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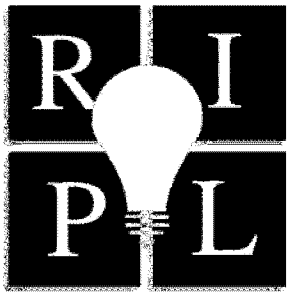

SMITHKLINE V. APOTEX: BROADENING THE SCOPE OF INHERENT ANTICIPATION AND ITS IMPACT ON THE PATENTABILITY OF CHEMICAL STRUCTURES

BRYAN WILLIAM JONES

ABSTRACT

In *SmithKline v. Apotex*, the Court of Appeals for the Federal Circuit invalidated the main patent on Paxil as inherently anticipated. In doing so, the court over-stepped the bounds of appellate review, and broadened the scope of the inherent anticipation doctrine to include chemical structures that are not measurably produced by strict practice of the prior art. This holding does not comport with well-settled precedent and could have dire consequences for the patentability of many chemical structures. A more equitable invalidity analysis would require a chemical structure to derive directly from a disclosed reaction in order to be anticipated; in all other cases, the chemical structure must be proven obvious.

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SMITHKLINE V. APOTEX: BROADENING THE SCOPE OF INHERENT ANTICIPATION AND ITS IMPACT ON THE PATENTABILITY OF CHEMICAL STRUCTURES

BRYAN WILLIAM JONES*

INTRODUCTION

The doctrine of inherent anticipation postulates that everything consistently resulting from the practicing of prior art is anticipated, regardless of whether such result was explicitly disclosed.[1] In order to establish inherent anticipation, positive evidence emanating directly from practice of the prior art must disclose the presence of the anticipated subject matter.[2] Moreover, production of the anticipated subject matter must be a necessary consequence of the prior art.[3] "An accidental achievement of a product or process does not constitute an anticipation."[4]

Despite these well-settled principles, the Court of Appeals for the Federal Circuit ("Federal Circuit") has recently expanded inherency beyond the traditional bounds. In *SmithKline v. Apotex*, the Federal Circuit applied the inherent anticipation doctrine to invalidate a patent on a novel three-dimensional chemical structure despite the fact that it was not measurably produced through strict practice of the prior art.[5] This case threatens the patentability of any chemical structure.

Patents are designed to strike a balance between increasing the store of public knowledge and encouraging innovation.[6] The holding in *SmithKline* indicates that

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[1] 1-3 DONALD S. CHISUM, CHISUM ON PATENTS § 3.03; *see also* Schering Corp. v. Geneva Pharms., Inc., 339 F.3d. 1373, 1377 (Fed. Cir. 2003); Brassica Prot. Prods LLC v. Sunrise Farms (*In re Cruciferous Sprout Litig.*), 301 F.3d 1343, 1350–51 (Fed. Cir. 2002); MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1366 (Fed. Cir. 1999).

[2] *See generally In re* Seaborg, 328 F.2d 996 (C.C.P.A. 1964) (holding that theoretical evidence establishing production of a radioactive isotope was insufficient to establish anticipation).

[3] *Schering*, 339 F.3d. at 1377; *MEHL/Biophile*, 192 F.3d at 1366.

[4] CHISUM, *supra* note 1, § 3.03.

[5] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1346 (Fed. Cir. 2005), *reversing*, 247 F. Supp. 2d 1011 (N.D. Ill. 2003). "This court's holding today merely precludes patent protection for the bare compound PHC hemihydrate as claimed in claim 1." *Id.* Process claims, purification claims, and utilization claims are unaffected. *Id.* (citing *Schering*, 339 F.3d at 1381).

[6] Special Equip. Co. v. Coe, 324 U.S. 370, 378 (1945) (noting that "[Congress] gave to the inventor limited opportunity to gather material rewards for his invention and secured to the public the benefits of full knowledge of the invention and the right to use it upon the expiration of the patent"); Omega Eng'g Inc. v. Raytek Corp., 334 F.3d 1314, 1325 (Fed. Cir. 2003) (reasoning that the Federal Circuit requires a clear disavowal of claim scope in order to "balance the importance of public notice and the right of patentees to seek broad patent coverage"); *see* U.S. CONST. art. I, § 8, ¶ 8 ("[Congress has the power] to promote the Progress of Science and useful Arts by securing for limited Times to . . . Inventors the exclusive Right to their . . . Discoveries"); Kimberly-Clark Corp. v. Johnson & Johnson, 745 F.2d 1437, 1453–54 (Fed. Cir. 1984) (noting that "the real meaning of 'prior

the Federal Circuit has tried to strike this balance in the chemical arts by deeming any undescribed chemical structure that derives from production of a prior art structure anticipated, regardless of the method of derivation. However, this opens the door to invalidating patents on chemical and pharmaceutical structures through anticipation based solely on scientific speculation. Inventions should not be excluded from patent protection on such a tenuous basis.

This comment will analyze the rationale and implications of the inherent anticipation doctrine as applied in *SmithKline*. First, the concepts of obviousness, anticipation, and inherency will be reviewed, and the facts underlying *SmithKline* will be introduced. Next, the Federal Circuit's decision in *SmithKline* will be discussed and criticized. Finally, *SmithKline's* implications will be analyzed and an alternate rubric for analyzing similar situations will be suggested.

I. BACKGROUND

At its core, patent protection rests on a quid pro quo between the inventor and society.[7] The inventor agrees to disclose something that is useful in exchange for the limited right to exclude others from making, using, offering to sell, or selling the innovation.[8] One consideration in this exchange requires the inventor to prove that her invention is novel and non-obvious.[9] Simply put, disclosure of something that does not increase society's store of knowledge does not warrant granting monopoly protection to the discloser.[10] To this end, Congress enacted 35 U.S.C. §§ 102 and 103.[11] Any disclosure that falls within the purview of § 102 lacks novelty and is deemed "anticipated" by the prior art, while one that falls within § 103 is "obvious."[12] First, the standards of patentability under these statutes will be introduced. Then, the facts and the procedural history underlying *SmithKline* will be discussed.

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art' . . . is knowledge that is available, including what would be obvious from it, at a given time, to a person of ordinary skill in the art.").

[7] *E.g.*, Lizardtech, Inc. v. Earth Res. Mapping, Inc., 433 F.3d 1373, 1375 (Fed. Cir. 2006).

[8] 35 U.S.C. § 271 (2000).

[9] 35 U.S.C. §§ 101–103 (2000).

[10] Bonito Boats v. Thunder Craft Boats, 489 U.S. 141, 148 (1989).

> Sections 102(a) and (b) operate in tandem to exclude from consideration for patent protection knowledge that is already available to the public. They express a congressional determination that the creation of a monopoly in such information would not only serve no socially useful purpose, but would in fact injure the public by removing existing knowledge from public use.

Id.

[11] (2000).

[12] *See id.*; WILLIAM H. FRANCIS & ROBERT C. COLLINS, 5 CASES AND MATERIALS ON PATENT LAW 183–86 (West 2002).

A. Obviousness, Anticipation, and Inherency

1. Obviousness

Section 103 was enacted to address situations where the claimed invention is not literally identical to the prior art, but the prior art nonetheless makes the claimed subject matter obvious to a person having ordinary skill in the art.[13] In litigation, an obviousness analysis consists of two steps: determining the scope of the patent claim and determining the differences between the claimed subject matter and the prior art.[14]

First, the scope of the patent claim is determined. A patent claim informs the public of the limits of the invention.[15] In order to properly construe the claims, a court must determine what the claims would mean to a person of ordinary skill in the art in light of the entire record.[16]

Second, the differences between the claimed subject matter and the prior art must be compared through the lens of one with ordinary skill in the art.[17] The invention is deemed obvious if this comparison shows (1) that the claimed subject matter *as a whole* would have been obvious to such a person *at the time of invention*, and (2) the prior art would enable her to produce the subject matter.[18] Courts consider the scope and content of the prior art, the level of ordinary skill in the art, and the differences between the claimed subject matter and the prior art.[19] Also, secondary considerations, such as "commercial success, long felt but unsolved needs, [and] failure of others," may be used to help arrive at such a conclusion.[20]

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[13] *See* Gillette Co. v. S.C. Johnson & Son, Inc., 919 F.2d 720, 724 (Fed. Cir. 1990); *In re* Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988); *In re* Nilssen, 1991 U.S. App. LEXIS 9796 *1–2 (Fed. Cir. 1991).

[14] Graham v. John Deere Co., 383 U.S. 1, 17 (1966). "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved." *Id.* "Against this background, the obviousness or nonobviousness of the subject matter is determined." *Id.*

[15] Permutit Co. v. Graver Corp., 284 U.S. 52, 60 (1931) (noting that "[t]he [patent] statute requires the patentee . . . to inform the public during the life of the patent of the limits of the monopoly asserted, so that it may be known which features may be safely used or manufactured without a license and which may not"); Schriber-Schroth Co. v. Cleveland Trust Co., 305 U.S. 47, 57 (1938) (noting that "[t]he object of the [patent statute] is to require the patentee to describe his invention so that others may construct and use it after the expiration of the patent").

[16] Markman v. Westview Instruments, Inc., 52 F.3d 967, 979–80 (Fed. Cir. 1995) (en banc), *aff'd*, 516 U.S. 1007 (1996). Claims are interpreted "in view of the specification . . . [for which] the description may act as a sort of dictionary, which explains the inventions and may define terms used in the claims." *Id.* at 979. The patent's prosecution history should be included in this analysis. *Id.* at 980. *See also* Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996).

[17] *Graham*, 383 U.S. at 17.

[18] 35 U.S.C. § 103(a) (2000); *In re* Lintner, 458 F.2d 1013, 1015 (C.C.P.A. 1972) (noting that, "it is necessary to ascertain whether or not the reference teachings would appear sufficient for one of ordinary skill in the relevant art having the references before him to make the proposed substitution, combination, or other modification").

[19] *Graham*, 383 U.S. at 17.

[20] *Graham*, 383 U.S. at 17–18 (noting that "such secondary considerations . . . might be utilized to give light to the circumstances surrounding the origins of the subject matter sought to be patented"); *In re Lintner*, 458 F.2d at 1015 (noting that "unexpectedly superior properties or

Eibel Process Co. v. Minn. & Ont. Paper Co. provides a good example of finding non-obviousness due to secondary considerations.[21] In *Eibel Process*, the Supreme Court held that an alteration in the pitch of a certain wire in a paper-making machine was a patentable invention because it increased the speed at which the paper could be made despite the fact that other references suggested increasing the pitch of the same wire.[22] According to the Court, this alteration was a patentable discovery because Eibel's patent was aimed increasing the speed of production, which was important to the art and distinct from the aims of the prior art.[23] As the Court noted, "[t]he fact that in a decade of an eager quest for the higher speeds this important chain of circumstances had escaped observation . . . leaves no doubt . . . that what [Eibel] saw and did was not obvious."[24] This holding means that a patent can be non-obvious even though prior art suggests a similar improvement when the effect of the alteration itself was not suggested by the prior art.

2. Anticipation and Inherency

Anticipation is similar to obviousness but with important distinctions. Whereas a patent claim can be obvious even when it differs from the prior art, a claim is anticipated only when it is identical to a prior art disclosure.[25] In order to be anticipated, every element of a claim must be present in a single prior art reference and set forth in an identical manner.[26] Although trial courts have found anticipation where the claim and the prior art were "substantially" the same, the Federal Circuit and the Supreme Court have repeatedly held that even a slight change defeats anticipation.[27] While a prior art reference most obviously anticipates a claim when it expressly discloses every element of the claim, such explicitness is not required.[28] Rather, a piece of prior art is anticipatory if it discloses every limitation of the claim *either expressly or inherently*.[29] Any result that is "[a] necessary consequence of

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advantages as compared to prior art" may be evidence of nonobviousness); *In re* Papesch, 315 F.2d 381, 387–88 (C.C.P.A. 1963) (holding that a chemical compound that was structurally similar to a prior art compound was nonetheless nonobvious because it possessed unexpected anti-inflammatory properties); *In re* Petering, 301 F.2d 676, 682 (C.C.P.A. 1962) (holding that properties of chemical homologs should be considered in determining obviousness).

[21] Eibel Process Co. v. Minn. & Ont. Paper Co., 261 U.S. 45 (1923).

[22] *Id.* at 67.

[23] *Id.*

[24] *Id.*

[25] *E.g.*, Gechter v. Davidson, 116 F.3d 1454, 1457 (Fed. Cir. 1997) (noting that "[e]very limitation of a claim must identically appear in a single prior art reference to anticipate the claim.").

[26] Studiengesellschaft Kohle, m.b.H. v. Dart Industries, Inc., 726 F.2d 724, 726–27 (Fed. Cir. 1984); CHISUM, *supra* note 1, § 3.02 [1][a].

[27] CHISUM, *supra* note 1, § 3.02 [1][a]&[b] (citing Butler v. Helms 550 F.2d 954, 193 (4th Cir. 1977) (noting "a merely extraneous structural feature recited in a claim . . . should not prevent invalidity for anticipation"); *Eibel Process*, 261 U.S. at 67 (holding that a change in the angle of one component of a paper-making apparatus was sufficient to make it a patentable invention); *Gechter*, 116 F.3d at 1457 (Fed. Cir. 1997) (noting that "[e]very limitation of a claim must identically appear in a single prior art reference to anticipate the claim.").

[28] Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047 (Fed. Cir. 1995).

[29] *Id.*

what was deliberately intended" is inherently anticipated.[30] However, the limits of necessary consequences of prior art are not entirely clear.[31] One line of cases in the Federal Circuit indicates that the inherent property must be recognizable to one skilled in the art in order to be inherently anticipated.[32] A second line indicates that prior art anticipates any natural consequence of its practice, regardless of whether it was recognizable to one of ordinary skill in the art.[33]

This split was ostensibly resolved in *Schering v. Geneva*.[34] *Schering* held that a drug patent inherently anticipated one of the drug's metabolites, even though the identity of the metabolite was unknown when the patent issued.[35] The metabolite was produced as a natural consequence of ingesting pills containing the prior art molecule.[36] In this respect, the *Schering* court extended the concept of necessary consequences to applications of prior art beyond those explicitly outlined in the reference. The court rejected any argument that such consequences needed to be appreciable in order to be inherently anticipated.[37] In *SmithKline Beecham Corp. v. Apotex Corp.*, this iteration of inherent anticipation was applied to invalidate a patent on a chemical compound related to the prior art compound, but not measurably produced by the method outlined in the prior art. [38]

B. SmithKline Beecham Corp. v. Apotex Corp.

1. Facts

In the late 1970s, a company named Ferrosan developed and patented the anti-

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[30] CHISUM, *supra* note 1, § 3.03(1).

[31] *See* Schering Corp. v. Geneva Pharms., Inc., 339 F.3d 1373 (Fed. Cir. 2004); Pfizer, Inc. v. Mylan Labs., Inc., 2005 U.S. Dist. LEXIS 27450, *11 (W.D. Pa. 2005); Harvest Techs. Corp. v. Cytomedix, Inc., 2004 U.S. Dist. LEXIS 18003, *27 (D. Mass. 2004). *See also* Cynthia Chen, Schering Corp. v. Geneva Pharmaceuticals, Inc.: *Clarification of the Inherent Anticipation Doctrine and Its Implications*, 20 BERKELEY TECH. L.J. 95, 99–104 (2005).

[32] Cont'l Can Co. USA v. Monsanto Corp. 948 F.2d 1264, 1268 (Fed. Cir. 1991) (noting that "evidence must make clear that the missing descriptive matter is *necessarily present* . . . and that it *would be so recognized by persons of ordinary skill*.") (emphasis added); *In re* Seaborg, 328 F.2d 996, 998–99 (C.C.P.A. 1964) (holding that practice of prior art that led to production of a radioactive isotope "in such minuscule amounts and under such conditions that its presence was undetectable" did not anticipated the isotope); *Glaxo*, 52 F.3d at 1047 (interpreting anticipation to require every limitation of the claim to be "appreciated by one of ordinary skill in the art").

[33] *E.g.*, Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999). In invalidating a claim for an explosive composition with "sufficient aeration" as the only part of the claim distinguishing it from prior art, the court noted that "artisans of ordinary skill may not recognize the inherent characteristics or functioning of prior art." *Id.* at 1345, 47. "However, the discovery of a previously unappreciated property of a prior art composition . . . does not render the old composition patentably new to the discoverer." *Id.* at 1347.

[34] Schering Corp. v. Geneva Pharms., Inc., 339 F.3d. 1373, 1378 (Fed. Cir. 2003).

[35] *Id.* at 1380. Note that the drug in question in this case is lortadine (better known as Claritin) and that the identified metabolite is the "active circulating metabolite" of lortadine. Chen, *supra* note 31, at 104–05.

[36] *Schering*, 339 F.3d at 1380 (noting that "ingesting lortadine would necessarily metabolize that compound to [the metabolite in the anticipated claim]").

[37] *Id.* at 1377–78.

[38] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1343–46 (Fed. Cir. 2005).

depressant compound paroxetine ("Ferrosan patent").[39] As Ferrosan had no experience in producing pharmaceuticals, it granted a license to SmithKline to bring paroxetine to market.[40]

When an manufacturer produces a drug in pill form, the manufacturer typically converts a pharmaceutically active compound into its salt.[41] While the Ferrosan patent disclosed a method of making a paroxetine maleate salt, a hydrochloride salt is generally preferred.[42] Through some difficulty, Ferrosan was able to produce a paroxetine hydrochloride salt ("PHC"), although this procedure was not disclosed by the Ferrosan patent.[43]

Initial tests indicated that PHC produced in this manner was anhydrous, meaning the crystalline structure did not contain bound water.[44] This anhydrousness made production of PHC in bulk extremely difficult because the PHC had a propensity to absorb atmospheric water.[45] As a result, SmithKline failed to find a suitable production method under the Ferrosan patent, which was approaching its expiration date.[46] This failure was an enormous concern because FDA requirements already greatly reduce the effective time of exclusive use of patented technologies.[47]

SmithKline sought to remedy the situation by experimenting with different production methods.[48] In the course of doing so, a SmithKline chemist observed a novel crystalline form of PHC, PHC hemihydrate.[49] The PHC hemihydrate solvate was more stable than the anhydrous form, making it much easier to package and preserve.[50] Recognizing the economic potential of this form of PHC, SmithKline patented PHC hemihydrate ("SmithKline patent").[51] SmithKline eventually switched focus to developing a drug under the SmithKline patent, now known as Paxil.[52]

PHC hemihydrate had a peculiar property. Once the hemihydrate was produced in a lab, the anhydrate form could no longer be produced; rather, procedures that formerly lead to anhydrate production would now lead to hemihydrate production.[53] Moreover, SmithKline detected hemihydrate in a few PHC batches from a previous manufacturing cycle that had yielded only anhydrate.[54] SmithKline explained these observations by a phenomenon called seeding. Seeding occurs when a crystal

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[39] U.S. Patent No. 4,007,196 (filed July 23, 1975) (claiming "[paroxetine] and a salt thereof with a pharmaceutically acceptable acid").

[40] SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d 1011, 1015 (N.D. Ill. 2003).

[41] *Id.*

[42] *Id.*

[43] *Id.* at 1016.

[44] *Id.* at 1017. In contrast, a hemihydrous crystal structure contains one molecule of water for every two molecules of the crystalline molecule. *Id.*

[45] *Id.*

[46] *Id.*

[47] *Id.*

[48] *Id.* at 1016.

[49] *Id.*

[50] *Id.* at 1017.

[51] U.S. Patent No. 4,721,723 (filed Oct. 23, 1986). The filing claimed, "[c]rystalline paroxetine hydrochloride hemihydrate" (claim 1) and "[c]rystalline paroxetine hydrochloride hemihydrate in substantially pure form" (claim 2). *Id.*

[52] *SmithKline*, 247 F. Supp. 2d at 1018.

[53] *Id.* at 1021.

[54] *Id.* at 1021–22.

structure becomes contaminated with small amounts of a similar, but more stable, form of the crystal.[55] The less stable form of the crystal then spontaneously converts to the more stable form.[56] Therefore, if the anhydrous form becomes contaminated with the more stable hemihydrous seeds, the anhydrous form will rapidly convert to hemihydrate. This seeding theory formed the basis of the infringement claim in *SmithKline*.

2. Court Proceedings

As the Ferrosan patent approached its expiration date, Apotex, a generic drug manufacturer, sought approval from the FDA to begin marketing a PHC anhydrous-based pharmaceutical.[57] In response, SmithKline initiated an infringement action against Apotex.[58] SmithKline theorized that if one produced the anhydrous form long enough in an industrial setting, the production facilities would inevitably become seeded with hemihydrate.[59] This seeding would make future production of anhydrate impossible because it would convert to hemihydrate, thereby infringing the SmithKline patent.[60] Apotex asserted that the Ferrosan patent inherently anticipated the SmithKline patent.[61] It theorized that hemihydrate is always present when PHC is produced, although it can remain undetectable for a long period of time.[62] Therefore, the Ferrosan patent inherently anticipated hemihydrate because it disclosed a method for producing it, albeit in undetectable amounts.

The district court conceded that the Apotex scenario is likely.[63] However, the court declined to invalidate the SmithKline patent because Apotex failed to prove by clear and convincing evidence that production of pure PHC anhydrate inevitably leads to production of PHC hemihydrate.[64] The district court was particularly swayed by the significant debate amongst scientists over the origin of different crystal structures.[65] Despite this, the district court ultimately rejected SmithKline's infringement action by construing the SmithKline patent to cover only "commercially significant quantities of hemihydrate."[66] Therefore, the SmithKline patent was held

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[55] *Id.* at 1019–20.

[56] *Id.* at 1020.

[57] *Id.* at 1023. The Hatch-Waxman Act allows generic manufacturers to eschew formal FDA safety requirements if it can show that its generic is a bioequivalent of a previously approved drug. *Id.* at 1018. To this end, generic manufacturers must file an Abbreviated New Drug Application ("ANDA"), which discloses bio-equivalents to the product. *Id.* Apotex's ANDA disclosed the active ingredient of its product as PHC anhydrate, which it claimed as bioequivalent to the PHC hemihydrate disclosed in the SmithKline patent. *Id.* at 1023. Apotex's ANDA further stated that its product would not infringe that patent. *Id.*

[58] *Id.* at 1013.

[59] *Id.* at 1013–14, 1019–20.

[60] *Id.* at 1019.

[61] *Id.* at 1024–25.

[62] *Id.* at 1025.

[63] *Id.* at 1022–23.

[64] *Id.* at 1025.

[65] *Id.* (noting "the uncertainties in the scientific community concerning the provenance and causality of polymorphs.").

[66] *Id.* at 1026–29.

valid, but not infringed, by Apotex's method for producing PHC anhydrate.[67]

II. DISCUSSION

Improper Application of the Inherent Anticipation Doctrine in *SmithKline*

The Federal Circuit reversed the district court's claim construction, but ultimately invalidated the SmithKline patent because it was inherently anticipated by the Ferrosan patent.[68] This was improper for two reasons. First, the court misconstrued the record and the district court's holding in finding the SmithKline patent anticipated. Second, the Federal Circuit's holding does not comport with precedent when the facts are properly interpreted.

A. The Federal Circuit erred in reversing the district court's finding that the Ferrosan patent did not anticipate the SmithKline patent.

An issued patent enjoys a presumption of validity which can only be rebutted by clear and convincing evidence.[69] Prior art anticipates a chemical structure only when it enables one skilled in the art to produce the identical structure.[70] Therefore, clear and convincing evidence must show that the Ferrosan patent *by itself* enabled a skilled practitioner to make hemihydrate in order to find anticipation. The Federal Circuit misconstrued SmithKline's infringement claim and misinterpreted the teachings of the Ferrosan patent, causing it to mistakenly find the district court's conclusion clearly erroneous.

1. Manufacture of PHC is not the same as practicing the Ferrosan patent.

SmithKline's argument that manufacture of PHC would inevitably lead to hemihydrate production formed a main foundation of the Federal Circuit's ruling.

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[67] *Id.* at 1052.

[68] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d. 1331, 1342–46 (Fed. Cir. 2005) (stating that "SmithKline admits, through its proffered arguments, that producing PHC anhydrate according to the [Ferrosan] patent inevitably results in the production of at least trace amounts of anticipating PHC hemihydrate").

[69] 35 U.S.C. § 282 (2000) (stating that "[a] patent shall be presumed valid [and] . . . [t]he burden of establishing invalidity . . . shall rest on the party asserting such invalidity"); Radio Corp. of Am. v. Radio Eng'r Lab., Inc., 293 U.S. 1, 8 (1934) (noting that "one . . . who assails the validity of a patent fair upon its face bears a heavy burden of persuasion, and fails unless his evidence has more than a dubious preponderance"); Union Oil Co. of Cal. v. Atl. Richfield Co., 208 F.3d 989, 995 (Fed. Cir. 2000) (requiring clear and convincing evidence to establish anticipation).

[70] *See SmithKline*, 403 F.3d at 1342 (noting that anticipation requires each and every limitation to be disclosed in a single prior art reference); Novo Nordisk Pharm. Inc., v. Bio-technology Gen. Corp., 424 F.3d 1347, 1354–55 (Fed. Cir. 2005) (reasoning that anticipation requires that the inherently disclosed feature be enabled to one of skill in the art); Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318, 1325 (Fed. Cir. 2005) (reasoning that "a patent claim 'cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled'").

The court reasoned that SmithKline "[admitted], through its proffered arguments, that producing PHC anhydrate according to the [Ferrosan patent] inevitably results in production . . . of anticipating PHC hemihydrate."[71] This rationale misinterprets SmithKline's core argument.

A claim is inherently anticipated only when it literally reads on something that is a necessary consequence of practicing a prior art reference.[72] SmithKline argued that its patent was infringed by manufacture of PHC anhydrate products, but that the Ferrosan patent did not anticipate it.[73] They hypothesized that manufacture of anhydrate products would cause the production facilities to become seeded with hemihydrate, which would then make production of pure anhydrate impossible.[74] The distinction between "practice of the Ferrosan patent" and "manufacture of anhydrate products" is crucial to the question of inherent anticipation.[75]

First, it is questionable whether production of PHC is indeed practice of the Ferrosan patent. The district court merely noted that production of hemihydrate was first observed "while following *more or less* the directions of the patent."[76] However, the Ferrosan patent does not explicitly disclose either PHC or a method aimed at producing PHC. Rather, the Ferrosan patent claims "[paroxetine] . . . and a salt thereof with a pharmaceutically acceptable acid" and discloses a general method for producing a single paroxetine salt.[77] This presents two problems. First, the patent discloses, at the most, a genus of paroxetine salts, of which PHC is a species. The problem is that a genus does not necessarily anticipate every species that falls within it.[78] Therefore, before the court could even get to the question of whether hemihydrate was anticipated by the Ferrosan patent, it first needed to address whether PHC, as a species of paroxetine salts, was disclosed by the Ferrosan patent. This question was never addressed by either court. Second, one cannot logically practice a patent on a chemical structure unless there is a procedure for producing it. If anticipation of a product is analogous with practicing prior art, then the prior art must enable production of the structure without undue experimentation.[79] As noted

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[71] *SmithKline*, 403 F.3d at 1344.

[72] *See, e.g.*, Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999).

[73] *SmithKline*, 403 F.3d at 1341.

[74] SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d. 1011, 1019 (N.D. Ill. 2003); *SmithKline*, 403 F.3d at 1335–36 (noting that "to show that manufacture of PHC anhydrate tablets necessarily creates PHC hemihydrate, SmithKline proffered expert testimony on the so-called 'seeding' or 'disappearing polymorph' theory").

[75] *SmithKline*, 247 F. Supp. 2d. at 1019. As the district court points out, the issue is that *manufacture* of pure anhydrate would be difficult or impossible. *Id.* Moreover, Judge Gajarsa pointed out that both SmithKline and the district court explicitly rejected the idea that anhydrate and hemihydrate always exist together and that SmithKline's scientists were "absolutely convinced" that hemihydrate was not produced "before December 1984." *SmithKline*, 403 F.3d at 1355–56 (Gajarsa, J. concurring).

[76] *SmithKline*, 247 F. Supp. 2d at 1025 (emphasis added).

[77] *See* U.S. Patent No. 4,007,196 (filed July 23, 1975) (claim 1 and example 2). Example 2 demonstrates a general method for making paroxetine maleate salts. *Id.*; *see also SmithKline*, 247 F. Supp. 2d. at 1015 (noting that "the patent specified paroxetine maleate as the paroxetine salt it was claiming"); U.S. Patent No. 4,721,723 (filed Oct. 23, 1986) (issued Jan. 26 1988) (citing Example 2 of the Ferrosan patent as an example of making paroxetine salts).

[78] Atofino v. Great Lakes Chem. Corp., 2006 U.S. App. LEXIS 7180, *20–21 (Fed. Cir. 2006).

[79] Novo Nordisk Pharm. Inc., v. Bio-technology Gen. Corp., 424 F.3d 1347, 1355 (Fed. Cir. 2005).

by the district court, the patent discloses "more or less" a procedure for producing PHC. This is a problem, however, because the court also noted that Ferrosan encountered "some travail" in producing PHC.[80] Importantly, the district court never addressed whether this difficulty amounted to undue experimentation. Although it is possible, and maybe even likely, that the court would have found that PHC was both disclosed and enabled by the Ferrosan patent, its failure to do so imparts doubt on the propriety of the Federal Circuit's holding.

Even assuming that the Ferrosan patent disclosed and enabled PHC production, manufacture of anhydrate products is not the same as practicing the Ferrosan patent. Even in its broadest sense, practicing the Ferrosan patent ends with the production of paroxetine salts. Manufacture of anhydrate products can involve steps beyond production of PHC, including high-pressure treatment to form pills and a final treatment with a water-based coating.[81] Furthermore, temperature and humidity fluctuations during manufacture and storage present limitations outside the bounds of the Ferrosan patent that could influence structural changes.[82] Finally, SmithKline argued that Apotex's production facilities were already seeded with hemihydrate from actively producing it for Hatch-Waxman purposes.[83] This is precisely the point; SmithKline's argument is that Apotex cannot possibly have a pure anhydrate product because use of PHC *under these circumstances* will inevitably result in hemihydrate production. These conditions simply do not read upon anything in the Ferrosan patent.[84]

The only way to reconcile the Federal Circuit's holding is to presume that a structural patent inherently contains the right to manufacture all commercial embodiments of the claimed product, which then passes to the public upon expiration. In this case, the Ferrosan patent must be construed to include all products that contain paroxetine salts. However, it is dogmatic that, while a patent contains the right *to exclude* others from using the claimed structure, it does not guarantee an absolute right *to use* the structure.[85] As noted in the Federal Circuit's concurring opinion, the right to use is traditionally limited to those means that are reasonably disclosed by the patent.[86] It logically follows that the benefit to the public

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[80] *SmithKline*, 247 F. Supp. 2d. at 1015.

[81] *Id.* at 1024, 1034, 1039, 1043–44.

[82] *Id.* at 1024.

[83] *Id.*

[84] *See generally* U.S. Patent No. 4,007,196 (filed July 23, 1975).

[85] JANICE M. MUELLER, AN INTRODUCTION TO PATENT LAW 14 (Aspen 2003) (noting that "a patent does not convey any *positive* or affirmative right to make use sell, offer to sell, or import an invention"). For example, assume that inventor A invents a straight back chair and obtains a broad patent covering chairs. *Id.* at 15. Inventor B subsequently invents a rocking chair. *Id.* Inventor B cannot make, use, or sell his rocking chair because it literally infringes A's patent. *Id.* Likewise, A cannot make sell or use a rocking chair because B has the right to exclude others from using it. *Id.*

[86] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1358 (Fed. Cir. 2005) (Gajarsa, J., concurring). Judge Gajarsa noted that:

> [w]hoever discovers that a certain useful result will be produced . . . by the use of certain means, is entitled to a patent for it; provided he specifies the means he uses in a manner so full and exact, that any one skilled in the science . . . can, by using the means he specifies, without any addition to, or subtraction from them, produce precisely the result he describes. And if this cannot be done by the means he describes, the patent is void. And if it can be done, then the patent confers on him the exclusive right to use the means he specifies to produce the result or

is limited to those means. The embodiment of PHC anhydrate and the means to produce it that SmithKline claims will infringe its patent simply are not disclosed, reasonably or otherwise, by the Ferrosan patent. SmithKline's arguments therefore do not admit that practice of the Ferrosan patent inevitably leads to production of PHC hemihydrate.

2. The facts as found by the district court were not clearly erroneous.

Without such an admission, Apotex needed to prove by clear and convincing evidence that hemihydrate is a necessary consequence of practicing the Ferrosan patent.[87] Hemihydrate production was observed only in two situations: (1) SmithKline's experiments with the procedures outlined by Ferrosan and (2) a few batches of PHC produced by SmithKline which contained hemihydrate.[88] The district court found this evidence insufficient to meet this burden.[89] To the Federal Circuit, however, this indicated that the Ferrosan patent inherently anticipated the SmithKline patent, rendering it invalid.[90] The Federal Circuit was unwarranted in reversing this finding of fact as clearly erroneous.[91]

The Federal Circuit misinterpreted the district court's holding. It read the decision as requiring Apotex to prove by clear and convincing evidence that hemihydrate existed before SmithKline discovered it.[92] While this was certainly an aspect of the holding, it is not the entire case. The district court was also unconvinced that Apotex had shown by clear and convincing evidence that hemihydrate is produced by following the Ferrosan patent in a non-seeded environment.[93] Apotex's expert posited that, under the Ferrosan specifications, hemihydrate exists in equilibrium with anhydrate, although at undetectable levels, while SmithKline's expert asserted that he was "'absolutely convinced' that no hemihydrate had existed before December of 1984."[94] The district court thought it likely that hemihydrate seeds are present in any batch of anhydrate, but nonetheless found it possible that pure anhydrate could be produced in a non-seeded

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effect he describes, and nothing more.

Id. (quoting O'Reilly v. Morse, 56 U.S. 62 (1853)).

[87] *See, e.g.*, Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999).

[88] *SmithKline*, 403 F.3d at 1344.

[89] *SmithKline*, 247 F. Supp. 2d. at 1025–26.

[90] *SmithKline*, 403 F.3d at 1347. The court found that SmithKline's "serendipitous" discovery of hemihydrate meant that anhydrate could spontaneously convert to hemihydrate. *Id.* at 1344.

[91] Novo Nordisk Pharm. Inc., v. Bio-technology Gen. Corp., 424 F.3d 1347, 1355 (Fed. Cir. 2005) (noting that "[w]hat a prior art reference discloses in an anticipation analysis is a factual determination that we review under the clearly erroneous standard"); Glaxo Group Ltd. v. Apotex, Inc., 376 F.3d 1339, 1346 (Fed. Cir. 2004) (stating that "a finding is clearly erroneous when, despite some supporting evidence, 'the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed.'").

[92] *SmithKline*, 403 F.3d at 1343 (interpreting the district court decision as requiring Apotex to prove, "by clear and convincing evidence that it was impossible to make pure PHC anhydrate in the United States before the critical date of the [SmithKline] patent").

[93] *SmithKline*, 247 F. Supp. 2d at 1026. Particularly, the district court was swayed by "the uncertainties in the scientific community concerning the provenance and causality of polymorphs . . . ." *Id.* at 1025.

[94] *Id.* at 1022.

environment.[95] Therefore, Apotex failed to meet its burden of proof.

This is a critical holding because the presence of seeds presents an extra limitation not described in the Ferrosan patent. Neither party presented evidence clearly showing that practice of the Ferrosan patent leads directly to formation of hemihydrate seeds.[96] SmithKline's experiments with the Ferrosan patent provided the only direct mechanisms for hemihydrate formation.[97] However, this does not mean that the Ferrosan patent anticipates seed formation, because at least one condition of this procedure was not taught by the Ferrosan patent.[98] Hemihydrate was subsequently observed every time SmithKline attempted to make anhydrate in the lab; however, this can be explained by seeds left from SmithKline's previous production of hemihydrate.[99] Therefore, SmithKline's experimental observation of hemihydrate conclusively was *not* anticipatory. The only other veritable observation of hemihydrate came while testing two batches manufactured prior to SmithKline's discovery of hemihydrate.[100] However, those samples were tested three months after they were made.[101] Without understanding what happened in those three months, one can only speculate as to the source of the hemihydrate.[102] For all anyone knows, those batches were pure anhydrate until they were seeded by the very scientists responsible for verifying their purity. The district court noted that someone carrying even trace amounts of hemihydrate on their clothing could seed anhydrate, converting it to hemihydrate.[103] The Ferrosan patent does not contemplate such an additional treatment of the end-product. In such a situation, hemihydrate production is not anticipated because it occurs as a result of a condition outside the purview of the Ferrosan patent.

Taken as a whole, the district court did not find these facts to clearly show that production of hemihydrate seeds naturally flows from practice of the Ferrosan

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[95] *Id.* at 1023, 1026. The district court also reasoned that "inherent anticipation may not be established by probabilities or possibilities." *Id.* at 1025 (citing MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1365 (Fed. Cir. 1999)).

[96] *See SmithKline*, 247 F. Supp. 2d at 1019–23.

[97] *Id.* at 1017 (noting that when hemihydrate was first observed, SmithKline's scientist had "made a batch of paroxetine, added isopropyl alcohol, . . . and found that the batch crystallized as hemihydrate instead of anhydrate"); *see also* U.S. Patent No. 4,721,723 (filed Oct. 23, 1986) (issued Jan. 26 1988).

[98] *See generally* U.S. Patent No. 4,007,196 (filed July 23, 1975). Example 2 demonstrates a general method of paroxetine crystal formation whereby the chemical is crystallized initially in an ether solution, resuspended in ethanol, and then recrystallized. *Id.* Addition of isopropyl alcohol constitutes an additional limitation not found in the Ferrosan patent. *See SmithKline*, 247 F. Supp. 2d. at 1017; U.S. Patent No. 4,721,723 (filed Oct. 23, 1986) (issued Jan. 26 1988) (reciting several methods for production of crystalline paroxetine hemihydrate distinguishable from those in the Ferrosan patent).

[99] *SmithKline*, 247 F. Supp. 2d. at 1021. The district court accepted that seeding was responsible for subsequent laboratory produced hemihydrate, noting that "the likeliest explanation is that the first batch of hemihydrate that he created had seeded his lab." *Id.*

[100] *Id.* at 1022.

[101] *Id.* at 1016, 1022 (noting that SmithKline's scientist discovered hemihydrate in March of 1985 and batches produced in December of 1984 and January of 1985 were subsequently tested and determined to contain hemihydrate).

[102] *Id.* at 1022 (characterizing Apotex's assertion that hemihydrate and anhydrate exist in equilibrium as conjecture "support[ed] . . . in SmithKline's own evidence").

[103] *Id.* at 1020–21.

patent.[104] The district court noted that, "[i]t is equally plausible . . . that practicing the [Ferrosan] patent in a non-seeded premises . . . would not have produced any hemihydrate."[105] This conclusion is supported by substantial evidence, therefore rendering the Federal Circuit's reversal unwarranted.[106]

B. The Federal Circuit's ruling over-extends the reach of inherent anticipation.

The extent to which the Federal Circuit has broadened the inherent anticipation doctrine presents an even more troubling problem than the impropriety of reversing the district court. First, the Federal Circuit essentially held that a by-product of a chemical reaction not directly taught by the patent was anticipated by the mere fact that the reaction was intended to produce a claimed structure. Second, the court held that such anticipation could be established solely upon a theoretical base even when faced with an equally plausible counter-theory, which is inconsistent with precedent.

1. SmithKline held that a chemical by-product of an undescribed chemical reaction is anticipated.

The first and most obvious point of error by both courts is that PHC is never explicitly described in the patent.[107] The Ferrosan patent claimed a class of molecules that includes paroxetine and "a pharmaceutically acceptable salt thereof" and only disclosed a method for making paroxetine maleate.[108] The claim of pharmaceutically acceptable salts is a genus claim, which does not necessarily encompass all members of the genus.[109] At best, such a genus could only generically anticipate PHC, but could not anticipate specific crystalline forms of PHC.[110]

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[104] *See id.* at 1025–26. Even though the opposite is likewise not clearly demonstrated, the district court pointed out that the burden upon the party challenging the validity of the patent is heavy. *Id.* The weight of the evidence failed to carry this burden. *Id.* at 1026.

[105] *Id.* at 1026.

[106] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1328, 1329 (Fed. Cir. 2005) (Newman, J., dissenting) (denying rehearing en banc) (noting that the majority's "findings of chemical fact are devoid of scientific support"); *see also* Anderson v. Bessemer City, 470 U.S. 564, 573–74 (1985) (noting that "if the district court's account of the evidence is plausible in the light of the record viewed in its entirety, the court of appeals may not reverse it even though convinced . . . it would have weighed the evidence differently."); Miles Lab. Inc. v. Shandon, Inc., 997 F.2d 870, 874 (Fed. Cir. 1993) (noting that "[w]here the fact-finder's account of the evidence . . . chooses one of two permissible views of the evidence, it has committed no clear error.").

[107] *See SmithKline*, 247 F. Supp. 2d at 1024 (noting that "[the Ferrosan patent] did not refer to paroxetine hydrochloride or to crystallinity, but to a set of compounds of which paroxetine maleate (another paroxetine salt) was one example.").

[108] U.S. Patent No. 4,007,196 (filed July 23, 1975).

[109] Atofina v. Great Lakes Chem. Corp., 2006 U.S. App. LEXIS 7180, at *20–21 (Fed. Cir. Mar. 23, 2006) (noting that, unless a genus claim is narrow, it does not necessarily anticipate every species); Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997) (noting that "[w]here there is unpredictability in performance of certain species . . . other than those specifically enumerated, one skilled in the art may be found not to have . . . a genus.").

[110] *See* SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d at 1024. The court noted

Even assuming that PHC anhydrate was a claimed end product, each of the processes that definitively led to hemihydrate production involved steps that were not contemplated by the Ferrosan patent.[111] Furthermore, the intended end product of each of these processes was anhydrate, not hemihydrate. Given this, the hemihydrate that was produced could be deemed a by-product of uncontemplated methods of producing a claimed end product. The crux of the issue is that different methods for producing the same intended end-product will often result in a distinct array of by-products. The question is whether a structure patent anticipates by-products of production methods that are distinct from what was disclosed. This proposition does not logically comport with precedent.

Anticipation requires that every limitation of the anticipated subject matter be contained within a single prior art reference.[112] Something simply is not contained within a prior art reference if one must go outside of that reference to produce it. Moreover, prior art inherently anticipates only those things which are necessary consequences of what was disclosed.[113] Again, something cannot be a necessary consequence when it only appears under certain conditions beyond the teachings of the prior art. There are simply too many steps required to get from the Ferrosan patent to hemihydrate in order to justify ruling that it contains every limitation of the SmithKline patent.

2. Neither Supreme Court nor Federal Circuit precedent supports anticipation of chemical by-products by undescribed chemical reactions.

Neither the structure of PHC hemihydrate nor the methods for producing it were disclosed by the Ferrosan patent. Well-established Supreme Court precedent holds that even slight variance between the assaulted subject matter and prior art defeats anticipation.[114] In *Eibel Process*, the Supreme Court unambiguously held that a claim is unanticipated even when every element of the prior art is present if they are put together in a distinct fashion.[115] Every instance in which hemihydrate was produced involved fashions of producing PHC anhydrate that are measurably distinct from those taught in the Ferrosan patent. Furthermore, *Tilghman v. Procter* explicitly rejected the argument that accidental and unwitting production of by-products in pursuit of other and different results is the same as anticipation.[116] PHC

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that SmithKline was able to patent other forms of anhydrate. *Id.* This indicates that the disclosure of the genus itself was insufficient to prevent the patentability of PHC anhydrate. Moreover, the court observed that the example of paroxetine maleate probably yielded an amorphous salt, which means that it was not crystalline. *Id.* This could be construed to indicate that significant experimentation would have been required to produce any crystalline structure, which would preclude anticipation of crystalline species.

[111] *Compare* U.S. Patent No. 4,007,196 (filed July 23, 1975) (Example 2), *with* U.S. Patent No. 4,721,723 (filed Oct. 23, 1986) (issued Jan. 26 1988).

[112] *See, e.g.*, Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999).

[113] *Id.*

[114] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1328, 1329–30 (Fed. Cir. 2005) (denying rehearing en banc) (Newman, J., dissenting) (citing Tilghman v. Proctor, 102 U.S. 707 (1881) and Eibel Process Co. v. Minn. & Ont. Paper Co., 261 U.S. 45, 67 (1923)).

[115] *Eibel Process*, 261 U.S. at 67.

[116] *Tilghman*, 102 U.S. at 711–12 (noting that there is no anticipation of "accidentally and

hemihydrate was produced as an accidental and unwitting by-product of an attempt to produce PHC anhydrate that was not described by the Ferrosan patent. Both cases are still good law and defeat any precedential basis for the Federal Circuit's holding.

One can also distinguish this case from Federal Circuit precedent. Much of the court's decision was based on the teachings of *Schering* and *Atlas Powder*.[117] Both cases involved claimed elements that were necessary for the prior art to function as intended.[118] Moreover, those anticipated by-products were invariably present when the intended result was obtained as described.[119] In contrast, hemihydrate production was an ancillary consequence of an alternate method of production.[120] Further, the district court found that it was reasonably possible to produce anhydrate in some settings without producing hemihydrate.[121] This sufficiently distinguishes *SmithKline* from *Schering* and *Atlas Powder* to avoid them as precedent.

The Federal Circuit also incorrectly distinguished this case from *In re Seaborg*. *In re Seaborg* held that a radioisotope was not anticipated by a prior art nuclear reaction because there was no "positive evidence" that the isotope was actually produced.[122] If anything, this case is directly on point. In both cases, anticipation

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unwittingly produced" results).

[117] *SmithKline*, 403 F.3d at 1343–46.

[118] *Atlas Powder*, 190 F.3d at 1347 (noting that a claim for "sufficient aeration" is anticipated when "[t]he trial record . . . shows that those of ordinary skill in this art at the time . . . knew that both interstitial and porous air enhance sensitivity."); *Schering*, 339 F.3d. at 1381 (holding that the a metabolite of a claimed product was anticipated).

[119] Schering Corp. v. Geneva Pharms., Inc., 275 F. Supp. 2d 534, 538 (D.N.J. 2002) (noting that the plaintiff consistently called the anticipated product "the major active circulating metabolite" of the anticipatory subject matter, which means that the anticipatory subject matter could not function as intended without forming that metabolite); *Atlas Powder*, 190 F.3d at 1344–45 (noting that sufficient aeration—which was the only distinguishing limitation between the claim in question and the prior art—was a critical element in the increased efficacy of prior art explosives as compared to others available at the time, therefore rendering that limitation inherent in the prior art).

[120] *See* SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d. 1011, 1022 (N.D. Ill. 2003).

[121] *Id.* at 1026.

[122] *In re* Seaborg, 328 F.2d 996, 999 (C.C.P.A. 1964). The court noted that:

> [In order for a] patent or other publication to be an anticipation [it] must bear within its four corners adequate directions for the practice of the patent invalidated. If the earlier disclosure offers no more than a starting point for further experiments, if its teaching will sometimes succeed and sometimes fail, if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation.

Id. at 997. In addition, the court stated:

> There is no positive evidence that americium was produced inherently in the natural uranium fuel . . . in the exemplary statement relied upon by the Patent Office. . . . The maximum amount of americium-241 which could have been produced by the operation of the reactor . . . would have been one billionth of one gram (1/1,000,000,000 gram). . . . If the one billionth of a gram were produced, it would have been completely undetectable, since it would have been diluted with the 40 tons of intensely radioactive uranium fuel which made up the reactor. The possibility that although a minute amount of americium may have been produced in the Fermi reactor, it was not identified (nor could it have been identified,(*sic*)

was inferred from a scientific theory.[123] In neither case was there any evidence shown that the anticipated molecules were actually being produced by the methods as described in the prior art.[124] Under *In re Seaborg*, a scientific theory cannot substitute for evidence showing production of hemihydrate flowing *directly* from practice of the Ferrosan patent.[125] Because Apotex could not produce such evidence, *In re Seaborg* required the court to reject the anticipation defense.

Finally, the court failed to distinguish this case from *Glaxo Inc. v. Novopharm, Ltd.*[126] In that case, the Federal Circuit affirmed a finding of non-anticipation of a novel crystalline form of an anti-ulcer drug.[127] The party asserting anticipation was able to definitively demonstrate that a crystallization procedure outlined in a prior art patent led directly to production of the claimed crystal.[128] However, the district court found non-infringement because the prior art form of the crystal could also be made by the procedure.[129] The Federal Circuit affirmed.[130] As the Federal Circuit explained in *In re Crish*, this holding was proper because the facts indicate that the claimed form of the crystal was not always made by the procedure outlined in the prior art patent.[131] Similarly here, the district court concluded that, although it is likely that hemihydrate is produced in trace amounts whenever anhydrate is made, this was not proven by clear and convincing evidence.[132] The finding of non-anticipation based on this finding of fact is clearly supported by *Glaxo* and *Crish* and should have been affirmed.

III. PROPOSAL

So What Is the Alternative? Applying Obviousness to Remedy the Flaws of *SmithKline*.

Despite the legal flaws, it is difficult to argue with the outcome of *SmithKline* from an equity standpoint. Neither logic nor equity supports precluding practice of

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> would preclude the application of the Fermi patent as a reference to anticipate the present invention.

Id. at 999. In short, this means that even though the party asserting anticipation proved with a fair degree of scientific precision that the alleged product was present in the prior art, this evidence was insufficient to establish inherency because there was no positive evidence *emanating from the practice of the prior art* to establish this theory.

[123] *Compare id.* at 998 (rejecting inherent anticipation because "its determination [in this case] is dependent to such a great extent upon inferences rather than upon definitely established facts"), *with* SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1335, 1344–45 (Fed. Cir. 2005) (finding inherent anticipation despite the fact that the movant did not show that practice of prior art directly leads to production of the anticipated subject matter).

[124] *In re Seaborg*, 328 F.2d at 998; *SmithKline*, 403 F.3d at 1335, 1344–45.

[125] *See In re* Seaborg, 328 F.2d 993, 994 (C.C.P.A. 1964).

[126] *See generally*, Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043 (Fed. Cir. 1995).

[127] *Id.* at 1045, 1047–48.

[128] *Id.* at 1047.

[129] *Id.*

[130] *Id.* at 1048.

[131] *In re* Crish, 393 F.3d 1253, 1259 (Fed. Cir. 2004).

[132] SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d. 1011, 1022–23, 1026 (N.D. Ill. 2003).

an expired patent on the theory that it infringes a subsequent patent. However, the inherent anticipation doctrine as applied in *SmithKline* could prove fatal to many chemical and biological structural patents.[133] First, the pitfalls of this doctrine will be discussed. Then, an alternate rubric for analyzing such situations will be addressed.

A. The Federal Circuit's current inherency doctrine could preclude patenting of useful chemical and biological structures.

PHC and other crystal structures are examples of macromolecules, a class of very large molecules composed of smaller subunits, which includes proteins, DNA, and polymers. Although macromolecular variability is most obvious when the chemical composition is changed, any macromolecule can exist in a multitude of three-dimensional structures.[134] These different structures often impart distinct physical, functional, and even pathological characteristics on the molecule.[135] The identification, production, and utilization of novel three-dimensional macromolecular structures has already proven to be fertile ground for advancement in the chemical, pharmaceutical, biotechnological, and nanotechnological arts.[136]

Under *SmithKline*, a competitor could invalidate patents on such structures merely by devising a scientifically plausible theory explaining the structure's undetected presence within the prior art. For example, various types of DNA structures have been observed *in vitro*.[137] Assume that a scientist, while attempting to increase the yield of one of these structures, alters the concentration of one reagent in a previously described protocol. As a result, she discovers a novel structure that unexpectedly proves useful in developing an AIDS vaccine. She applies for and

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[133] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1328, 1329 (Fed. Cir. 2005) (en banc) (Newman, J., dissenting) (listing specific classes of chemicals that will become unpatentable as a result of *SmithKline*).

[134] Piero A. Temussi, Laura Masino, & Annalisa Pastore, *From Alzheimer to Huntington: why is a structural understanding so difficult?*, 22 EMBO J. 355, 355 (2003) (noting that "the 'one gene, one protein, one function' hypothesis has by now been contradicted more often than confirmed" in respect to genetic disorders and that neurodegenerative diseases are characterized by protein "misfolding" events); G. Bitan et. al., *Neurotoxic Protein Oligomers—What You See Is Not Always What You Get.*, 12 AMYLOID 88, 88–95 (2005). For example, the beta-amyloid protein can exist as a monomer or can self-associate to form globular and fibrillar quaternary structures, depending on a variety of factors. *Id.* at 88–92.

[135] *See generally* C. Hetz & C. Soto, *Protein Misfolding and Disease: The Case of Prion Disorders*, 60 CELL. MOL. LIFE SCI. 133 (2003) (noting that the only difference between the normal protein and a pathogenic prion is a "misfolding" event that induces a different three-dimensional structure to the prion).

[136] *See generally* William L. Klein, *Abeta toxicity in Alzheimer's disease: globular oligomers (ADDLs) as new vaccine and drug targets*, 41 NEUROCHEMISTRY INT'L 345 (2002) (demonstrating the disparate pathological characteristics of three different three-dimensional forms of a protein implicated in Alzheimer's Disease and discussing the potential of one of these forms as a drug target); Amanda J. Haes, Lei Chang, William Klein, & Richard Van Duyne, *Detection of a biomarker for Alzheimer's disease from synthetic and clinical samples using a nanoscale optical biosensor*, 127 J. AM. CHEM. SOC'Y 2263 (2005) (demonstrating use of a novel three-dimensional structure of Aß as a diagnostic tool for Alzheimer's Disease).

[137] *See* JEREMY M. BERG, ET. AL., III BIOCHEMISTRY §27 (W.H. FREEMAN, 5TH ED. 2002); *available at* http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=stryer.section.3847.

obtains a patent on this structure. A competitor then asserts that the structure was a necessary, but immeasurable, result of the prior art protocol, explaining that an equilibrium existed between the structures that was dependant on the concentration of that reagent. Such a theory would be sufficient to prove the novel structure was anticipated under a strict factual comparison to *SmithKline*.[138]

In the hypothetical, the general mechanism of a prior art reaction was being followed, but with a slight modification. Similarly, the hemihydrate that was first observed in SmithKline arose from a slight change in a prior art protocol.[139] The hypothetical actually presents a less radical situation because the only modification concerns the concentrations of a single reagent, whereas in *SmithKline*, a completely different reagent was involved. As the new DNA form in the hypothetical arose from a reaction more similar to the prior art than the reaction leading to hemihydrate production, *SmithKline* would counsel that the new DNA form was inherently anticipated.

The problem with *SmithKline's* rubric is that it allows a court to infer the results of a chemical reaction from those of a closely related, but distinct, reaction. However, what is and is not produced as a result of a chemical reaction is often dependant on every limitation of that reaction. Even the slightest change can significantly alter the outcome. To say that a single method for producing a certain end-product anticipates everything that results from every production method is scientifically untenable and does not comport with prior precedent.[140]

Perhaps the *SmithKline* court was motivated by an interest in stemming the tide of similar infringement cases. It is worth noting that both *SmithKline* and *Schering* originated as infringement actions against generic drug manufacturers attempting to practice prior art.[141] Moreover, at the time of trial, the Federal Trade Commission was investigating whether follow-up patents were being used by pharmaceutical companies to unfairly compete with generic companies.[142] This is rough justice strongly in favor of the broadest public use of patented technology after the patent term ends, regardless of the motivation. The majority rationalized this course by suggesting alternatives to the structural claim that would not be precluded from patent protection, such as "substantially pure" forms, process claims, or pharmaceutical compositions.[143] This does not solve the problem, as the usefulness

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[138] *See generally* SmithKline Beecham Corp. v. Apotex Corp., 247 F. Supp. 2d. 1011 (N.D. Ill. 2003).

[139] *Compare id.* at 1017 (noting that hemihydrate was observed when isopropanol was used as a solvent), *with* U.S. Patent No. 4,007,196 (filed July 23, 1975) (Example 2) (using ether and 99% ethanol-ether as solvent).

[140] *See* SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1328, 1329 (Fed. Cir. 2005) (en banc) (Newman, J., dissenting) (noting that inherent anticipation relates only to "situations where the common knowledge of technologists is not recorded in the reference" and that "[the majority's] findings of chemical fact . . . are devoid of scientific support") (citation omitted); *In re* Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970) (noting that most chemical reactions are unpredictable and therefore the extent to which a certain reaction enables should be considered narrowly).

[141] *See generally SmithKline*, 247 F. Supp. 2d. 1011; Schering Corp. v. Geneva Pharms., 339 F.3d 1373 (Fed. Cir. 2003).

[142] *SmithKline*, 247 F. Supp. 2d at 1024.

[143] SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1346 (Fed. Cir. 2005); S*chering*, 339 F.3d at 1381 (stating that patentees may still benefit from their discoveries through method claims, claims for the substantially pure form of the subject matter, and claims for pharmaceutical compositions).

and importance of a chemical discovery is not always realized by packaging it into a pill or concentrating it because the structure itself may have properties unrelated to the use contemplated by the discoverer. For example, benzene is a common organic solvent.[144] However, benzene is also commonly used as a precursor for other chemicals.[145] Suppose, *arguendo*, that someone invented benzene while experimenting with prior art reactions as in *SmithKline*. He acquires a patent on benzene, knowing only that it can be used as a solvent. If he is restricted to the types of claims outlined in *Schering*, others will be free to use it as starting material to make other new and useful products if they can do so without using substantially pure benzene or can develop alternate mechanisms for making it.[146] In essence, this invites competitors to freely experiment with the structure and obtain their own patents relating to the uses. This inequitably limits the inventor's right to exclude others from capitalizing on his innovation.

B. What is a court to do? Limiting the scope of inherent anticipation by using § 103 to analyze whether a chemical by-product of producing of a claimed end product is patentable.

This leaves us where we started. SmithKline's intent in filing both the patent and the infringement suit was clear: they wanted to be the exclusive marketer of a hugely profitable drug.[147] Their discovery contributed nothing to the efficacy of the drug, but did make it easier to manufacture.[148] By a quirk of chemistry, the prior art form of the drug cannot be manufactured in the preferred pharmaceutical embodiment without, at some point, infringing SmithKline's patent.[149] Therefore, SmithKline can presumably prevent anyone from manufacturing it even though the actual drug predates SmithKline's patent. This does not, and should not, feel right. However, an alternate analytical framework could avoid some of the most serious problems.

First, a chemical structure should only be anticipated when it arises as a direct result of an explicitly described prior art reaction. As a corollary to that, any alteration of a prior art reaction intended to produce a prior art molecule should preclude finding anticipation of other chemical structures produced as a result. These principles should insert more certainty into anticipation by more specifically defining anticipatory sources. Moreover, this narrow interpretation of anticipation more delicately balances protection of public knowledge with protection of novel ideas by restricting anticipation to the real anticipatory source: the chemical reaction. After all, prior art chemical structures themselves do little to inform the public of the existence of alternate structures or enable the public to make them. It is the reaction that both informs and enables.

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[144] 2 NEW ENCYCLOPAEDIA BRITANNICA 115 (Robert P. Gwinn, et. al., eds., 15th ed. 1992).

[145] *Id.*

[146] *See* Schering Corp., 339 F.3d at 1381.

[147] *See* Aaron Smith, *New profit twist for drugmakers*, CNNMoney.com, (May 11, 2005), http://money.cnn.com/2005/05/11/news/fortune500/generic/ (last visited Apr. 1, 2006); *SmithKline*, 247 F. Supp 2d. at 1017.

[148] *SmithKline*, 247 F. Supp 2d. at 1017.

[149] *Id.* at 1019–21.

Second, chemical structures that are by-products of undisclosed reactions should be patentable unless they are obvious. The anticipation doctrine applied in *SmithKline* renders any chemical structure related to a prior art reaction unpatentable, regardless of the predictability or utility of the structure. In contrast, obviousness predicates invalidity on the predictability of conceiving of the structure and the properties entailed by such a structure.[150] This presents a more equitable invalidity analysis because it differentiates between truly novel discoveries and pseudo best modes. The best way to illustrate the point is to consider how *SmithKline* and the DNA example would be treated under § 103.

Even though the district court found that the SmithKline patent was non-obvious, there is a reasonable argument that PHC hemihydrate was obvious in light of the Ferrosan patent. Claim interpretation and comparison is relatively easy. The SmithKline patent is quite clear, claiming "paroxetine hydrochloride hemihydrate."[151] The Ferrosan patent disclosed the broad class of pharmaceutically acceptable paroxetine salts.[152] The only specific example provided was a paroxetine maleate salt.[153] Therefore, the SmithKline patent and the Ferrosan patent differed only in the specificity of the salt claimed. The identity of hemihydrate is obvious simply by the disclosure of pharmaceutically acceptable salts of paroxetine. As a general proposition, a chemical structure is obvious when the identity and benefits of it would be known to a person of ordinary skill in the art.[154] The district court noted that pharmaceutical producers prefer hydrochloride salts.[155] This means that PHC generically is obvious.[156] Given the general knowledge that crystals can exist in multiple arrangements and that PHC made according to the Ferrosan patent had an affinity for water, an ordinarily skilled crystal chemist would conclude that PHC could exist in a hydrated form.[157] Therefore, the Ferrosan patent fairly suggests the existence of hemihydrate.[158] The benefits of hemihydrate would likewise be obvious. The problem addressed by addition of water is one of handling; anhydrate did not handle well in the pill making process because of its hygroscopicity.[159] Hemihydrate solved this problem because it is not hygroscopic.[160] As the district court pointed out,

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[150] DeMaco Corp. v. F. Von Langsdorff Licensing Ltd., 851 F.2d 1387, 1392 (Fed. Cir. 1988) (holding that a wildly successful, but simple, improvement over prior art was not obvious because the commercial success was evidence that the difference had unexpected quality making it more desirable); *In re* Papesch, 315 F.2d 381, 391 (1963) (holding that both the compound's chemical composition and properties must be obvious in order to be make the structure non-patentable).

[151] U.S. Patent No. 4,721,723 (filed Oct. 23, 1986).

[152] U.S. Patent No. 4,007,196 (filed July 23, 1975).

[153] *Id.* (Example 2).

[154] *In re* Lintner, 458 F.2d 1013, 1016 (C.C.P.A. 1972) (holding that *prima facie* obviousness requires that the reference teachings be sufficient to suggest the modification); *DeMaco*, 851 F.2d at 1393 (noting that commercial success must be due to properties separate from those disclosed by prior art to prove nonobviousness).

[155] SmithKline Corp. v. Apotex Corp., 247 F. Supp 2d 1011, 1015 (N.D. Ill. 2003).

[156] *Id.* at 1016. Because hydrochlorides are preferred, an ordinarily skilled practitioner would likely devise PHC immediately upon hearing the words "pharmaceutically acceptable salts thereof."

[157] *See Id.* at 1016–17.

[158] *See In re* Baird, 16 F.3d 380, 383 (Fed. Cir. 1994) (noting that "a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests").

[159] *SmithKline*, 247 F. Supp 2d at 1017.

[160] *Id.*

this property is not surprising as hemihydrate "has already drunk, as it were."[161] The fact that this property of hemihydrate was indeed predictable indicates that it is obvious.

In contrast, the DNA hypothetical would not be obvious. Despite the fact that the prior art disclosed a class of molecules related to it, nothing in the prior art suggests that particular structure. Furthermore, nothing about the function of the prior structures would allow one to predict its utility for treating AIDS. Given the lack of predictability of structure or function, this structure is non-obvious and thus should be patentable.

CONCLUSION

SmithKline rates fairly well as an equitable decision on the facts. SmithKline still has a monopoly over one iteration of a commercially successful product, albeit more restricted in scope than the one they wanted. Apotex, meanwhile, has the opportunity to enter the market as a competitor. On the other hand, *SmithKline* is woefully lacking as precedent. It has opened the door to invalidating too many truly useful patents by allowing defendants to demonstrate anticipation by mere possibility that a structure is present but undetectable in prior art. This cannot be allowed to stand. The Supreme Court should grant certiorari and set clear limits to the applicability of the inherent anticipation doctrine.

If *SmithKline* is vacated, then the Federal Circuit should adjust its analytical rubric for similar cases. First, inherent anticipation should not apply if any amount of experimentation is required to get from the prior art to the claimed subject matter. In such cases, three-dimensional isoforms of the prior art molecule should be proven obvious in light of the prior art before they can be deemed unpatentable. If these steps are taken, the types of vexing problems presented by *SmithKline* can largely be avoided.

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[161] *Id.* *But see In re* Petering, 301 F.2d 676, 683 (C.C.P.A. 1962) (finding non-obviousness when "there is no evidence in the record of the instant case which would teach one of ordinary skill in this art that the differences in molecular structure . . . would cause this difference in properties").