir. 1984) (emphasis in original); *see also Muniauction, Inc.,* 532 F.3d at 1324 ("When reviewing the denial of a JMOL motion, this court reviews a jury's conclusions on obviousness, a question of law, without deference, and the underlying findings of fact, whether explicit or implicit within the verdict, for substantial evidence.") (citation omitted).

> carboxyphthalide thus obtained, wherein the process is conducted in an open, non-pressurized reactor.
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> "24. A process for the synthesis of citalopram, comprising the process for the synthesis of 5-carboxyphthalide according to claim 23."[13]

This Court on a motion for summary judgment prior to trial held Claims 1 and 21 of the '973 Patent invalid as obvious.[14] The remaining asserted claim of the '973 Patent, Claim 24, differs from invalidated Claim 21 only with respect to the "open, non-pressurized reactor" limitation.[15] The Court, however, held that there remained questions of fact as to whether the prior art would have suggested to those of ordinary skill in the art that they should carry out the claimed reaction in an open, non-pressurized reactor and whether they would have had a reasonable expectation of success by so doing.[16] It noted that, although at least two prior art references each disclose the use of an open, non-pressurized reactor, neither on its face discloses a reaction conducted in oleum.[17] In consequence, the Claim 24 obviousness analysis properly focuses on whether it would have been obvious in light of the prior art to conduct the reaction in oleum in an

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13 DTX 1 at col. 7:2-27; col. 8:20-23; col. 8:25-56.

14 *See Infosint*, 612 F. Supp. 2d at 421.

15 As this Court has discussed previously, a non-pressurized reaction includes, but is not limited to, a reaction conducted at atmospheric pressure. It would be obvious to one with ordinary skill in the art that a reaction conducted at atmospheric pressure could be conducted in a "non-pressurized" reactor. *Id.* at 415.

16 *Id.*

17 *See id.* (citing DTX 2, DTX 70).

open, non-pressurized reactor.[18]

The determination whether an invention would have been obvious under Section 103 of the Patent Act[19] is a legal conclusion based on factual findings as to (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) any relevant secondary considerations.[20] The "burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed

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18 The Court of course accepts the propositions that "each claim of a patent is entitled to a presumption of validity and is to be treated as a complete and independent invention" and that a "domino approach in which each successively narrower claim is compared with the one before it, not with the prior art, is inappropriate since it improperly gives prior-art effect to the subject matter of an invalid claim." *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1137 (Fed. Cir. 1985). The Court, however, previously has found that the following limitations of Claim 21 of the '973 Patent are disclosed by the prior art: (1) the specification that the fuming sulfuric acid or oleum contain "at least 20 % of SO3," (2) the heating of the mixture to 120-145 degrees Celsius, (3) the isolation of the 5-carboxyphthalide compound, and (4) "[a] process for the preparation of citalopram." *Infosint*, 612 F. Supp. 2d at 412-415. It follows that the identical limitations of Claim 24 are disclosed by and obvious in light of the very same prior art. In consequence, it is not necessary to replicate the Court's previous discussion of the obviousness of these limitations. *See, e.g.*, *Bourns, Inc. v. United States*, 537 F.2d 486, 494 (Ct. Cl. 1976) ("That the subject matter of a claim must be considered as a whole is a position with which there is 'no quibble.' . . . But the practicalities are to look to the distinguishing features incorporated into the claims and the validity determination necessarily focuses on these features.") (citing *Graham v. John Deere Co.*, 383 U.S. 32, 86 S. Ct. 684 (1996)).

19 35 U.S.C. § 103.

20 *Id.*; *Graham*, 383 U.S. at 17.

The Federal Circuit "has articulated a subsidiary requirement for the first *Graham* factor, the scope and content of the prior art. . . . Where, as here, all claim limitations are found in a number of prior art references, the factfinder must determine 'what the prior art teaches, whether it teaches away from the claimed invention, and whether it motivates a combination of teachings from different references.'" *Dystar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1359-61 (Fed. Cir. 2006) (quoting *In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004)).

process, and would have had a reasonable expectation of success in doing so."[21]

Infosint and defendants agree as to the first and second factors. It is undisputed that the prior art includes LeRoy S. Forney's *Reaction of Terephthalic Acid with Formaldehyde in Sulfur Trioxide Media* ("Forney 1970"), Forney's *Reaction of Formaldehyde with Deactivated Benzoic Acids* ("Forney 1971"), U.S. Patent No. 3,607,884 (the "'884 Patent"), International Patent Application WO 98/19513 (the '513 application"), and J.R. LeBlanc's *Di and Tetracarboxydiphenlmethanes and Derivatives* ("LeBlanc"). The parties agree that one of ordinary skill in the art would have a master's degree and two years of laboratory experience in organic chemistry and would have been familiar with the prior art.[22] They agree also that the secondary considerations include any unexpected or superior results achieved by the claimed process and any prior or simultaneous invention of the claimed process.

As to the third factor, the differences between the prior art and the claimed process, defendants maintain that Forney 1970 and Forney 1971 each disclose each and every limitation of Claim 24, including the use of oleum as a solvent in open, non-pressurized conditions. Infosint, on

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21 *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007) (reversing district court's denial of defendant's motion for judgment as a matter of law that patent was invalid as obvious despite opinion of plaintiff's expert that "persons of skill in this field would not have had a reasonable expectation of success in carrying out the claimed process" in light of prior art); *R.R. Dynamics, Inc.*, 727 F.2d at 1511 ("When a jury verdict of validity is tested by a motion for JNOV . . . the district court must determine whether the patent challenger's evidence met the burden imposed by § 282.")

22 Trial Tr. 680:17-681:10 (Williams), 973:17-25 ("This is a hypothetical person who has a broad knowledge of the literature, and I assumed in this case that Dr. Williams' definition of a person having a master's degree and a couple of years of professional experience was a reasonable description.") (Gokel). Plaintiff, however, requested a jury charge that the person of ordinary skill in the art "is an individual who would have a bachelor's degree in organic chemistry, or equivalent thereof, with experience in organic chemistry synthesis." Pl. Charge at 22.

the other hand, contends that Forney 1970 taught away from the use of oleum as a solvent and that Forney 1971 taught away from the use of an open, non-pressurized reactor.

1. The Prior Art

a. Forney 1970

Forney 1970 describes the production of 5-carboxyphthalide "cleanly and in excellent yield" when terephthalic acid and formaldehyde are reacted in "sulfur trioxide media."[23] The experimental section of Forney 1970 nevertheless describes a reaction involving 98 percent sulfuric acid, not oleum containing more than 20 percent sulfur trioxide.[24]

At trial, however, defendants adduced evidence that the reaction of terephthalic acid and formaldehyde to create 5-carboxyphthalide necessarily produces water.[25] The water produced by this reaction in turn reacts with sulfur trioxide present in the reaction mixture to create sulfuric acid.[26] The resulting mixture of the sulfuric acid and the unreacted sulfur trioxide is by definition "fuming sulfuric acid" or oleum.[27] Defendants' expert witness, Dr. Robert Williams, opined that one

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23 DX 70 at FL/I 001194 ("We wish to report the condensation of terephthalic acid with formaldehyde in sulfur trioxide media, a process which produces 5-carboxyphthalide . . . cleanly and in excellent yield.").

24 *See id.*

25 *Id.* (fig. 2); Trial Tr. 690:2-691:9, 1005:20-23 (Gokel).

26 Trial Tr. 690:2-694:1.

27 *Id.* at 692:11-23. Fuming sulfuric acid is formed even if the reaction described in Forney 1970 begins with pure sulfur trioxide instead of "sulfur trioxide media." *Id.* at 690:2-694:1; DTX 1045.

of ordinary skill in the art would have understood the product of the reaction to be thirty-six percent sulfuric acid and sixty-four percent sulfur trioxide, which is sixty-four percent oleum.[28] Infosint neither disputed nor challenged that conclusion.[29]

Moreover, the Forney 1970 reaction indisputably takes place in open, non-pressurized conditions. Forney 1970 noted when a reaction described therein was carried out in sealed rather than open containers.[30] The Court previously found that the omission of such a specification in the article's description of the 5-carboxyphthalide reaction therefore indicated that the Forney 1970 reaction used an open reactor.[31] Dr. Williams indeed opined that "since there is no specific mention

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28 *Id.* at 690:2-694:1.

29 *See Integra Lifesciences I, Ltd. v. Merck KGaA*, 496 F.3d 1334, 1345 (Fed. Cir. 2007) ("[T]he court should give credence to the evidence favoring the nonmovant as well as that 'evidence supporting the moving party that is uncontradicted and unimpeached.'" (quoting 9A WRIGHT & MILLER § 2529)) (reversing jury finding of patent infringement as unsupported by substantial evidence); *PharmaStem Therapeutics, Inc.*, 491 F.3d at 1351 (reversing jury finding of infringement, crediting "uncontradicted evidence at trial" that favored defendant); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1362 (Fed. Cir. 2007) (reversing jury verdict and holding patent obvious as matter of law, finding that "unrebutted testimony from [defendant's] expert, which we find compelling, supports an inference that the skilled artisan actually would have been encouraged, rather than discouraged" to combine prior art references); *see also County of Suffolk v. Long Island Lighting Co.*, 907 F.2d 1295, 1314-15 (2d Cir. 1990) (affirming district court's grant of motion for judgment notwithstanding verdict in fraud suit and stating that "unimpeached and uncontradicted evidence favorable to the movant [] can be considered by us in evaluating the merits of a denial of a motion for judgment n.o.v.") (citing 9A WRIGHT & MILLER § 2529).

Dr. Gokel acknowledged that in the Forney 1970 reaction "you may have sulfuric acid in the presence of SO_3, you can call that oleum." *Id.* at 978:2-7. Infosint, however, argues that the sulfuric acid produced by the reaction is a "minute amount[]" that "has no impact on the reaction between terephthalic acid and formaldehyde." Pl. Mem. 7 n.3. *See* discussion *infra* at 13.

30 *Infosint*, 612 F. Supp. 2d at 415.

31 DTX 70 at FL/I 001194; *id.*

of a type of reactor used, skilled chemists would understand that the default position is always that . . . this would be a glass round bottomed flask that would be open."[32] He opined also that Forney 1970's reference to "excess sulfur trioxide distilled off"[33] "would indicate that the reaction was open."[34] Infosint neither disputed nor challenged Williams's opinion. Thus, undisputed evidence showed that Forney 1970 describes the use of an open, non-pressurized reactor.[35]

The remaining limitation of Claim 24, the use of 5-carboxyphthalide to make citalopram, was disclosed by the '513 application, which was filed more than a year before plaintiff's '973 Patent application.[36] The 5-carboxyphthalide made by the Forney 1970 process could be used to create citalopram according to the process described by the '513 application.[37] In consequence, Forney 1970 describes the same reaction to create 5-carboxyphthalide from terephthalic acid and

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32 Trial Tr. at 688:20-689:9.

33 DTX 70 at FL/I 001194; Trial Tr. 688:22-689:9.

34 Trial Tr. 688:20-689:9.

35 *See supra* note 29.

36 DTX 9.

37 *Id.*; Trial Tr. 696:18-697:11. Infosint's argument that the '513 application teaches away from using 5-carboxyphthalide made by the claimed process as a "starting material for making citalopram" is without merit. Pl. Mem. 8-9. As an initial matter, Professor Gokel conceded that the '513 application is a "method for the preparation of citalopram" in which "[t]he starting material is 5-carboxyphthalide." Trial Tr. 891:9-15. While the '513 application does not itself disclose the claimed process for making 5-carboxyphthalide, that process concededly was known to those of ordinary skill in the art through the Forney publications. In any event, there is nothing in the '513 application that "criticizes, discredits, or otherwise discourages" the use of the claimed process to make citalopram. *See In re Fulton*, 391 F.3d at 1201.

formaldehyde in oleum in open, non-pressurized conditions as is claimed by Claim 24.[38]

Infosint responds that Forney 1970 "actually teaches away" from using oleum in a reaction of terephthalic acid and formaldehyde to produce 5-carboxyphthalide.[39] Its expert, Dr. George Gokel, opined that Forney 1970 discusses the use of oleum as a solvent only in reference to LeBlanc, which describes the reaction in oleum of isophthalic acid and formaldehyde to produce a diphenyl methade derivative rather than a phthalide.[40] It contends that, based on the teachings of Forney 1970, a person of ordinary skill in the art would not expect that a reaction between terephthalic acid and formaldehyde in oleum would yield 5-carboxyphthalide. Infosint's argument is unavailing.

"A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant."[41] A reference, however, does not teach away if it "merely expresses a general preference for an alternative invention but does not 'criticize, discredit, or otherwise discourage' investigation into the invention claimed."[42]

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38 *Cf. SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343-44 (Fed. Cir. 2005) (finding patent claim anticipated by prior art where prior art "discloses a method of manufacturing PHC anhydrate that naturally results in the production of [the claimed] PHC hemihydrate").

39 Pl. Mem. 6.

40 *See* Trial Tr. 892:15-896:18, 974:15-975:24; DTX 70 at FL/I 001194 (citing LeBlanc); DTX 82.

41 *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (Fed. Cir. 2009) (quoting *Ricoh Co., Ltd. v. Quanta Computer Inc.*, 550 F.3d 1325, 1332 (Fed. Cir. 2008)).

42 *Id.* (quoting *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004)).

Forney 1970 does not criticize, discredit, or otherwise discourage the use of oleum as a solvent in the 5-carboxyphthalide process. Instead, it describes the production of 5-carboxyphthalide through the interaction of terephthalic acid and formaldehyde in "sulfur trioxide media."[43] Indeed, as shown above, the Forney 1970 reaction necessarily proceeds in oleum for the majority of its duration. LeBlanc concededly describes a different reaction involving isophthalic acid rather than terephthalic acid.[44] LeBlanc therefore does not address the reaction between terephthalic acid and formaldehyde here at issue.

Infosint rejoins that Dr. Gokel opined that in Forney 1970 "you may have sulfuric acid in the presence of SO_3, you can call that oleum, but that's not the reaction medium in which this reaction is being run."[45] Infosint therefore argues "a person of ordinary skill in the art would not have read Forney 1970 as disclosing a reaction in oleum despite the small quantities of oleum that might be formed as a by-product of the reaction itself."[46] But that argument fares no better, as indicated by this Court's claim construction and Forney 1971.

This Court has construed the phrase "fuming sulfuric acid containing at least 20%

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43 DX 70 at FL/I 001194 ("We wish to report the condensation of terephthalic acid with formaldehyde in sulfur trioxide media, a process which produces 5-carboxyphthalide . . . cleanly and in excellent yield.").

44 *See* DTX 82; Trial. Tr. 893:12-20 ("In the LeBlanc article, they use instead of terephthalic acid, they use isophthalic acid.") (Gokel).

45 Trial Tr. 978:2-7.

46 Pl. Mem. 7.

SO_3" to mean "20% SO_3 up to an amount to which sulfuric acid would be considered an impurity."[47] Thus, any amount of sulfuric acid above an amount that would be "an impurity" is fuming sulfuric acid or oleum. Infosint's contention that the thirty-six percent sulfuric acid generated in the reaction is a "small quantit[y]" or a "minute amount[]"[48] therefore is inapposite.

In any event, Forney 1971 expressly describes the use of oleum as a solvent in a reaction to produce 5-carboxyphthalide.[49] This Court previously found that Forney 1971 would have indicated unequivocally to those of ordinary skill in the art that they could synthesize 5-carboxyphthalide using oleum as a solvent and that they could expect a reasonable degree of success if they did so.[50] Dr. Gokel in fact conceded that the use of oleum as a solvent in a reaction of terephthalic acid and formaldehyde "was not new" at the time that plaintiff filed its patent application.[51] In consequence, any contention that Forney 1970 teaches away from the use of oleum, even if that argument were persuasive, would be immaterial in light of Forney 1971, the more recent prior art reference.

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47 *Infosint, S.A. v. H. Lundbeck A/S*, 603 F. Supp. 2d 748, 758 (S.D.N.Y. 2009) (adopting Report and Recommendation finding that the limitation "does not include pure SO_3 which contains sulfuric acid as an impurity"); DI 113 at 11.

48 Pl. Mem. 7 n.3.

49 *See* DTX 71 at FL/I 001208-09.

50 *Infosint*, 612 F. Supp. 2d at 414.

51 Trial. Tr. 1010:2-1011:17.

b. Forney 1971

Defendants argue also that Forney 1971 discloses each and every limitation of Claim 24, including the use of oleum as a solvent, in an open, non-pressurized reactor. Infosint responds that it adduced substantial evidence through Dr. Gokel that Forney 1971 teaches away from the use of open, non-pressurized conditions.

Forney 1971 compares a series of reactions of formaldehyde and terephthalic acid in oleum to a series of reactions of the same two compounds in dimethyl sulfate media containing varying amounts of sulfur trioxide.[52] The experimental section of Forney 1971 discusses the reaction of formaldehyde and terephthalic acid in dilute oleum in the conditions described in Forney 1970.[53] Dr. Gokel indeed admitted that "[t]his reaction, as far as I can tell, is run in an open reactor. And not a sealed glass tube."[54]

In opposition to defendants' motion for summary judgment, Infosint argued that Forney 1971 required sealed and pressurized conditions for a reaction in oleum.[55] At trial, however, Dr. Williams opined that sealed glass tubes were used in Forney 1971 for "small-scale experiments" where it was necessary to "prevent loss of any of the reagents or reactants."[56]

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52 DTX-71.

53 *Id.* at FL/I 001211 (citing Forney 1970).

54 Trial Tr. 1001:19-20.

55 Infosint Invalidity S.J. Opp. Mem. 22 ("[A]s Dr. Gokel points out, the fact that SO_3 boils at 45º C would have motivated a person skilled in the art away from using an open, non-pressurized reactor.") (discussing Forney 1971).

56 Trial Tr. 703:12-704:9.

Infosint now argues that Forney 1971 teaches that the reaction of terephthalic acid and formaldehyde in dilute oleum produces both 5-carboxyphthalide and an "unwanted byproduct" known as terephthalyloxyacetic acid. It contends that "even were such reactions run in open reactors, they would have taught the person of skill not to use an open reactor to make 5-carboxyphthalide, because the primary product of the reaction is the wrong compound."[57] Infosint's argument is immaterial.

As an initial matter, the experimental section of Forney 1971 concededly discloses the reaction of terephthalic acid and formaldehyde in dilute oleum in open, non-pressurized conditions to create 5-carboxyphthalide.[58] It describes the formation of the byproduct terephthalyloxyacetic acid in a reaction involving ninety-eight percent sulfuric acid, not oleum containing twenty percent sulfur trioxide as claimed by the '973 Patent.[59] Forney 1970 nevertheless discloses that the byproduct can be avoided by using "sulfur trioxide media" such as oleum containing greater than twenty percent sulfur trioxide.[60] In any event, the formation of the byproduct is irrelevant because Claim 24 contains no limitation as to the purity or yield of 5-carboxyphthalide.[61]

The prior art therefore does not teach away from the use of oleum as a solvent in an

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57 Pl. Mem. 10 (citing Trial Tr. 1018:5-18 (Gokel)).

58 Trial Tr. 998:16-1001:20 (Gokel).

59 DTX-71 at FL/I 001211.

60 DTX 70 at FL/I 001194 ("The reaction is generally free of by-product formation over a fairly wide range of reaction conditions, although terephthaloyloxyacetic acid . . . has been identified (as its dimenthyl ester) from reaction in the presence of excess formaldehyde and from reaction media containing <20% SO_3."); Trial Tr. 684:6-685:1.

61 Trial. Tr. 992:9-18 (Gokel).

open, non-pressurized reactor.

* * *

In consequence, Forney 1970 and Forney 1971 each disclose each and every limitation of Claim 24 – the reaction of terephthalic acid and formaldehyde in oleum in open, non-pressurized conditions to produce 5-carboxyphthalide.[62] The prior art plainly would have indicated to those of ordinary skill in the art that they could run the claimed reaction in oleum in an "open, non-pressurized reactor" and that they could expect a reasonable degree of success if they did so. Defendants have demonstrated clearly and convincingly that Claim 24 would have been obvious in light of each prior art reference and the knowledge of one of ordinary skill in the art. There is no legally sufficient evidentiary basis for a reasonable jury to find in favor of Infosint.

The Court therefore turns to Infosint's attempt to rebut the *prima facie* case of obviousness with secondary considerations of nonobviousness.[63]

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62 The Court previously held that the 120-145º C temperature limitation of Claim 24 was disclosed by the prior art and an optimization within the ordinary skill in the art. *See* DX 70 (heating mixture to 120-130º C); DX 2 (heating mixture to 120-180º C, with range of 120-150º C preferred); DX 71 (heating mixture to 150º C); *Infosint*, 612 F. Supp. 2d at 414.

Moreover, the '884 Patent discloses a similar reaction involving sulfur trioxide run "at atmospheric pressure." *See* DTX 2, at Col. 1, lines 23-26. LeBlanc and Lundbeck's IPC application and authorization each disclosed the use of an open reactor for running reactions using formaldehyde and isophthalic action or terephthalic acid in oleum. *See* DTX 66; DTX 80; DTX 82; DTX 1052; Trial Tr. 720:10-721:20.

63 *See, e.g., Muniauction, Inc. v. Thompson Corp.*, 532 F.3d 1318, 1327 (Fed. Cir. 2008) (considering plaintiff's "attempt to rebut" defendant's *prima facie* showing of obviousness with secondary considerations of nonobviousness).

2. Secondary Considerations

Among the secondary considerations of nonobviousness are unexpected or superior results achieved by the claimed process.[64] Infosint contends that it adduced "unrebutted evidence" that the Claim 24 process yields results superior to those of Forney 1971. It maintains that the "particular set of conditions [of the claimed process] provides an exceptional yield, exceptional purity, and a relatively simple process suitable for industrial use."[65]

As an initial matter, Infosint does not contend that the use of an open, non-pressurized reactor produced any unexpected or superior results. Moreover, Infosint's evidence of unexpected results is insubstantial because it does not compare the claimed process to Forney 1970, which, as shown above, discloses each limitation of Claim 24, including open, non-pressurized conditions. In any event, evidence of unexpected results is not availing where, as here, there is an overwhelming *prima facie* case of obviousness.[66]

3. Routine Optimization

As discussed, Claim 24 differs from invalidated Claim 21 only with respect to the

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64 *See, e.g.*, *Pfizer, Inc.*, 480 F.3d at 1372.

65 Pl. Mem. 12, 18.

66 *See Agrizap, Inc. v. Woodstream Corp.*, 520 F.3d 1337, 1342-43 (Fed Cir. 2008) ("Even when we presume the jury found that the objective evidence of nonobviousness favored Agrizap, this evidence is insufficient to overcome the overwhelming strength of Woodstream's *prima facie* case of obviousness."); *Pfizer, Inc.*, 480 F.3d at 1372 ("[W]e hold that even if Pfizer showed that amlodipine besylate exhibits unexpectedly superior results, this secondary consideration does not overcome the strong showing of obviousness in this case. . . . Here, the record establishes such a strong case of obviousness that Pfizer's alleged unexpectedly superior results are ultimately insufficient.").

"open, non-pressurized reactor" limitation. Defendants argue in the alternative that "[e]ven if the use of an open, non-pressurized reactor had not been disclosed in the prior art for reactions of terephthalic acid and formaldehyde in oleum, such conditions were on the established menu of options" and therefore are a matter of routine optimization.[67] The Federal Circuit has explained that the use of "routine research methods to prove what was already believed to be the case" is within the skill of the art.[68]

As the 5-carboxyphthalide reaction generates gas, there were at most three different types of reactors in which the claimed reaction could be run: an open, non-pressurized reactor, an open, pressurized reactor, and a closed, pressurized reactor.[69] Infosint's process chemistry expert, Dr. Jon Scott, testified that "[t]here are two types of reactors. There is what would be normally called the standard reactor. However, there are certain types of chemistry that requires substantial pressures in order for the reaction to take place. And when we have a reaction of that sort, we use a pressure reactor."[70]

The reaction here at issue concededly does not require pressure. Moreover, the open, non-pressurized reactor – described by Infosint as a "standard" or "conventional" reactor[71] – was well

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67 Def. Mem. 6.

68 *PharmaStem Therapeutics, Inc.*, 491 F.3d at 1363-64 (Fed. Cir. 2007); *see also Ritchie v. Vast Res., Inc.*, 563 F.3d 1334, 1337 (Fed. Cir. 2009).

69 Trial Tr. 714:7-716:20.

70 *Id.* at 195:21-25.

71 *Id.* at 195:19-196:14 (Scott).

known in the field.[72] In these circumstances, it would have been obvious for a person of ordinary skill in the field of synthetic organic chemistry to try the claimed reaction in an open, non-pressurized reactor.[73]

Infosint responds that its claimed process was more than mere routine optimization in light of its (1) "rejection of Forney's command to use 100% SO_3, and use oleum instead," (2) "rejection of the use of 150º C and a closed container," and (3) unexpected results.[74] Its arguments are unpersuasive.

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72 *See, e.g.*, DTX 2, at Col. 1, lines 23-26 (reaction involving sulfur trioxide "at atmospheric pressure"); DTX 66 (open reactor); DTX 70 (reaction in system in which "excess sulfur trioxide distilled off"); DTX 71 (reaction in dilute oleum in open reactor, citing Forney 1970); DTX 80 (open reactor).

73 *See KSR Int'l Co.*, 550 U.S. at 421, 127 S. Ct. at 1742 ("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 has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.") (holding that court of appeals "conclude[d], in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try'"); *see e.g.*, *Bayer Schering Pharma AG v. Barr Labs., Inc.*, 575 F.3d 1341 (Fed. Cir. 2009) ("[T]he prior art was not vague in pointing toward a general approach or area of exploration, but rather guided the formulator precisely to the use of either a normal pill or an enteric-coated pill . . . . Because the selection of micronized drospirenone in a normal pill led to the result anticipated by the Krause series, the invention would have been obvious."); *Ecolab, Inc. v. FMC Corp.*, 569 F.3d 1335, 1349-50 (Fed. Cir. 2009) (holding claimed method obvious where all but one limitation disclosed in single prior art reference, and the "advantages" of the additional limitation, pressure of "at least 50 psi," "were known"); *Pfizer, Inc.*, 480 F.3d at 1366-67 (holding patent obvious where prior art "clearly pointed the skilled artisan to 53 anions that, as of 1974, were pharmaceutically acceptable" and "one of ordinary skill in the art was capable of further narrowing that list of 53 anions to a much smaller group, including benzene sulphonate, with a reasonable expectation of success").

Lundbeck process chemist Poul Dahlberg Nielsen indeed testified that he replicated the Forney 1970 reaction using oleum as a solvent in "his very first experiment" in 1981. Trial Tr. 563:8-564:3, 564:21-566:12.

74 Pl. Mem. 17-18.

First, Forney did not "command" the use of one hundred percent sulfur trioxide. In fact, the Court previously held that Forney 1971 expressly provided a clear alternative to the use of sulfur trioxide, which one trained in the art would have known "combine[d] with water with explosive violence" and emitted "dense white fumes" when exposed to the air.[75] It previously held also that the temperature was an optimization that would have been within the ordinary skill in the art.[76] Further, a number of prior art references disclose the use of an open, non-pressurized reactor.[77] Finally, Infosint's assertion of unexpected results is flawed and insubstantial for the reasons previously discussed.

In consequence, the '973 Patent is invalid for the independent reason that the use of an open, non-pressurized reactor in the claimed reaction of terephthalic acid and formaldehyde in oleum was an optimization that would have been within the ordinary skill in the art.

Conclusion

For the foregoing reasons, defendants' renewed motion for judgment as a matter of law on the ground that the '973 Patent is invalid as obvious [DI 186] is granted. Defendants' motions for judgment as a matter of law as to infringement [DI 180] and for reconsideration [DI 183] are denied as moot. Infosint's motions to amend the judgment [DI 189] and for judgment as a matter of

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75 DTX 90; *Infosint*, 612 F. Supp. 2d at 413-14.

76 *Infosint*, 612 F. Supp. 2d at 414.

77 *See* DTX 2, at Col. 1, lines 23-26 (reaction involving sulfur trioxide "at atmospheric pressure"); DTX 66 (open reactor); DTX 70 (reaction in system in which "excess sulfur trioxide distilled off"); DTX 71 (reaction in dilute oleum in open reactor, citing Forney 1970); DTX 80 (open reactor).

law [DI 191] are denied.

SO ORDERED.

Dated: June 17, 2010

Lewis A. Kaplan
United States District Judge

(The manuscript signature above is not an image of the signature on the original document in the Court file.)