United States District Court,
D. Delaware.

NOVARTIS PHARMACEUTICALS CORPORATION, Novartis AG, Novartis Pharma AG, and Novartis International Pharmaceutical Ltd,
Plaintiffs.
v.
EON LABS MANUFACTURING, INC,
Defendant.

No. CIV.A.00-800-JJF

Aug. 9, 2002.

Pharmaceutical company sued competitor for infringement of patent for hydrosol compositions. Construing claims, the District Court, Farnan, J., held that: (1) "hydrosol" composition was synthetic pharmaceutical preparation in solid particle form; (2) "stabilizer" was excipient, in which drug was not soluble, which completely surrounded solid particles of drug and kept their size distribution constant for at least six hours; and (3) requisite weight ratio of drug to water was from 1:250 to 1:1549.

Claims construed.

5,389,382. Construed.

Stuart B. Young, Esquire of Young, Conaway, Stargatt & Taylor, Wilmington, Delaware, Of Counsel: Robert L. Baechtold, Nicholas N. Kallas, and Brian V. Slater, Esquires of Fitzpatrick, Cella, Harper & Scinto, New York City, for Plaintiffs.

George H. Seitz, III, Esquire of Seitz, Ogtrop and Green, P.A., Wilmington, Delaware, Of Counsel: Martin B. Pavane, and Mindy H. Chettih, Esquires of Cohen, Pontani, Lieberman & Pavane, New York City, for Defendant.

MEMORANDUM OPINION

FARNAN**, District Judge.**

This action was brought by Plaintiffs Novartis Pharmaceuticals Corporation, Novartis AG, Novartis Pharma AG, and Novartis International Pharmaceutical Ltd. (collectively "Novartis") against Defendant Eon Labs Manufacturing, Inc. (hereinafter "Eon") alleging infringement of U.S. Patent No. 5,389,382 (hereinafter the " '382 Patent"). The issue currently before the Court is the interpretation of certain claim language of the '382 Patent. The parties briefed their respective positions on claim construction, and the Court held a *Markman* hearing on July 2, 2002. This Memorandum Opinion presents the Court's construction of the

disputed terms and phrases.

I. BACKGROUND

Novartis' '382 Patent relates to hydrosol compositions of pharmaceutically active agents, including the immunosuppressive drug cyclosporin, which are suspended or re-suspendable in an aqueous medium. (D.I. 298 at 2). Specifically, these hydrosol compounds are comprised of several elements, including solid particles of cyclosporin which have a weight ratio to water of "about 1:300 to about 1:500," as well as a separate "stabilizer which maintains the size distribution of said particles." (D.I. 298 at 6).

Novartis alleges infringement of independent Claim 1, which defines one of the several hydrosol compositions covered by the '382 Patent. (D.I.1). Specifically, Claim 1 discloses a:

[h]ydrosol which comprises solid particles of a cyclosporin and a stabilizer which maintains the size distribution of said particles, wherein said cyclosporin has a water solubility below 0.5 grams per 100 milliliters, and said particles have a weight ratio of cyclosporin to water of about 1:300 to about 1:500 and a weight ratio of cyclosporin to said stabilizer of about 1:1 to about 1:50.

(D.I. 303 at A7, '382 Patent, col. 9, lines 21-28).

After hearing the parties' arguments and reviewing their contentions, the Court finds that the parties' dispute centers on the meaning of the terms "hydrosol" and "stabilizer," as well as the phrases "which maintains the size distribution of [cyclosporin] particles" and "weight ratio of cyclosporin to water of about 1:300 to about 1:1500." (D.I. 298 at 2; D.I. 302 at 12). Accordingly, to the extent the parties address the construction of other terms and phrases in their briefing the Court declines to provide a construction at this time. If the parties believe further claim construction is necessary, the parties shall inform the Court what additional terms are in dispute as of the first day of trial.

II. THE LEGAL PRINCIPLES OF CLAIM CONSTRUCTION

[1] [2] [3] [4] Claim construction is a question of law. Markman v. Westview Instruments, Inc., 52 F.3d 967, 977-78 (Fed.Cir.1995), *aff'd,* 517 U.S. 370, 388-90, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). When construing the claims of a patent, a court considers the literal language of the claim, the patent specification and the prosecution history. Markman, 52 F.3d at 979. A court may consider extrinsic evidence, including expert and inventor testimony, dictionaries, and learned treatises, in order to assist it in construing the true meaning of the language used in the patent. Id., at 979-80 (citations omitted). A court should interpret the language in a claim by applying the ordinary and accustomed meaning of the words in the claim. Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 759 (Fed.Cir.1984). However, if the patent inventor clearly supplies a different meaning, the claim should be interpreted accordingly. Markman, 52 F.3d at 980 (noting that patentee is free to be his own lexicographer, but emphasizing that any special definitions given to words must be clearly set forth in patent). If possible, claims should be construed to uphold validity. In re Yamamoto, 740 F.2d 1569, 1571 & n. * (Fed.Cir.1984) (citations omitted).

III. DISCUSSION

A. The Meaning Of The Disputed Term "Hydrosol"

[5] Novartis contends that the term "hydrosol" should be construed to mean "solid particles, varying in size

from 1 nanometer to 10,000 nanometers (10 microns) in diameter, dispersed in an aqueous (*i.e.,* water-containing) medium" (D.I. 298 at 2, 6). Novartis contends that this definition is consistent with what one of ordinary skill in the art would construe the term "hydrosol" to mean, namely solid particles dispersed in any aqueous medium (i.e. a water-containing environment), which could include the stomach of a patient. (D.I. 298 at 6). Novartis also contends that this definition is supported by the '382 Patent specification, which requires that the solid particles range in size from 1 nanometer to 10,000 nanometers. (D.I. 298 at 6).

Eon contends that the term "hydrosol" should be construed to mean "a synthetic pharmaceutical preparation, i.e., it does not encompass a dispersion of solid particles of cyclosporin which only forms in the stomach of a patient; a formulation in which all the solid particles are smaller than 7 microns in diameter, and in any event smaller than about 10 microns in diameter; all the cyclosporin is in solid particle form and not in solution, excepting for a very small amount of cyclosporin which the water in the hydrosol can solubilize." (D.I. 302 at 4). According to Eon, this definition is supported by the specification and prosecution history, which limit all solid particles to about seven microns in diameter, and confirm that the '382 Patent only contemplates synthetically stabilized hydrosols formed outside of the body. (D.I. 302 at 13, 15, 16).

In construing the term "hydrosol," the Court has considered the claim language, specification, and prosecution history of the '382 Patent. (*See* D.I. 303, '382 Patent, col. 9, lns. 21-29, col. 1, lns. 21-23, 48-51, D.I. 303 at A59, A66). The specification of the '382 Patent indicates that the hydrosol contemplated in Claim 1 is in "intravenously" acceptable and "injectable" form. The specification does not support an interpretation regarding hydrosols formed naturally upon ingestion. (*See,* D.I. 303 at A3, '382 Patent, col. 1, lns. 21-23; at A5, col. 5, lns. 62-65). Moreover, in the applicants' Amendment dated March 17, 1989, they describe how the invention is prepared and administered:

...a solution of a difficulty [sic] water soluble drug compound in an organic solvent miscible with water is *poured out into water* [, t]hus forming finely divided solid drug compound particles in amorphous colloid form...;

The removal of organic solvent from the colloidal aqueous dispersion is not detrimental, as the stabilization of the drug colloid particles is maintained. The protective colloid is, and remains absorbed on the solid drug particles. The resulting dispersion contains particles of such small diameters that they *can be administered by* intravenous injection. From the particles the drug compound is then *immediately released without any measurable delay*.

(D.I. 303 at A66) (emphasis added). When read together, the Court is persuaded that the specification and prosecution history require that the term "hydrosol" be limited in scope to synthetic pharmaceutical preparations which are not formed within the stomach of a patient. With regard to the parties' dispute concerning the size of the solid particles, the Court declines to provide a construction, because the specification of the '382 Patent unambiguously resolves the issue. (*See* D.I. 303 A3, '382 Patent, col. 1, lns. 14-18). As for the remaining issue, namely whether hydrosol is comprised of solid particles, it appears that the parties are in agreement, and thus, the Court will adopt Eon's proposed definition.

For all of the above reasons, the Court construes the term "hydrosol" to mean: a) a synthetic pharmaceutical preparation, i.e., it does not encompass a dispersion of solid particles of cyclosporin which only forms in the stomach of a patient; and b) all the cyclosporin is in solid particle form and not in solution, excepting for a very small amount of cyclosporin which the water in the hydrosol can solubilize.

B. The Meaning Of The Disputed Term "Stabilizer" And The Disputed Phrase "Which Maintains The Size Distribution Of [Cyclosporin] Particles"

[6] Novartis contends that the phrase "a stabilizer which maintains the size distribution of said [cyclosporin] particles" should be construed to mean "a substance which inhibits an increase in the size of the solid particles of cyclosporin." (D.I. 298 at 2, 9).

Eon contends that the term "stabilizer" should be construed to mean: a) an excipient which forms a "protective colloid" about solid particles of cyclosporin, i.e., completely surrounds the solid particles of cyclosporin; b) an excipient in which cyclosporin is not soluble; and c) a gelatin. (D.I. 302 at 4). Under this construction, Eon further contends that the phrase "a stabilizer which maintains the size distribution of said [cyclosporin] particles" should be construed to mean: a) the stabilizer keeps the size distribution of the solid particles constant, i.e., the stabilizer prevents the solid particles of cyclosporin from increasing or decreasing in size; and b) the stabilizer maintains the size distribution of the particles for at least several hours after the hydrosol is formed. (D.I. 302 at 4).

In construing the term "stabilizer" and the phrase "a stabilizer which maintains the size distribution of said [cyclosporin] particles," the Court has considered the claim language, specification, and prosecution history of the '382 Patent. (*See* D.I. 303, '382 Patent, at A4, col. 4, lns. 35-40, 49-53, at A6, col. 7, lns. 29-39, at A5, col. 6, lns. 12-17; D.I. 303, at A66, pgs. 2, 4, at A345, para.para. 113, 114). Based upon this review, the Court concludes that there is support for Eon's position. Specifically, the specification provides that:

One difference from the prior art process is that the...hydrosol particles are bound-when a water soluble colloid stabilizer is used-to exchangeable colloid molecules....

(D.I. 303 at A5, '382 Patent, col. 6, lns. 12-17). Additionally, the prosecution history indicates:

To avoid coagulation and crystallization, *a protective colloid must be present* during the formation of the drug compound colloid particles.

(D.I. 303 at A66). In view of this language, the Court is persuaded that a protective colloid must be present in the disclosed stabilizer, and, in order to "avoid coagulation and crystallization," such a colloid must not be soluble in the target "drug compound", i.e., cyclosporin. (*See* D.I. 303 at A345, para.para. 113, 114). As for whether the term "stabilizer" includes a gelatinous component, the Court concludes that the specification discloses such a vehicle only as a preferred embodiment, and therefore does not require such a form. (*See* D.I. 303 at A4, '382 Patent, col. 4, lns. 49-53, 65-68).

Turning to the disputed phrase "which maintains the size distribution of [cyclosporin] particles," the '382 Patent specification describes the function of the disclosed stabilizer as follows:

In order to inhibit an increase in the size of the particles of active agent in water, e.g. to prevent an increase in the size of the larger particles at the expense of the smaller particles, a stabilizer is preferably added, *which maintains the size distribution* of the active hydrosol particles in the dispersion *constant*.

(D.I. 303 at A4, '382 Patent, col. 4, lns. 35-40) (emphasis added). The Court is persuaded that this language contemplates a stabilizer which, in addition to inhibiting particle growth, also "maintains" and keeps "constant" the size distribution of the hydrosol particles. The Court concludes that a person of ordinary skill

in the art would understand that pharmaceutical preparations, including the invention disclosed in the '382 Patent, must remain stable for at least six hours so as to ensure their pharmacological integrity. (*See* D.I. 303 at A605-606, para. 6).

For all of the above reasons, the Court construes the term "stabilizer" to mean: a) an excipient which forms a "protective colloid" about solid particles of cyclosporin, i.e., completely surrounds the solid particles of cyclosporin; and b) an excipient in which cyclosporin is not soluble. In addition, the Court construes the phrase "a stabilizer which maintains the size distribution of said [cyclosporin] particles" to mean: a) the stabilizer keeps the size distribution of the solid particles constant, i.e., the stabilizer prevents the solid particles of cyclosporin from increasing or decreasing in size; and b) the stabilizer maintains the size distribution of the particles for at least six hours after the hydrosol is formed.

C. The Meaning Of The Phrase "Weight Ratio Of Cyclosporin To Water Of About 1:300 To About 1:1500"

[7] Novartis contends that the phrase "weight ratio of cyclosporin to water of about 1:300 to about 1:1500" should be construed to mean a "weight ratio of solid cyclosporin particles to water of 1:255 to 1:1725." (D.I. 298 at 2). According to Novartis, the term "about" in the disputed phrase allows for an actual range of plus or minus fifteen percent at each listed value. (D.I. 298 at 9). Specifically, Novartis contends that a person of ordinary skill in the art would use this figure because it is listed in the United States Pharmacopeia (hereinafter "USP"), a standard-setting body in the field of pharmacology. (D.I. 298 at 12).

Eon contends that the disputed phrase should be construed to mean a weight ratio of cyclosporin to water of 1:250 to 1:1549. (D.I. 302 at 4). Specifically, Eon contends that since the specification and prosecution history of the '382 Patent do not provide a specialized definition, the term "about" should be given its ordinary meaning in a mathematical context, whereby decimals are rounded up or down to the nearest integer according to numeric value. (D.I. 302 at 33). Furthermore, because the applicants' added the disputed phrase to Claim 1 in response to the Examiner's request for elaboration, Eon contends that Novartis is estopped from claiming a broader range of ratios than will approach exactness in quantity. (D.I. 302 at 35).

In construing the phrase "weight ratio of cyclosporin to water of about 1:300 to about 1:1500," the Court has considered the claim language, specification, and prosecution history of the '382 Patent. (D.I. 303, '382 Patent, A4, col. 4, lns. 54-57, A7, col. 9, lns. 21-28; D.I. 299 at para.para. 3, 29; D.I. 303 at A262-63, A265). Based upon this review, the Court concludes that there is support for Eon's position. Although the drug monographs listed in the USP commonly include values in the fifteen percent range, this figure is not exclusive, as Novartis has recognized in its briefing. (*See* D.I. 298 at 12). Moreover, in response to an Office Action, which required the applicants to "provide more definite claim wording so as to clearly distinguish the present claims from that of the prior art" and to limit the claims to the invention for which "the disclosure is enabling," the applicants amended Claim 1 by adding the disputed phrase. (D.I. 303 at A 258-265). In view of these circumstances, the Court concludes that the term "about" in the disputed phrase must be given a more limited construction. Accordingly, the Court will construe the phrase "weight ratio of cyclosporin to water of about 1:300 to about 1:1500" to mean a weight ratio of cyclosporin to water of 1:250 to 1:1549.

IV. CONCLUSION

An appropriate Order will be entered.

ORDER

At Wilmington this 9th day of August, 2002, for the reasons set forth in the Memorandum Opinion issued this date;

IT IS HEREBY ORDERED that:

1) the term "hydrosol" is construed to mean: a) a synthetic pharmaceutical preparation, i.e., it does not encompass a dispersion of solid particles of cyclosporin which only forms in the stomach of a patient; and b) all the cyclosporin is in solid particle form and not in solution, excepting for a very small amount of cyclosporin which the water in the hydrosol can solubilize;

2) the term "stabilizer" is construed to mean: a) an excipient which forms a "protective colloid" about solid particles of cyclosporin, i.e., completely surrounds the solid particles of cyclosporin; and b) an excipient in which cyclosporin is not soluble;

3) the phrase "a stabilizer which maintains the size distribution of said [cyclosporin] particles" is construed to mean: a) the stabilizer keeps the size distribution of the solid particles constant, i.e., the stabilizer prevents the solid particles of cyclosporin from increasing or decreasing in size; and b) the stabilizer maintains the size distribution of the particles for at least six hours after the hydrosol is formed;

4) the phrase "weight ratio of cyclosporin to water of about 1:300 to about 1:1500" is construed to mean a weight ratio of cyclosporin to water of 1:250 to 1:1500.

D.Del.,2002.
Novartis Pharmaceuticals Corp. v. EON Labs Mfg., Inc.