United States District Court,
D. New Jersey.

BRISTOL-MYERS SQUIBB COMPANY,
Plaintiff.
v.
IMMUNEX CORPORATION, Zenith Goldline Pharmaceuticals, Inc. and IVAX Corporation, Boehringer Ingelheim Corp., Ben Venue Laboratories and Bedford Laboratories,
Defendants.

Nos. CIV. A. 97-6050 (WHW), 98-159(WHW), 98-1412(WHW)

March 2, 2000.

Owner of patented regimen for administration of anti-cancer drug taxol sued competitors for infringement, and they counterclaimed for patent invalidity on grounds of anticipation and obviousness. Construing claim language, the District Court, Walls, J., held that preamble phrases were merely statements of purpose and not claim limitations.

Ordered accordingly.

5,641,803, 5,670,537. Cited.

Andrew T. Berry, McCarter & English, Newark, NJ, for Bristol-Myers Squibb Co.

William Mentlik, Arnold Krumholz, Paul Kochanski, Michael Teschner, Lerner, David, Littenberg, Krumholz & Mentlik, Westfield, NJ, for Immunex Corp., Zenith Goldline Pharmaceuticals, Inc., Ivax Corp.

H. Curtis Meanor, Podvey, Sachs, Meanor, Catenacci, Hildner & Cocoziello, Newark, NJ, for Ben Venue Laboratories, Bedford Laboratories.

OPINION

WALLS**, District Judge.**

Defendant-counterclaimants Immunex Corporation, Zenith Goldline, and IVAX Corporation (collectively "IVAX defendants") move for a *Markman* claim interpretation ruling and for partial summary judgment of noninfringement of U.S. Patent No. 5,641,803 ("the '803 patent"), owned by plaintiff Bristol-Myers Squibb Co. ("Bristol") and asserted in these infringement actions. Patentee Bristol opposes the motion. This Opinion sets out the construction of the two patents in suit. The IVAX defendants' motion for partial summary judgment of noninfringement of the '803 patent is denied.

ANALYSIS

1. "*Markman*" *Rulings*: *Standards for Claim Construction*

[1] The construction of patent claims is a matter of law exclusively for the court. Markman v. Westview Instruments, 52 F.3d 967 (Fed.Cir.1995).

[2] [3] [4] The court must look first to the "intrinsic evidence," which consists of the patent claims, the specification, and the prosecution history if in evidence. "Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996). The court should presume that the terms in the claim mean what they say, and, unless otherwise compelled, give full effect to the ordinary and accustomed meaning of claim terms. *See* Johnson Worldwide Associates, Inc. v. Zebco Corp., 175 F.3d 985, 989 (Fed.Cir.1999). Of course, "claim construction is not philosophy ... [it] is firmly anchored in reality by the understanding of those of ordinary skill in the art." K-2 Corp. v. Salomon S.A., 191 F.3d 1356 (Fed.Cir.1999). And though the prosecution history can and should be used to understand the language used in the claims, it may not be used to "enlarge, diminish, or vary" the limitations in the claims. Markman, 52 F.3d at 979 (citation omitted).

[5] "In most situations, an analysis of intrinsic evidence alone will resolve any ambiguity in a disputed claim term. In such circumstances, it is improper to rely on extrinsic evidence," such as expert testimony, treatises and dictionaries, and articles. Vitronics, 90 F.3d at 1583. Accordingly, where the patent documents are unambiguous, expert testimony is entitled to no weight. *See id*. Prior art may serve as a guide to the meaning of a disputed term and, particularly, as a time-saving demonstration of how a disputed term is used by those skilled in the art. *See id*. at 1584. Finally, "opinion testimony on claim construction should be treated with the utmost caution," because such testimony "amounts to no more than legal opinion-it is precisely the process of construction that the court must undertake." Id. at 1585 (citation omitted).

2. *Construction of the '537 Patent Claims*

United States Patent No. 5,670,537 (" '537 patent") issued from a chain of applications prosecuted by Bristol over a period of five years beginning in 1992. The first, "grandparent application," serial number 923,628 ("the '628 application"), was filed in August 1992 to provide Bristol with patent coverage of certain inventions resulting from a multinational study of taxol to treat refractory ovarian cancer known as the "OV.9 study." Later, "parent application" number 109,331 ("the '331 application") was filed as a division of the grandparent in June 1993 pursuant to 35 U.S.C. s. 121. In January 1995, the patent examiner entered a restriction requirement directed to claims which mentioned premedication to prevent hypersensitivity reactions ("HSRs"). "Child application" number 544,594 ("the '594 application") was filed in October 1995. FN1 Finally, for lack of a better description, "grandchild" application number 08/715,914 ("the '914 application") was filed on September 19, 1996 as a continuation of the '594 application. The '537 patent issued from the '914 application on September 23, 1997. The specifications submitted in support of each application and the issued patent were identical. However, throughout this period, Bristol amended, added and deleted various claims submitted to the United States Patent and Trademark Office (PTO).

FN1. The '803 patent issued from this application on June 24, 1997.

The '537 patent contains ten claims, divided between independent and dependent claims. Claims 1 and 5 are

representative of claims 2-4 and 6-10, respectively, and read:

1. A method for treating a patient suffering from a taxol-sensitive tumor comprising

(i) premedicating said patient with a medicament that reduces or eliminates hypersensitivity reactions, and

(ii) parenterally administering to said patient about 135-175 mg/m ^{2} taxol over about three hours.

5. A method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity, said method comprising

(i) premedicating said patient with a medicament that reduces or eliminates hypersensitivity reactions, and

(ii) parenterally administering to said patient about 135-175 mg/m^2 taxol over about three hours.

The element common to each claim is premedication to reduce or eliminate hypersensitivity reactions ("HSRs"), an element missing from claims of the '803 patent.

The construction of claims 1-4 of the '537 patent is not disputed. *See* BMS Opp. Brf. to Ben Venue's Motion for Summary Judgment of Invalidity at 11 (stating that the parties largely agree on the limitations of the '537 Patent). FN2 The import of the phrase "[a] method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity," in claims 5-10, however, is contested. Id.

FN2. The briefs referenced by the Court in constructing the '537 patent are those submitted by the parties in a related motion for summary judgment of invalidity of the two patents in suit because of anticipation, 35 U.S.C. s. 102(b), and/or obviousness, 35 U.S.C. s. 103.

Whether the phrase, "[a] method for treating a cancer ***patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity," in claims 5-10, is properly understood as a claim limitation.***

Ben Venue argues that the phrase, "[a] method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity," in claims 5-10 of the '537 patent, is not a claim limitation "but rather a statement of the object of practicing the method set forth" in the claims. Ben Venue '537 Brf. at 17. Bristol responds that a review of the patents, FN3 their prosecution history and specifications, makes clear that "reducing hematologic toxicity while achieving [antitumor] efficacy is a key element of the invention." BMS Opp. Brf. at 17; *see also* '537 Patent, cols. 8-10 (Efficacy & Safety; Hematologic Toxicity). Thus, the references to reducing toxicity and shrinking tumors are "necessary to give life and meaning" to Bristol's inventions. Brf. at 17. Bristol also relies on the presumption of claim differentiation to buttress its argument-if the Court ignores the preamble of the '537 patent (claims 5-10) as a limitation, claim 5 is identical to claim 1. Claim differentiation teaches that "each claim of a patent constitutes a separate invention." *See* P.A.T. Co. v. Ultrak, Inc., 948 F.Supp. 1506, 1511 (D.Kan.1996).

FN3. The two patents in suit ('803 and '537) have a similar prosecution history and nearly identical specifications.

A patent claim is normally divided into three sections: (1) the preamble; (2) the transition; and, (3) the body. *See* STX, Inc. v. Brine, Inc., 37 F.Supp.2d 740, 752 (D.Md.1999). "The preamble is that portion of the claim preceding the word 'comprising.' " Boehringer Ingelheim Animal Health, Inc. v. Schering-Plough Corp., 984 F.Supp. 239, 247 (D.N.J.1997). "The preamble is an introductory phrase that may summarize the invention, its relation to the prior art, or its intended use or properties .... [i]t may also constitute a limitation." *See* Donald A. Chisum, *Patents* s. 8.06 (1994). "[A] claim preamble has the import that the claim as a whole suggests for it." Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620 (Fed.Cir.1995). On the other hand, claim limitations serve to "point out distinctly the process, machine, manufacture or composition of matter which is patented ... not its advantages." *See* Preemption Devices, Inc. v. Minnesota Mining & Manuf. Co., 732 F.2d 903, 907 (Fed.Cir.1984); 35 U.S.C. s. 101. Thus, whether a preamble contains a limitation or merely a statement of purpose can only be decided "on review of the entirety of the patent to gain an understanding of what the inventors actually invented." Rowe v. Dror, 112 F.3d 473, 477 (Fed.Cir.1997); *see also* General Electric Co. v. Nintendo Co., 179 F.3d 1350, 1361 (Fed.Cir.1999).

Though still somewhat "opaque," certain rules for analyzing preambles have developed. *See* Patrick J. Flimm, Claim Construction Trends in the Federal Circuit, 572 PLI/PAT 317, 335-36 (1999) (characterizing the preamble/limitations test as "opaque" and without a set framework). However, "[t]he Federal Circuit has made it reasonably clear that the mere fact that a patentee finds something useful in a claim preamble in the [patent] litigation does not alone justify treatment of a claim preamble as a limitation." *See* STX, 37 F.Supp.2d at 752. If the body of the claim sets out a "structurally complete" invention, it is not a limitation. *See* Rowe, 112 F.3d at 478. Thus, where:

the body of the claim fully and intrinsically sets forth the complete invention,including all of its limitations, and the preamble offers no distinct definition of any of the defined claims limitations, but rather merely states, for example,the purpose or intended use of the invention, then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation.

Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305 (Fed.Cir.1999). Conversely, where the claim preamble "is necessary to give life, meaning, and vitality to the claim" or is "essential to point out the invention defined by the claim," it should be construed as a claim limitation. *See* Pitney Bowes, 182 F.3d at 1305-06; Boehringer, 984 F.Supp. at 247; *see also* General Electric, 179 F.3d at 1361.

[6] From examination of the patent, the Court finds that, as in *STX,* "the [disputed] phrase is a shorthand encapsulation of the advantages of the invention." 37 F.Supp.2d at 752. The body of the '537 patent recites a structurally complete invention. Put differently, to achieve the beneficial results promised in the preamble, a practitioner need only follow the method steps recited in the body of the claim-"(i) premedicating said patient with a medicament that reduces or eliminates hypersensitivity reactions, and (ii) parenterally administering to said patient about 135-175 mg/m^2 taxol over about three hours." '537 Patent, Claim 5; *see generally* Rowe, 112 F.3d at 478 (a statement of the "intended use" of an invention is not a claim limitation). The Court cannot transform a statement of objective into a structural limitation. *See* STX, 37 F.Supp.2d at 753. Moreover, where the preamble "simply states the intended use or purpose of the invention ... [it] usually does not limit the scope of the claim unless the preamble provides antecedents for ensuing claim terms." C.R. Bard, Inc. v. M3 Sys., Inc., 157 F.3d 1340, 1350 (Fed.Cir.1998) (citations omitted). Here the preamble phrase need not be referenced to practice the invention set out in the body of the claim. *See*

Biacore, AB v. Thermo Bioanalysis Corp., 79 F.Supp.2d 422 (D.Del.1999) (where the preamble "offers no distinct definition of any of the claimed invention's limitations, but rather merely states ... the intended use, then the preamble is of no significance"); *cf.* Boehringer, 984 F.Supp. at 247-48 (finding that the preamble included "an integral part of the process which cannot be separated" from the rest of the patent). The objectives of toxicity reduction and tumor regression are not "intimately meshed with the ensuing language in the claim." Pitney Bowes, 182 F.3d at 1306.

Additionally, Bristol asserts that the patent examiner insisted on dividing those claims which specifically addressed a reduction in toxicity and tumor size (claims 5-10) from those which did not (claims 1-4). *See* Oral Arg. (Feb. 15, 2000). That the examiner insisted on including certain language in claims 5-10, however, does not automatically make the claims' preambles limitations. *See* STX, 37 F.Supp.2d at 752 ("I decline to undertake the impossible task of divining what was in the examiner's mind"). As said, the '537 patent's limitations stand alone; the preamble sections express only the intended use of the invention. FN4

FN4. Bristol also advanced, at oral argument on February 15, 2000, that the desired results of practicing the method steps set out in the patent(s)-namely reducing toxicity and tumor size-give "meaning" to the invention because these results were unexpected as compared to previous studies. *See generally* Rowe, 112 F.3d at 478. Where, however, a court determines that the preamble "is a statement of intended use which is devoid of any structural elements .... [it cannot] be relied upon to distinguish over prior art." Heidelberg Harris, Inc. v. Mitsubishi Heavy Indus. Ltd., No. 95-0673, 1998 WL 42277, at (N.D.Ill. Jan.29, 1998).

[7] Bristol's final argument, based on the presumption of claim differentiation, is inapplicable. The doctrine of claim differentiationapplies when a broad claim is interpreted narrowly such that it is coextensive with a narrower claim. *See* General Electric Co. v. Hoechst Celanese Corp., 698 F.Supp. 1181, 1185-85 (D.Del.1988); *see also* D.M.I. Inc. v. Deere & Co., 755 F.2d 1570, 1574 (Fed.Cir.1985). Such is not here. Rather, the arguably narrower claim, claim 5, is interpreted to be coextensive with the broadest claim of the patent, claim 1; the "limitations" of claim 5 are not "being read into unlimited claims." Hoechst, 698 F.Supp. at 1185 (construing the doctrine narrowly to apply only when limitations of one claim are sought to be read into unlimited claims); *see* Dow Chem. Co. v. United States, 20 Cl.Ct. 623, 643 (1990) ("narrow limitations contained in one claim should not be read into other claims in which there is no such limitation").

Even if the presumption of validity created by claim differentiation could be relied upon, it should not be used to create a claim limitation where none exists. "[I]f a claim will bear only one interpretation, similarity will have to be tolerated." *See* Laitram Corp. v. Morehouse Indus., Inc., 143 F.3d 1456, 1462 (Fed.Cir.1998) (citing Autogiro Co. of Amer. v. United States, 181 Ct.Cl. 55, 384 F.2d 391, 404 (1967)); Clintec Nutrition Co. v. Baxa Corp., 988 F.Supp. 1109, 1119 (N.D.Ill.1997). To repeat, "the mere fact that a patentee finds something useful in a claim preamble in the [patent] litigation does not alone justify treatment of a claim preamble as a limitation." *See* STX, 37 F.Supp.2d at 752.

3. *Construction of the '803 Patent Claims*

The '803 patent has four independent claims and two dependent ones. *See* Mentlik Decl. Exh. A. Claims 1 and 2 are representative:

1. A method for reducing hematologic toxicity FN5 in a cancer patient undergoing Taxol treatment comprising parenterally administering to said patient an antineoplastically effective FN6 amount of about

135-175 mg/m^2 taxol over a period of about three hours.

FN5. Bristol defines "hematologic toxicity" simply as blood damage. Bristol Br. at 8. Similarly, the IVAX defendants state: " 'Hematologic toxicity' is one of several terms used by Bristol to describe the same phenomenon, others being hemotoxicity, neutropenia and myelosuppression. All refer to the same phenomenon: while chemotherapy drugs like taxol kill cancer cells, they are extremely toxic and also kill bone marrow cells which are essential to human life, as they manufacture white blood cells." IVAX Br. at 2 n. 4. Thus, the parties agree upon a definition of this term which is supported by the '803 patent specification. *See* '803 Patent, col. 9, lns. 60-67 ("Another aspect of the present invention is the reduction in hematologic toxicity associated with the treatment of cancer with taxol. The 157 patients who received taxol had blood counts performed weekly. White blood cell (WBC) counts, absolute neutrophil count (ANC), platelet counts, and hemoglobin (Hb) concentration were the primary variables to evaluate treatment related myelosuppression..")

FN6. Bristol claims: "It is ... clear that the words 'antineoplastically effective' refer to efficacy in fighting cancer." Bristol Br. at 8. Bristol's definition is supported by the patent specification. *See* '803 Patent, cols. 3-4 ("[I]t is highly desirable that the infusion duration not exceed 6 hours, yet the infusion dosage should provide the patient sufficient taxol to have an anti-neoplastic effect." Again, "It is another object of the present invention to provide a new method for administration of taxol which reduces the amount of taxol administered to a patient, without sacrificing the anti-neoplastic effects desired by administering taxol.") The IVAX defendants do not define this term.

2. A method for reducing both hematologic toxicity and neurotoxicity in a cancer patient undergoing Taxol treatment comprising parenterally administering to said patient an antineoplastically effective amount of about 135 mg/m^2 taxol over a period of about three hours.

[8] Bristol argues that together, the two passages "a method for reducing hematologic toxicity" and "an antineoplastically effective amount" "capture the essence of the meaning of Claim 1 of the '803 patent-namely, achieving *efficacy* and *reducedhematologic toxicity*." Bristol Br. at 8. In contrast, the IVAX parties charge that while the '537 patent claims are directed to methods for treating cancer, the '803 patent defines methods to reduce hematologic toxicity. IVAX Br. at 12. The Court accepts neither interpretation.

Of course, the '803 claims must be analyzed pursuant to the guidelines used to construct the '537 patent. Accordingly, the Court finds that the phrases "[a] method for reducing hematologic toxicity [and in claims 2, 3, and 5, neurotoxicity as well] in a cancer patient undergoing Taxol treatment" (Claims 1, 2, 3 and 6) and "[a] method for reducing hematologic toxicity [and in claim 5, neurotoxicity] in patients suffering from ovarian cancer FN7 and undergoing Taxol treatment [for such cancer]" (Claims 4 and 5) are not claim limitations, but preambles containing statements of purpose or intended use. Rowe v. Dror, 112 F.3d at 477; C.R. Bard, 157 F.3d at 1350.

FN7. There is no dispute that the treatment of ovarian cancer, and other types of cancer named in the claims, constitute claim limitations.

In turn, the transition of each of the claims is the phrase "comprising parentally administering [to said patient]." Boehringer Ingelheim Animal Health, Inc., 984 F.Supp. at 247.

Finally, the body of the representative claims describes two limitations. First is the administration of "an antineoplastically effective amount" of either 135-175 mg/m^2 or 135 mg/m^2 taxol. Despite Bristol's intimations to the contrary,FN8 it is clear from both the claim syntax and the patent specification that the phrase "an antineoplastically effective amount," which describes anti-cancer efficacy, is inseparable from the specific concentrations described in the claims. The specification merely recognizes that concentrations as low as 135 mg/m^2 can have an anti-cancer effect:

FN8. In its submissions to the Court concerning the defendants' motions for summary judgment of anticipation and obviousness, Bristol implies that the phrase "an antineoplastic amount," as opposed to the enumerated concentrations of 135-175 mg/m^2 and 135 mg/m^2, constitutes a claim limitation. *See* Bristol Br. in Opp. to Ben Venue's Motions for Summary Judgment of Invalidity at 8, 10 (arguing that Claims 1 and 2 "define three principal limitations," including "the administration of an antineoplastically *effective* amount of taxol. This means that the amount of paclitaxel administered according to the prescribed regimen is sufficient to achieve an antitumor response.") Having thus framed the question, Bristol then argues that its purported efficacy limitation is not disclosed or anticipated by the prior art, specifically Kris et al. and the handout distributed by Bristol at a 1991 conference of the National Cancer Institutes of Canada. The Court here rejects that interpretation.

It has also been surprisingly discovered that lower taxol dosages, such as about 135 mg/m^2 can be administered via infusions lasting about 3-hours to about 28-hours, and still be antineoplastically effective.... The present invention provides an improvement in the treatment of all types of cancer which can be treated with taxol, since by use of the administration protocol of the present invention, lower toxicities and/or less time is required than that associated with the prior art protocols for administering antineoplastically effective amounts of taxol.
'803 Patent, col. 5, lns. 40-44, 59-65. The second limitation is the infusion duration, which in all claims is "about three hours."
The prosecution history cited by Bristol does not persuade the Court otherwise. The patentee asserts that immediately before the examiner allowed the patent to issue, the inventors amended each claim to recite administration of "an antineoplastically effective amount" of paclitaxel. Bristol Br. at 15. The inventors remarked:

Applicants' amendment would more particularly recite that, not only is the claimed regimen effective in reducing hematologic toxicity, but it is simultaneously effective in causing an anti-tumor response. That is, the claimed regimenachieves both an antineoplastic effect while reducing hematologic toxicity, and Applicants show that this is accomplished by administering paclitaxel (taxol) to patients at a dosage of about 135-175 mg/m^2 over a duration of about 3 hours. Such an amendment would further distinguish the claimed invention from references teaching that regimens involving such a duration of infusion effected no observable antitumor response.

This passage enforces the Court's conclusion that the heralded anti-cancer efficacy of the invention flows inexorably from administration of the referenced concentrations. It does not constitute a separate claim limitation.

The Court holds that the '803 patent claims describe methods to treat various types of cancer through the

injection ("parenterally administering") of between 135 and 175 mg/m^2 taxol over a period of about 3 hours. Such steps present a structurally complete invention. And under *Rowe v. Dror, supra,* this Court reads the claims to include no more and no less. Employing the same rationale, the Court holds that the reduction of hematologic and neurologic toxicities are purposes of the invention comprising the stated method steps.

Reducing Toxicity: IVAX's "Literal" Interpretation

[9] As said, the Court finds that the passage "a method for reducing hematologic (and neurologic) toxicity" is not a claim limitation. However, the meaning of the phrase is disputed and will be addressed.

The IVAX defendants offer a purportedly "literal" interpretation. They argue that the claims of the '803 patent recite methods for reducing hematologic toxicity, and in some claims, neurotoxicity in a cancer patient by taxol administration. IVAX Br. at 6-7.FN9 However, the defendants note that when patients are given taxol, their levels of hematologic toxicity typically increase, not decrease. Put simply, they claim that blood damage is a side effect of the administration of taxol. Thus, they assert that their proffered claim interpretation defines a method that cannot work. And because "no doctor, nurse, pharmacist or any other health professional" would administer taxol for the purpose of reducing hematologic toxicity caused by taxol in the first place, the IVAX defendants conclude that a literal interpretation of the claims justifies a grant of partial summary judgment of noninfringement.

FN9. IVAX fully explains its position: "All claims of the '803 patent thus literally recite and should be interpreted to define, not methods for treating cancer with taxol, but methods for reducing hematologic toxicity (and in some cases, neurotoxicity) in a cancer patient undergoing taxol treatment by giving more taxol." IVAX Br. at 6-7.

Bristol readily agrees that hematologic toxicity is a side effect of taxol, and that the administration of a drug to reduce its own side effects would be "absurd." However, the plaintiff rejects the defendants' interpretation as unsupportable. Bristol Br. at 17 ("Defendants have grafted 'by administering paclitaxel' onto 'reducing hematologic toxicity;' but the resulting phrase 'a method of reducing hematologic toxicity by administering paclitaxel' ... is nowhere found in the claims, specification or prosecution history.") Instead, Bristol argues, "the clear meaning of [the claim language] is that the reduced toxicity occurs in a patient receiving paclitaxel, not *by* administering paclitaxel in the first place". Bristol Br. at 18.

At this stage, the dispute between the parties centers upon whether the '803 patent claims refer to a method for reducing blood damage in a cancer patient *by* administering taxol (IVAX's interpretation), or a method for reducing blood damage *resulting from* taxol treatment (Bristol's reading).

The Court looks to the patent specification for guidance. "Claims must be read in view of the specification, of which they are a part .... the description may act as a sort of dictionary, which explains the invention and may define terms used in the claims." Markman, 52 F.3d at 979. "[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." Vitronics, 90 F.3d at 1582.

The specification makes clear that the defendants' proffered interpretation is off target. First, it refers repeatedly to myelosuppression and myelotoxicity as side effects of taxol treatment. *See, e.g.,* '803 Patent, "Detailed Description of the Invention" ("Of great significance is a surprising discovery that the short term

infusion causes less myelosuppression, which leads to a lower incidence of infections and fever episodes (e.g., febrile neutropenia)."), col. 5, lns. 24-28; "Hematologic Toxicity" ("Another aspect of the present invention is the reduction of hematologic toxicity associated with the treatment of cancer with taxol."), col. 9, lns. 60-63, and ("Leukopenia and neutropenia were the most frequent and severe hematologic adverse effects observed during the first course of treatment."), col. 10, lns. 3-5.

Further, the structure of the specification confirms that the hematologic results described are part of Bristol's randomized comparative study of taxol ("the OV.9 study") in patients suffering from ovarian cancer. That study reviewed the "objective response rates" of patients to taxol treatment, as well as various side effects of such, including hematologic toxicity, hypersensitivity reactions, and peripheral neurotoxicity. There is no suggestion that taxol should be administered in order to counteract its own side effects; instead, the specification quantifies comparative levels of blood damage in patients receiving the drug. The "literal interpretation" offered by the IVAX defendants fails.

"Reducing Hematologic Toxicity": IVAX's Alternative Interpretation

Alternatively, the IVAX defendants assert that only one other interpretation of the '803 patent claims is plausible. They advance that the reference to "reducing hematologic toxicity" describes a two-step scenario in which a patient undergoing taxol treatment experiences a high level of hematologic toxicity, and whose treatment regimen is adjusted to the duration and levels described in the claims. They quote a section of the patent specification entitled "Hematologic Toxicity":

Thus, it is clear that both reducing the dosage and the infusion time will lower hematologic toxicity; however, reducing the infusion to 3 hours from 24 hours appears to have a greater impact on reducing toxicity than reducing the taxol dosage from about 175 mg/m^2 to 135 mg/m^2.

From this, defendants argue that the '803 patent claims define a method in which "the dosing regimen is changed from a 24-hour infusion to a 3-hour infusion to reduce the level of hematologic toxicity experienced at the longer infusion rate." IVAX Br. at 9.

Bristol counters that the phrase, properly interpreted, has "only one meaning- administering between 135 mg/m^2 and 175 mg/m^2 of paclitaxel over about 3 hours to achieve both an antineoplastic effect and a reduction in hematologic toxicity ... and neurotoxicity. ., *as compared to that normally experienced in a 24-hour infusion*." (Emphasis added.) Bristol Br. at 7. Though Bristol admits that the claims do not expressly refer to the 24-hour infusion regimen, it asserts that a skilled reader would clearly have understood this comparison from context.

In essence, the parties debate the meaning of the phrase "reducing hematologic toxicity." IVAX contends that the adjusted 3-hour treatment regimen described in the claims reduces the blood damage levels of a single patient already undergoing 24-hour taxol treatment. Yet Bristol insists that the reduction refers to hemotoxicity levels in a patient undergoing 3-hour treatment which are lower than those witnessedin other patients treated by the conventional, 24-hour infusion regime. The dispute over the meaning of "reducing ... neurotoxicity" (Claims 2, 3 and 5) involves basically the same issues.

Again the Court rejects IVAX's interpretation based on a reading of the patent specification. The passage quoted by defendants is from the "Experimental Protocol" section of the specification, which details the research methods used in the OV.9 study. There, researchers enrolled each patient in one of four treatment

arms with set infusion periods and concentrations of taxol: 1) 24-hour infusion duration at a dosage level of 175 mg/m^2 (Arm A); 2) 3-hour duration at 175 mg/m^2 (Arm B); 3) 24-hour duration at 135 mg/m^2 (Arm C); or 4) 3-hour duration at 135 mg/m^2 (Arm D). *See* '803 Patent, col. 6, lns. 15-20. The investigators then compared, *inter alia,* relative levels of hematologic toxicity observed in patients in the four study arms. *See* '803 Patent, Table 2 and Table 3, col. 10-11. They concluded in the cited passage that blood damage was lower in patients in the low-dose, or "reduced," 135 mg/m ^{2} arms than in the 175 mg/m^2 arms, and also lower in the short-term, or "reduced," 3-hour infusion arms than in the 24-hour arms. Notably, the specification contains no affirmance of IVAX's suggestion that patients who began a 24-hour regimen were later "adjusted" to the 3-hour regimen. The OV.9 researchers observed the hematologic damage effected in patients receiving the set taxol regimens imposed in arms A, B, C, and D of the study. The specification provides no support that they considered IVAX's purported Arm E. And the IVAX parties admit as much. *See* IVAX Br. at 9 ("[N]one of the subjects of the study as reported in the patent first received taxol over 24 hours and then had their infusion schedule reduced to three hours.")

Other references in the specification enforce the Court's position: In the "Hematologic Toxicity" section, the specification repeatedly compares hematologic results among the four study arms. *See, e.g.,* '803 Patent, col. 10, lns. 10-14 ("Of particular significance is that Grade IV neutropenia was reported almost five times more frequently in the patients treated with the 24-hour taxol infusion than the patients treated with a 3-hour taxol infusion."); col. 10, lns. 45-48 ("When the incidence of grade 3 and grade 4 are pooled, it is clear that severe leukopenia occurs more frequently in patients treated with a 24-hour taxol infusion than with a 3-hour infusion.")

Further, the "Background of the Invention" employs comparative language as it purports to describe the differences between the prior art and the stated invention. That section is context for the patent claims at issue:

Although it appears possible to minimize the side effects of administering taxol in an emulsion by use of a long infusion duration, the long infusion duration is inconvenient for patients, and is expensive due to the need to monitor the patients for the entire 6 to 24-hour infusion duration; Further, the long infusion duration requires that patients spend at least one night in a hospital or treatment clinic.

Thus, it is highly desirable to develop a taxol infusion protocol which would allow for recipients to be treated on an out-patient basis.

* * * * * *

It is also highly desirable to decrease the time required to administer taxol to patients to minimize patient discomfort and expense.

Thus, there is a need for a new method of administration of taxol which utilizes less taxol and/or requires less infusion time.

Therefore, it is a primary object of the present invention to provide a new method for administering taxol over a shorter period of time than the present 6 to 24-hour infusion protocols, while minimizing toxic effects induced by the administration of taxol.

* * * * * *

It is yet a further object of the present invention to provide a new method for administration of taxol which utilizes both lower dosages of taxol and shorter infusion periods, without sacrificing the anti-neoplastic benefits of the administration of taxol.

('803 Patent, cols. 3-4.) With IVAX's lack of other evidence to support its position, these paragraphs persuade the Court that the OV.9 study and the patent specification overall do not countenance the two-stage process proposed by defendants.

That determination does not change when the Court considers the prosecution history of the '803 patent. The IVAX defendants emphasize that Bristol repeatedly changed the wording of its claims throughout the five-year course of prosecution and chain of three applications which in June 1997 resulted in the issuance of the '803 patent. IVAX Br. at 10-12. They note, without challenge from Bristol, that in September 1995, the patent examiner refused to consider Bristol's new claims directed to reducing hematologic toxicity because they were "not readable on the elected invention" of treating cancer patients. *See* Mentlik Decl. Exh. B at 210-211. They argue, this time disputed, that while the '803 patent is directed solely to methods for reducing hematologic toxicity with taxol, the '537 patent addresses the treatment of cancer with the drug. IVAX Br. at 12. From there, the IVAX parties leap to the conclusion that the '803 patent necessarily describes either one of the methods described in their proffered claim interpretations.

Unfortunately, that leap is a misstep. The foregoing evidence does not permit the Court to accept IVAX's "alternative" interpretation.

4. ***IVAX's Motion for Summary Judgment of Noninfringement***

As patentee, Bristol bears the burden to prove infringement at trial. Consequently, to survive summary judgment, Bristol must identify specific, material facts showing a genuine issue for trial as to infringement. S. Bravo Systems, Inc. v. Containment Technologies Corp., 96 F.3d 1372, 1376 (Fed.Cir.1996).

Here, because Bristol has pulled the Hatch-Waxman "trigger" FN10 when the defendants filed ANDAs with the FDA, Bristol must produce evidence that their actions to sell paclitaxel-based drugs would infringe the '803 patent if and when FDA approval was received. Glaxo Inc. v. Novopharm Ltd., 110 F.3d 1562, 1564 (Fed.Cir.1997). The question is whether the defendants' proposed package insert (the proposed label for Zenith Goldline's generic paclitaxel-based drug Paxene(R)) could by its terms induce infringement of the '803 patent claims.

FN10. *See* 35 U.S.C. s. 271(e)(2)(A).

To begin, IVAX admits that, pursuant to FDA regulation, the proposed paclitaxel label of IVAX defendant Zenith Goldline contains "essentially the same information" as that of Bristol's Taxol(R) product. IVAX Br. at 17. Nonetheless, the IVAX defendants argue that the taxol administration methods recited in their label do not infringe Bristol's rights under the claims of the '803 patent. Simplified, IVAX's position is that the patent claims describe methods of taxol administration which the IVAX defendants do not reference in their label.

That argument is premised on the assumption that the Court would accept either IVAX's "literal" or

"alternative" claim interpretation. The Court has already rejected IVAX's suggested claim interpretations. So now, IVAX's avowal that it does not practice methods according to those interpretations is wholly irrelevant. Bristol points to the purported admissions of IVAX's expert, Dr. James F. Holland, in an effort to demonstrate that physicians are induced by the methods described in IVAX's label to use paclitaxel in a manner that would infringe Bristol's rights were IVAX's product involved. Bristol Br. at 25. The Court need not rely upon this evidence to determine that summary judgment of noninfringement in favor of IVAX is inappropriate now.

CONCLUSION

The two patents in suit are constructed as set out in this Opinion. IVAX's motion for summary judgment of noninfringement is denied.

ORDER

This matter is before the Court on the motion by defendant-counterclaimants Immunex Corporation, Zenith Goldline, and IVAX Corporation (collectively "IVAX defendants") for a *Markman* claim interpretation ruling and for partial summary judgment of noninfringement of U.S. Patent No. 5,641,803 ("the '803 patent"). Having heard oral argument on February 14-15, 2000, upon consideration of the submissions of the parties, and for the reasons stated in the accompanying opinion, it is on this day of March, 2000:

ORDERED that the claims of U.S. Patent Nos. 5,641,803 and 5,670,537 are constructed as set forth in the accompanying Opinion, and it is further

ORDERED that the IVAX defendants' motion for summary judgment of noninfringement is DENIED.

D.N.J.,2000.
Bristol-Myers Squibb Co. v. Immunex Corp