United States District Court,
S.D. New York.

In re OMEPRAZOLE PATENT LITIGATION

May 31, 2001.

OPINION

JONES**, J.**

Pursuant to 28 U.S.C. s. 1407, the Judicial Panel on Multidistrict Litigation consolidated for pre-trial purposes before this Court the patent infringement suits filed by Astra Aktiebolag, Aktiebolaget Hassle, KBI-E, Inc., KBI, Inc. and Astrazeneca, L.P. (collectively "Astra") in response to various pharmaceutical companies' requests for permission from the Food and Drug Administration (FDA) to market generic versions of Prilosec, Astra's highly profitable gastric acid inhibiting drug. Having completed consolidated discovery, defendants Genpharm, Inc. ("Genpharm") and Cheminor Drugs Ltd., Reddy-Cheminor, Inc. and Schein Pharmaceutical, Inc. (collectively "Cheminor") now move pursuant to Fed.R.Civ.P. 56 for an order granting summary judgment against Astra on its claims of infringement of U.S. patent No. 4,636,499 ("the '499 patent"), because the patent is invalid as anticipated by prior art, or in the alternative because the movants' generic omeprazole will not infringe the '499 patent. Because Genpharm and Cheminor attack the validity of the '499 patent for nearly identical reasons, the Court addresses both motions in this opinion, and for the reasons set forth below grants them.

The Hatch-Waxman Act, also known as The Drug Price Competition and Patent Term Restoration Act, Pub.L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. s. 355 and 35 U.S.C. s. 271(e)(1994)), amended the Federal Food, Drug, and Cosmetic Act ("FDCA"), Pub.L. No. 52-675, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. s.s. 301-397 (1994)), to permit filing of an Abbreviated New Drug Application ("ANDA") to expedite FDA approval of a generic version of a drug previously approved by the FDA. *See* Bayer AG v. Elan Pharm. Research Corp., 212 F.3d 1241, 1244 (Fed.Cir.2000). Under the ANDA procedure, an applicant may seek FDA approval to market a generic drug without undergoing the same expensive and time-consuming FDA approval process undergone by the maker of the branded version of the drug, often called the pioneer drug, 1) by demonstrating that the generic drug is the bioequivalent of the branded drug and 2) by certifying that manufacturing, marketing and selling the drug will not infringe the rights held by the patentee of the pioneer drug.

Under the FDCA, the holder of the NDA for the previously approved drug lists all of its patents that claim the drug or a use of the drug in the book "New Drug Products With Therapeutic Equivalence Evaluations" (referred to as "the Orange Book") published by the FDA. In its ANDA, the generic applicant must certify one of the following four statements with respect to each patent listed under the pioneer drug in the Orange Book: no patent information has been filed (paragraph I certification), the patent has expired (paragraph II certification), the patent soon will expire on a specified date (paragraph III certification), or the patent "is

invalid or will not be infringed by the manufacture, use, or sale of the new drug" covered by the ANDA (paragraph IV certification). *See* 21 U.S.C. s. 355(j)(2)(A)(vii)(I)-(IV).

Although Astra's basic patent covering the chemical formula for omeprazole and its oral administration for gastric acid inhibition, U.S. Patent No. 4,255,431 ("the '431 patent"), will expire on October 5, 2001, FN1 the '431 patent is not the only patent Astra has listed for omeprazole in the Orange Book. The patent at issue on this motion, the '499 patent, claims both a class of chemical compounds called sulphenamides and the administration of sulphenamides for the treatment of inflammatory diseases of the human gastrointestinal tract. The '499 patent will expire on May 30, 2005. Genpharm and Cheminor both certified in their ANDAs for generic omeprazole that the '499 patent "is invalid or will not be infringed by the manufacture, use, or sale" of its generic omeprazole. *See* 21 U.S.C. s. 355(j)(2)(A)(vii)(IV).

FN1. U.S. Patent No. 4,255,431 expired on April 5, 2001; however the FDA granted Astra a six-month pediatric exclusivity extension of the patent term pursuant to 21 U.S.C. s. 355a.

Although no actual infringement can possibly have taken place because the movants' omeprazole product has not been released in the market, 35 U.S.C. s. 271(e)(2)(A) "define[s] a new (and somewhat artificial) act of infringement for a very limited and technical purpose that relates only to certain drug applications." Eli Lilly and Co. v. Medtronic, Inc., 496 U.S. 661, 676 (1990). Section 271(e)(2)(A) provides a patentee with a cause of action for patent infringement based solely upon the filing of an ANDA containing a paragraph IV certification naming the patentee's patent. The artificial infringement arising by operation of law is an integral part of a statutory scheme designed to allow pharmaceutical manufacturers to market generic drugs as soon as possible after the expiration of patents covering them. This is accomplished because it allows the patentee, in this case Astra, "to challenge the certification-i.e. to assert inter alia that the commercial manufacture, use or sale of the new drug *would infringe* its patent" and the Court to efficiently resolve patent issues in advance of the drug's release. Glaxo, Inc. v. Boehringer Ingelheim Corp., 954 F.Supp. 469, 473 (D.Conn.1996) (emphasis added).

Based on the movants' ANDA filings, Astra filed suit pursuant to s. 271(e)(2)(A), alleging that the generic omeprazole products for which Genpharm and Cheminor were seeking approval would induce and contribute to the infringement of the '499 patent because they would be used by doctors and patients for the treatment of inflammatory diseases of the gastrointestinal tract via the administration of the claimed sulphenamides, in contravention of Astra's rights under the patent. Genpharm and Cheminor now move for an order granting summary judgment of invalidity of the '499 patent, or in the alternative an order granting summary judgment of non-infringement.

I.

Summary Judgment Standard

Summary judgment may not be granted unless "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Fed.R.Civ.P. 56(c); *see also* Celotex Corp. v. Catrett, 477 U.S. 317, 322 (1986); Gallo v. Prudential Residential Servs., Ltd. Partnership, 22 F.3d 1219, 1223 (2d Cir.1994). In determining whether summary judgment is appropriate, the Court must resolve all ambiguities and draw all reasonable inferences against the moving party. *See* Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp., 475 U.S. 574, 587 (1986) (citing United States v. Diebold, Corp., 369

U.S. 654, 655 (1962)). Summary judgment is improper if there is any evidence in the record from any source from which a reasonable inference could be drawn in favor of the nonmoving party. *See* Chambers v. TRM Copy Ctrs. Corp., 43 F.3d 29, 37 (2d Cir.1994). Because each claim of a patent is presumed valid, in considering a motion for summary judgment of invalidity the Court must consider the facts in view of the clear and convincing evidentiary burden placed on the moving party. *See* Monarch Knitting Machine Corp. v. Sulzer Morat Gmbh, 139 F.3d 877, 880 (Fed.Cir.1998).

II.

Claim Construction of the '499 Patent

Astra was granted U.S. Patent No. 4,255,431 in 1981. The patent claims a chemical compound called omeprazole, whose basic structure is 2-pyridyl methylsulfinyl benzimidazole, and its oral administration for inhibiting gastric acid secretion. Astra's scientists had found that when omeprazole was ingested by a human, the enzyme responsible for gastric acid secretion in the stomach lining, $H^+ K^+$ ATPase, was inhibited.

The '499 patent, granted in 1987, claims a class of substances called sulphenamides, and also the administration of the claimed sulphenamides to effect gastric acid inhibition. Astra argues that Genpharm and Cheminor's proposed practice of the oral administration of omeprazole, as described in the soon to be expired '431 patent, will infringe the '499 patent because when a patient takes the Genpharm and Cheminor products, sulphenamides will form in the patient's body.

In the first of the two steps necessary to the infringement analysis the Court construes the allegedly infringed patent claims to establish their meaning and scope. *See* Markman v. Westview Instruments, Inc., 52 F.3d 967 (Fed.Cir.1995), *aff'd,* 517 U.S. 370 (1996). The primary claim construction dispute between the parties turns on the meaning of the word "compound" as used in claims 1, 2, and 3 of the patent.FN2 Astra argues that the term refers to both sulphenamides made synthetically outside the body as well as those produced by the in vivo conversion of omeprazole. Genpharm and Cheminor argue that the inventors of the '499 patent intended to claim only synthetically produced sulphenamides when they used the term "compound." Astra concedes that if the '499 patent is construed to claim only synthetic sulphenamides, the defendants' products will not infringe it. See May 10, 2001 Tr. at 23 ("[w]e have not developed evidence of infringement by synthetic production against the defendants in the first wave of cases.").

FN2. Claim 1 reads: "A compound according to the formula IIIa wherein" and goes on to describe the various components of the sulphenamide. Importantly, the claim ends "and x is a pharmaceutically acceptable anion." Claims 2 and 3 depend upon claim 1, and claim variants of the formula set forth therein. For example, claim 2 claims "[a] compound according to claim 1 wherein the pharmaceutically acceptable anion is Cl, Br, I, BF_4, PF_6, or $AuCl_4$."

Astra relies heavily on the Federal Circuit's opinion in Zenith Labs., Inc. v. Bristol-Myers Squibb Co., 19 F.3d 1418 (Fed.Cir.1994), for the proposition that "when a patent claims a compound by its chemical formula (as the '499 patent does), the patent covers that compound regardless of whether it is made synthetically or is produced in the body after ingestion of a different compound." Genpharm and Cheminor in turn rely on Marion Merrell Dow, Inc. v. Baker Norton Pharmaceuticals, Inc., 948 F.Supp. 1050 (S.D.Fla.1996).

In *Marion Merrell Dow,* the Court declined to find a per se rule in *Zenith* which would require "that all claims which describe a compound be construed as covering both the metabolically produced and synthetically produced forms of the compound, without regard to the language of the claims, the specification of the patent or the prosecution history." Id. at 1054 n.4. Instead, the court held that it should construe the claims pursuant to the *Markman* procedure. This Court agrees.

It cannot be that a claim to a "compound" covers the compound whether it is made synthetically or produced in vivo, regardless of whether such a construction is supported by the evidence intrinsic to the patent. As in *Marion Merrell Dow,* the Court construes the claims of the '499 patent according to the hierarchy of evidence articulated in *Markman,* looking first to the intrinsic evidence of the patent:

[T]he court has the power and obligation to construe as a matter of law the meaning of language used in the patent claim. As such, "[a] patent covers the invention or inventions which the court, in construing its provisions, decides that it describes and claims." ... "To ascertain the meaning of claims, we consider three sources: The claims, the specification, and the prosecution history."

52 F.3d at 979 (citations omitted).

A. The Claim Language

In construing the patent, the Court looks first to the language of the disputed claims. *See* Autogiro Co. v. United States, 384 F.2d 391, 395-96 (C.C.P.A.1967) ("[t]he claims of the patent provide the concise formal definition of the invention"). While Astra notes FN3 that no language in claims 1, 2 or 3 explicitly limits those claims to sulphenamides in their synthetic or pre-ingested form, neither can Astra point to any language explicitly claiming sulphenamides formed in vivo. Genpharm and Cheminor, however, do point to specific language in claims 1-3 which support their argument that the '499 patent does not claim sulphenamides formed in vivo.

FN3. Because the briefs submitted by the parties on these motions for summary judgment did not sufficiently address the issue of claim construction, the Court requested additional briefs from all of the parties to the consolidated litigation specifically addressing claim construction and held a hearing pursuant to *Markman* on May 10, 2001.

Claim 1, referring to the drawing at the top of column 21 of the patent, describes the general formula of sulphenamides and notes that the X shown in the drawing represents "a pharmaceutically acceptable anion." *See* U.S. Patent No. 4,636,499 at Col. 21 line 1 to Col. 22 line 1. Genpharm and Cheminor argue that because in vivo the sulphenamides exist as a free amine base without an anion component, the inclusion of the term "pharmaceutically acceptable anion" demonstrates that the '499 patent claims a pharmaceutically prepared stable sulphenamide salt. *See* Defs. Consol. Claim Cnstr. Memo. at 6-7.

Astra counters that sulphenamides are permanent cations which are always associated with an anion, whether they are found in vivo or in pharmaceutical preparations. *See* May 10, 2001 Markman Hearing Tr. at 58. Even accepting Astra's assertion that in vivo sulphenamides are always associated with an anion, "in vivo sulphenamides do not incorporate an anion that has been selected on the basis of its pharmaceutical acceptability." Defs. Consol. Claim Cnstr. Memo. at 7. By describing the invention in terms of an anion

chosen pursuant to pharmaceutical standards, the inventors of the '499 patent suggested a degree of control over the formulation of the sulphenamide; such control is available only in the synthetic context and is nonsensical in the in vivo context. *See* Marion Merril Dow, 948 F.Supp. at 1055 (finding that inventors' use of term "pharmaceutically acceptable" in the patent at issue constituted "further evidence that the inventors sought a patent on chemical formulations of TAM only.").

Moreover, Astra admits that some of the anions listed in claim 2 as "pharmaceutically acceptable" do not occur in vivo, further supporting the defendants' arguments that those claims refer to synthetic sulphenamides only. *See* 5/10/2001 Tr. at 59.FN4 Accordingly, the primary intrinsic evidence, the language of the claims at issue, supports defendants' contentions that the inventors of the '499 patent intended to claim synthetic sulphenamides only.

FN4. Although counsel for Astra said "admittedly, the list of cations include things that are not naturally within the body" it is clear from the context that he meant that the listed anions, rather than cations, are not naturally within the body. Opposing counsel had earlier argued that tetraflourobromide, or BF., one of the anions listed in claim 2, is not found in vivo. *See* 5/10/2001 Tr. at 32.

Defendants' claim construction is also supported by the language of the '499 patent claims not in dispute. Aside from claim 8 and claims 12-14, which Astra concedes are directed to sulphenamides in their pre-ingested form only, the defendants note that other claims demonstrate similar limitations. Claims 4 and 5 refer to "a compound according to claim 1" but require that the compound include chemical components not found in vivo, and thus must also refer only to synthetic sulphenamides. *See* Defs. Claim Cnstr. Memo. at 8; *see also* id. at 10 (claims 9-11 also must claim synthetic sulphenamides because they describe processes for preparation of the compound and refer to "isolating" sulphenamides, which according to the specification cannot be done in vivo).

Astra argues in response that because the claims not in dispute clearly and explicitly claim sulphenamides in their synthetic pre-ingested form while claims 1-3 are silent with respect to form, pursuant to the doctrine of claim differentiation the limitations to synthetic sulphenamides expressed in claim 8 and claims 12-14 should not be read into claims 1-3. *See* Pl.'s Opp. to Defs.' MSJ at 28-29. Astra is correct that where some claims are broad and others narrow, the narrow claim limitations should not be read into the broad. *See DMI, Inc. v. John* Deere, Inc., 755 F.2d 1570, 1574 (Fed.Cir.1985). In this case, however, the limitation to pre-ingestion synthetic sulphenamides advanced by the defendants is not imported from narrower claims within the patent but rather evidenced within the disputed claims themselves by the language "pharmaceutically acceptable." The patent claims not in dispute simply provide further evidence of the meaning of the "pharmaceutically acceptable" limitation contained in the disputed claims.

Astra also argues that the doctrine of claim differentiation demands that the Court read claims 1-3 as encompassing in vivo sulphenamides because to read them as only encompassing pre-ingestion sulphenamides would render the language "in solid form" contained in claim 8 FN5 superfluous. However, the defendants correctly note that the language "in solid form" may be interpreted not to distinguish synthetic sulphenamides from those formed in vivo, but rather to distinguish sulphenamides contained in a pharmaceutical preparation that takes a solid form from a pharmaceutical preparation that takes a liquid, or parenteral form. *See* U.S. Patent No. 4,636,499 at col. 5 lines 34-36 ("[f]or clinical use the compounds of the invention are formulated into pharmaceutical formulations for oral, rectal, parenteral or other mode of administration.... The carrier may be in the form of a solid, semisolid or liquid diluent"); *see also* 5/10/2001

Tr. at 42-43. Accordingly, construing claims 1-3 as claiming only synthetic sulphenamides does not render the "in solid form" language in claim 8 superfluous and thus does not invite application of the doctrine of claim differentiation.

FN5. Claim 8 reads "[a] compound according to one of the claim 1-6 wherein compound III(a) is in solid form."

B. The Specification Language

Having determined that the language of all of the claims of the '499 patents substantiates the defendants' construction, the Court next directs its analysis to the specification of the '499 patent. Astra argues that the '499 patent specification expressly discloses in col. 1, line 56 to col. 2, line 18 that the claimed sulphenamides may be formed in the body and that the specification describes the in vivo conversion of omeprazole to sulphenamides in col. 4 lines 3-49. The first portion of the specification cited by Astra reads:

BACKGROUND OF THE INVENTION

* * *

The in vivo inhibiting effect of the compounds with the general formula I [omeprazole] is not, however, exerted by the compounds as such but by one or more degradation products.

OUTLINE OF THE INVENTION

According to the present invention, it has now been surprisingly found that the above mentioned degradation reaction of the sulphoxides with the general formula I is a complicated transformation reaction to the new sulphenamides with the general formula III ..."
U.S. Patent No. 4,636,499, Col. 1 lines 56-68 (emphasis added).
Clearly these portions of the specification, which begin under the heading "Background of the Invention" and continue into the "Outline of the Invention" reveal that sulphenamides are formed in the body when omeprazole is ingested. This reference to omeprazole's in vivo conversion to sulphenamides, however, merely provides a description of the prior art which gives the context for the discovery of the claimed invention. If anything, it is an implied admission that the sulphenamides formed in vivo are inherent in the prior omeprazole art.

Furthermore, another portion of the "Outline of the Invention" section of the specification cited by Astra does not support its claim construction. It begins with the language "[c]ompounds of the general formula IIIa above [sulphenamides] may be prepared by the following method," followed by a drawing. *See* U.S. Patent No. 4,636,499, at col. 4, lines 3-5. The words "prepared by the following method" connote at the outset that a pharmaceutical preparation, rather than an in vivo transformation, is being described. The specification then reads "[t]he transformation reaction *probably goes via* the sulphenic acid IIa, which may also be an in vivo inhibitor, *when a sulphoxide with the general formula Ia [such as omeprazole] has been administered*." Col. 4 lines 41-45 (emphasis added). The Court reads this portion of the "Outline of the Present Invention" section cited by Astra only as a further reference to the "Background of the Invention" portion of the patent noting that an omeprazole degradation product, rather than omeprazole itself, is responsible for the acid inhibiting effect attributed to omeprazole.

The detail of the description of the processes for the synthesis of the claimed sulphenamides contained in the patent also demonstrate an intention to teach and claim those synthetic processes that is absent from the description of the in vivo formation of sulphenamides. The language "probably goes via" describing the in vivo pathway lacks the detail and certainty of the claimed synthetic processes, and reveals on its face no intent to claim and teach sulphenamides formed in vivo. Moreover, directly following the vague language Astra relies upon, the specification reads "[e]specially preferred acids for preparation of the compounds with the general IIIa are ...." and begins a detailed description of methods for the in vitro synthesis of sulphenamides. *See* U.S. Patent No. 4,636,499, col. 4 lines 51-53. Accordingly, the specification language cited by Astra does not persuade the Court that the '499 patent claims encompass sulphenamides formed in vivo.

C. The Prosecution History

The final source of intrinsic evidence the Court examines to determine the meaning of the disputed claim language is the prosecution history of the patent. Each side argues that its claim construction is supported by the same exchange between Astra and the patent examiner during the prosecution of the '499 patent. The examiner initially denied Astra's claims to sulphenamides because he determined that European patent 05129 disclosed them. The examiner noted "[n]o distinction can be seen between the compounds of formula III [sulphenamides inherent in omeprazole European patent 05129] and formula III(a) [those claimed in the '499 patent]" and rejected them under 35 U.S.C. s. 103. *See* Exh. 17 to Decl. of David M. Conca. This finding that the claims were invalid due to obviousness leads the defendants to argue that the examiner must have read the patent to claim only synthetic sulphenamides, because in light of the prior disclosures that sulphenamides operated to inhibit gastric acid secretion in vivo, creating synthetic sulphenamides would be obvious and thus unpatentable. Had the examiner thought that Astra intended to claim in vivo sulphenamides, presumably he would have declared the claim invalid due to anticipation either instead of or in addition to obviousness. *See* 35 U.S.C. s. 102.

After the examiner's initial rejection Astra reasserted the validity of the claims and persuaded the patent examiner to allow them to stand, citing *Ex Parte Biel,* Patent Appeal No. 223-47 (Oct. 14, 1964). The defendants argue that in light of the examiner's initial rejection on obviousness grounds, when Astra persuaded the patent examiner to allow the claims to stand by citing *Ex Parte Biel,* the examiner was allowing them to stand as claims to synthetic sulphenamides only. *See* Defs.' Claim Cnstr. Memo. at 17-21. Since the examiner cites *Biel* without any analysis or explanation, this interpretation is uncertain.

What is clear is that nothing in the prosecution history explicitly demonstrates that the examiner recognized that the claims of the '499 patent covered sulphenamides in their in vivo form. Astra cites nothing more in support of its position than the examiner's response "Claims 1-7, 9 and 18-27 are allowed in view of the *Ex Parte Biel* decision cited by Applicants." Exh. 17 to Decl. of David M. Conca, '499 file history 136-137. These different conclusions and arguments by the parties highlight the ambiguity of the exchange but do not favor either party's claim construction. The Court thus accords no weight to the prosecution history in determining the scope and meaning of the claims.

In light of the language of the claims in dispute and those not asserted, in conjunction with the specification of the patent, the Court is persuaded that the inventors of the '499 patent claimed only synthetic sulphenamides in claims 1-3 of that patent. Accordingly, disputed claims 15 & 16 are also construed to cover only synthetic sulphenamides, because those claims refer to "a compound according to claim 1." *See*

U.S. Patent No. 4,636,499 at col. 24 line 66-col. 25 line 7.

In the second phase of the patent infringement analysis, the factfinder compares the properly construed claims against the allegedly infringing devices. *See* Carroll Touch, Inc. v. Electro Mechanical Sys., 15 F.3d 1573, 1576 (Fed.Cir.1993). In this case, however, as previously noted no such comparison is necessary because Astra concedes that if the '499 patent is construed only to cover synthetic sulphenamides the defendants will not infringe it. Defendants' motions for summary judgment of non-infringement are therefore granted.

III.

Validity of the '499 Patent

The Federal Circuit has emphasized that when a district court is faced with questions of infringement and invalidity, in the interests of finality and judicial efficiency, the district court should consider both questions. *See* Multiform Desiccants, Inc. v. Medzam, Ltd., 133 F.3d 1473, 1481 (Fed.Cir.1998). Accordingly, the Court turns to Genpharm and Cheminor's contention that any claim to sulphenamides produced in vivo upon the oral administration of omeprazole is inherently anticipated by prior art.

A patent may not issue where the claimed invention

was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States ...

35 U.S.C. s. 102(b). Pursuant to s. 102(b), an invention may be patented only if it is novel in relation to the prior art available to the public at the time the patent application is filed. When the claimed invention "reads on" a prior art reference, the invention is said to be anticipated by that reference, and any claim purporting to patent the invention is deemed invalid. *See* Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1346 (Fed.Cir.1999) (citing Titanium Metals Corp. v. Banner, 778 F.2d 775, 781 (Fed.Cir.1985)).

As discussed above, the '499 patent describes the Astra scientists' discovery that it is not omeprazole as such that inhibits gastric acid secretion, but rather the sulphenamides produced when omeprazole reacts with chemicals in the body. Genpharm and Cheminor argue that the in vivo formation of sulphenamides upon the oral administration of omeprazole was inherently disclosed in the '431 patent as well as in numerous prior art references published more than a year before Astra's application for the '499 patent. Both argue that because the practice of the '431 art inevitably results in the production in vivo of the sulphenamides claimed by the '499 patent, the '499 patent runs afoul of the axiom "that which would infringe if later, anticipates if earlier."

To show that a patent is invalid by anticipation one must normally present a prior art reference disclosing each and every limitation of the claim. *See* Standard Havens Prods., Inc. v. Gencor Indus., Inc., 953 F.2d 1360, 1369 (Fed.Cir.1991). However, a prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent in it.

Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates ... the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.

Atlas Powder Co. v. IRECO, Inc., 190 F.3d 1342, 1347 (Fed.Cir.1999). Anticipation is a question of fact, including whether or not an element is inherent in the prior art. *See* In re Schreiber, 128 F.3d 1473, 1477 (Fed.Cir.1997).

In support of the position that the sulphenamides claimed by the '499 patent were inherently anticipated by the prior omeprazole art, the movants cite the testimony of Astra employees and witnesses, including the inventors of the '499 patent that "the necessary and inevitable result of the administration of omeprazole, as specifically taught by the basic omeprazole patent, is the in vivo (in the living body) conversion of omeprazole to a sulphenamide." *See* Def.'s Memo. at 5. Two of the three inventors of the '499 patent, Per Lindberg and Bjorn Wallmark, stated under oath that omeprazole converts to sulphenamides after administration to a human and that the sulphenamide is responsible for the inhibition of gastric acid. Dr. Lindberg testified:

Q: If one administers omeprazole to a patient and observes inhibition of gastric acid secretion, has there been acid-induced conversion of omeprazole to the sulphenamide?

A: That's my belief.

Lindberg May 26, 2000 Tr. at 202. Dr. Lindberg also stated in sworn testimony that it is his belief that when a person ingests orally administered omeprazole the sulphenamide always forms. *See* id. at 239:15-20. Dr. Wallmark testified:

Q: Tell me how omeprazole is changed after administration to a human to the active inhibitor for the gastric acid proton pump.

A: Okay. The neutral form of omeprazole is passing the biological membranes of the parietal cell, the neutral non-charged species penetrates the membranes of the parietal cell. It converts, as I said previously, by an intramolecular reaction, by a series of intramolecular reactions to the sulfenamide, which is the inhibitor of the H^+K^+ ATPase, not omeprazole itself.

Wallmark Mar. 22, 2000 Tr. at 75. Astra vice president Mats Parup also stated "[o]ur position is that any omeprazole product will, when administered, form sulphenamides, and therefore falling (sic) under [the claims of the '499 patent]." Parup Sept. 2, 1999 Tr. at 123:11-14.

Both movants argue that the fact that sulphenamides inevitably form upon the ingestion of omeprazole necessitates the conclusion that sulphenamides and their acid-inhibiting properties were inherently disclosed in the prior art sources discussing the administration of omeprazole to effect gastric acid inhibition. As Genpharm notes, each prior art publication FN6 discloses "compositions containing omeprazole administered to humans resulting in the inhibition of gastric acid secretion one year before the filing of the SULPHENAMIDE PATENT." Genpharm Memo. at 8. Dr. Lindberg testified that he had determined that the claimed sulphenamide formed in each reference. *See* Lindberg Nov. 17, 2000 Tr. at 298 (as to the '465 patent); id. at 296 (as to Ekenved); id. at 283 (as to Lind); id. at 253 (as to McArthur). He also testified with respect to the experiment described in the Gustavsson article not only that the sulphenamides formed, but also that they were responsible for inhibiting gastric acid. *See* id . at 298. Furthermore, Lindberg stated that the mechanism of omeprazole has not changed since at least the publication of the Ekenved article in 1981. *See* Nov. 18, 2000 Lindberg Tr. at 427-28.

FN6. Genpharm cites the following prior art as anticipating the '499 claims: U.S. Patent No. 4,359,465 issued on November 16, 1982; Sven Gustavsson, et al., *Rapid Healing of Duodenal Ulcers with Omeprazole: Double-Blind Dose-Comparative Trial,* The Lancet, July 16, 1983, at 124-125; G. Ekenved, et al., *Studies With 168/68, a Novel Gastric Acid Secretion Inhibitor,* The British Society of Gastroenterology, GUT, 1981, at A862-A900; Tore Lind, et al., *Effect of Omeprazole-A Gastric Proton Pump Inhibitor-On Pentagastrin Stimulated Acid Secretion in Man,* GUT, 1983, at 270-276; K.E. McArthur, et al., *Omeprazole as a Single Daily Dose as Effective Therapy in Zollinger-Ellison Syndrome,* 86 Gastroenterology 1178 (1984).

Cheminor, like Genpharm, also cites Lind, Gustavsson, and McArthur as prior art sources. In addition Cheminor cites U.S. Patent no. 4,255,431 and Lamers, et al., *Omeprazole in Zollinger-Ellison Syndrome,* 310 N. Eng. J. Med. 758-761 (1984).
Despite these admissions that omeprazole converted to sulphenamides and inhibited gastric acid secretion in the prior art, Astra argues that a factual dispute precluding entry of summary judgment exists with respect to whether the prior art cited by Genpharm and Cheminor discloses the sulphenamides claimed in the '499 patent, and whether a person of ordinary skill in the art would have recognized as much. *See* Astra Opp. Memo. to Defs. MSJ at 11. Much of Astra's argument on this point fails to address inherent, as opposed to explicit, anticipation. Whether a person ordinarily skilled in the art would have recognized the inherent characteristics of the functioning of the prior art is irrelevant, if those inherent characteristics indeed exist. *See* Atlas Powder, 190 F.3d at 1347 ("[i]nsufficient prior understanding of the inherent properties of a known composition does not defeat a finding of anticipation.") (citing Titanium Metals, 778 F.2d at 782)).

Astra's testimony and documentary evidence do not raise a genuine factual dispute regarding whether sulphenamides form after oral administration of omeprazole and act as gastric acid inhibitors. Astra's evidence on the issue devolves into two categories: (1) nonresponsive testimony that recent scientific literature suggests that sulphenic acid, or some other omeprazole degradation product, rather than sulphenamides, may under some circumstances be the *primary* gastric acid inhibitor among the omeprazole degradation products, and (2) testimony by Dr. Lindberg that suggests an abstract possibility that sulphenamides do not always form upon oral administration of omeprazole. This latter category of testimony is in conflict not only with Lindberg's prior May, 2000 deposition testimony, but also with his expert opinion-given in the same November, 2000 deposition-that the movants' generic omeprazole would infringe the '499 patent because upon oral administration of their product sulphenamides will necessarily form.

For example, Dr. Lindberg testified in his November 2000 deposition about scientific literature regarding the *possiblity* that in some instances the protonated form of omeprazole or sulphenic acid, rather than a sulphenamide, inhibits gastric acid secretion. In that case, Dr. Lindberg testified "the sulfenamide doesn't have to be formed." *See* Decl. of David M. Conca, Exh. 16 at 163:16-17; *see also* id., at 157:14-158:14 ("there has been an *increasing awareness* that it's not necessarily the sulfenamide that is the active inhibitor, it may as well be the sulphenic acid"). This testimony is mere speculation. Lindberg offers no evidence of experiments where the sulphenamides were determined not to have formed. Indeed, Lindberg was only willing to suggest that a recent scientific article, G. Sachs, et al ., *The Pharmacology of the Gastric Acid Pump: The* H^+K^+ *ATPase,* 35 Ann. Rev. of Pharmacology and Toxicology 277 (1995), might allow the possibility that sulphenamides occur in slighter concentrations relative to protonated omeprazole under certain conditions, but not that sulphenamides are not formed and do not act as inhibitors. Lindberg testified:

Q: Yes. What I'm asking, Dr. Lindberg, is where he says that the labelling results show that the sulfenamide does not form?

A: He doesn't say that it does not form in this particular article, but.... That means that the fraction of the unprotonated form is very low, it's maybe one per mill of the prot-compared to the protonated form....

Q: Well, okay. So what I get, but what I hear you saying is-well, he doesn't actually say even if protonated omeprazole is doing binding-

A: Doing?

Q: Binding.

A: That is, his proposal is that a possible explanation for the results that he has is that the protonated form itself binds.

Q: Now, that doesn't exclude sulfenamide molecules from binding; isn't that fair?

A: It doesn't exclude it, but it-we come into a situation where it's-you need an explanation for certain results, and the only-one proposal is that he is doing here is that the protonated Omeprazole is the one that is bound. I mean, that's something is ... binding to the enzyme, and that is the protonated form, which renders the concentration of the unprotonated form very low, which means that if that is true, the potential of forming sulfenamide is much lower.

Conca Decl. Exh. 16, at 166:21-167:15.

Furthermore, Dr. Lindberg's testimony in the November 2000 deposition is inherently suspect. As previously noted, Dr. Lindberg testified on numerous occasions, including in his May 2000 deposition six months earlier, that sulphenamides always form after oral administration of omeprazole. Even within the November 2000 deposition he testified that it was his belief that in all prior art references sulphenamides were formed and in one case acted as a gastric acid inhibitor. For example, Dr. Lindberg gave testimony that makes clear that in his expert opinion, to administer omeprazole is to administer sulphenamides:

Q: Now, in the same scenario, you wouldn't speak of administering a sulphenamide, would you?

A: It will eventually lead to administering the sulphenamide.

Q: If the doctor administers omeprazole to the patient in the way that we just said, has he administered the sulfenamide?

A: Yes.

See Conca Decl. Exh. 16 at 110:14-110:4. However, when the questioner mentioned the possible invalidity of the '499 patent later in the deposition, Lindberg's testimony became evasive and inconsistent.

Q: Are you aware that some of the defendants are trying to invalidate the '499 patent?

A: I heard that.

Q: As you sit here today, are you aware of whether omeprazole, I'm not talking about the Prilosec formulation, I'm talking about the compound omeprazole, if it is administered intravenously in a therapeutically effective amount, will the sulfenamide always form?

A: No, I'm not aware of that.

....

Q: Do you know one way or another whether the sulfenamide will always form in such a case?

A: I wouldn't say it's always form.

Q: Why not?

A: Because there are disagreements today in the literature about what is the active species.

Q: Well, even in those cases of disagreement about what the active species is, isn't it true that the sulfenamide will always form?

A: No.

Q: Why do you say that?

A: Because I'm not absolutely sure about that.

Conca Decl. Exh. 16 at 122:7-123:8.

In order to defeat a properly supported motion for summary judgment, a posited factual dispute must be genuine and material. Dr. Lindberg's testimony does not create a genuine issue of fact. Lindberg offers only the weak statement "because I'm not absolutely sure about that" in response to the question of whether sulphenamides are always formed. Speculative testimony that there exists "some metaphysical doubt" about a fact issue is insufficient to defeat a motion for summary judgment. *See* Matsushita Elec. Indus. Co. v. Zenith Radio, 475 U.S. 574, 586 (1986); Kulak v. City of New York, 88 F.3d 63, 71 (2d Cir.1996) (speculation by nonmovant will not defeat summary judgment). Dr. Lindberg's testimony does not create a genuine dispute of material fact that upon the oral administration of omeprazole sulphenamides are formed and inhibit gastric acid secretion.

By claiming patent protection for sulphenamides formed in vivo after the oral administration of omeprazole, Astra has merely attempted to patent the unpatentable-"a scientific explanation for the prior art's functioning." Atlas Powder, 190 F.3d at 1347. Astra's suggestion that omeprazole degradation products other than sulphenamides may have acid inhibiting properties does not call into question the acid-inhibiting properties of sulphenamides. Astra presented no evidence that in those cases where scientists posit that an omeprazole degradation product other than sulphenamides operates on a molecular level to inhibit gastric acid secretion, sulphenamides were not also on a molecular level in the same instance inhibiting gastric acid secretion elsewhere in the gastric mucosa.

Had Astra demonstrated that the mechanism of omeprazole and sulphenamides in vivo had changed since the publication of the prior art sources, it would have been relevant to the anticipation analysis because it would have created a factual issue with respect to what occurred in the prior art. Astra has done the opposite. Dr. Lindberg testified that the acid-inhibiting mechanism of omeprazole and sulphenamides has not changed since the prior art was published. *See* Lindberg Nov. 18, 2000 Tr. at 247-48. Accordingly, the evidence presented by Astra on the issue does nothing to change the conclusion that the in vivo formation of sulphenamides upon the oral administration of omeprazole, and the role of sulphenamides in effecting gastric acid inhibition, whether large or small, is inherently anticipated by the prior art.

As a result, even if the Court were not persuaded that the patent claims, specification, and prosecution history demonstrate that the '499 patent does not claim sulphenamides produced in vivo, the Court would construe the patent to claim only pre-ingestion sulphenamides in order to preserve the patent's validity, because any claim to sulphenamides produced in vivo upon the oral administration of omeprazole is inherently anticipated by prior art.

Conclusion

For the foregoing reasons, Genpharm and Cheminor's motions for summary judgment of non-infringement of U.S. Patent No. 4,636,499 are granted.

S.D.N.Y.,2001.
In re Omeprazole Patent Litigation