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

UNIGENE LABORATORIES, INC. and Upsher-Smith Laboratories, Inc,
Plaintiffs.
v.
APOTEX INC. and Apotex Corp,
Defendants.

No. 06 CV. 5571(RPP)

Aug. 28, 2008.

John F. Sweeney, Joseph A. DeGirolamo, Seth J. Atlas, Andrea L. Wayda, Joshua H. Harris, Sean E. Jackson, Morgan & Finnegan, LLP, New York, NY, for Plaintiffs.

Robert S. Silver, Manny D. Pokotilow, William J. Castillo, Allan H. Fried, Marc B. Bassler, Caesar, Rivise, Bernstein, Cohen & Pokotilow, Ltd., Philadelphia, PA, for Defendants.

OPINION AND ORDER

ROBERT P. PATTERSON, JR., **District Judge.**

Plaintiffs Unigene Laboratories, Inc., and Upsher-Smith Laboratories, Inc. brought suit against Defendants Apotex Inc. and Apotex Corp. alleging infringement of claim 19 of U.S. Patent No. 6,440,392 ("the '392 patent" or "the patent-in-suit"). From July 14, 2008, to July 16, 2008, the Court held a claim construction hearing. FN1 At the hearing, the parties limited the claim construction to the meaning of "about 20 mM citric acid," as used in claim 19. The following opinion constitutes the Court's construction of that claim term as a matter of law.

FN1. On July 14, 2008, prior to the hearing, the Court granted Defendants' motion in limine (Doc. No. 109) to preclude the testimony of Plaintiffs' patent law expert Dr. Robert Raymond, Esq. on the grounds that it addressed legal conclusions already presented in the Plaintiffs' briefs. (Tr. at 2:8-14.)

BACKGROUND

Plaintiffs are the owner and licensee of the '392 patent entitled "Nasal Calcitonin Formulations," which was issued on August 27, 2002. On February 5, 2004, Plaintiffs filed an application with the United States Patent and Trademark Office (the "PTO") for the reissue of the '392 patent due to errors made by the applicant during the prosecution. Although claim 19 is currently rejected by the patent examiner as being invalid over the prior art, the reissue proceeding is ongoing.

The patented formulation is currently sold as a nasal spray under the trademark Fortical(R). Plaintiffs allege that Defendants are liable for infringing claim 19 of the '392 patent based on Defendants' filing of an Abbreviated New Drug Application ("ANDA") to the Food and Drug Administration on or about June 1, 2006, to market a generic version of Fortical(R). Defendants' defense is that the patent-in-suit is invalid.

A. The '392 Patent **and Specification**

The '392 patent is directed to liquid pharmaceutical compositions, in a form suitable for nasal application, comprising calcitonin as an active ingredient, and specific concentrations of citric acid or a salt thereof, which act as a stabilizer and absorption enhancer, in a concentration from about 10 mM to about 50 mM. (PMX 1 ('392 Patent), Abstract). The patent specification discloses that use of citric acid or a salt thereof at a concentration from about 10 mM to about 50 mM increases both the stability of salmon calcitonin and the bioavailability levels of salmon calcitonin by conferring beneficial advantages to the nasal absorption characteristics. (Id., col. 2.)

The '392 patent issued with 23 claims. Claims 1-19 are composition of matter claims, and claims 20-23 are method claims. Only claim 19 is asserted by Plaintiffs against Defendants in this suit. As issued, claim 19 reads as follows:

A liquid pharmaceutical composition comprising about 2,200 MIC [FN2] units of salmon calcitonin, about 20 mM citric acid, about 0.2% phenylethyl alcohol, about 0.5% benzyl alcohol, and about 0.1% polyoxyethylene(20) sorbitan monooleate.

FN2. The parties stipulated that "MIC" is a typographical error and should read "MRC," which is a unit of measurement equivalent to "IU" (International Units).

(Id., col. 7, l. 21-col. 8, l. 3). haVing stipulated to the meaning of all the other terms in claim 19, the parties seek claim construction of only the term "about 20 mM citric acid."

The patent specification contains three illustrative examples of the inventor's studies. Example 1 of the '392 patent examines the effect of the concentration of citric acid on the bioavailability and plasma concentration of nasally administered salmon calcitonin (abbreviated "sCT"). (Id., col. 5, ll. 8-10.) Table 1 of the '392 summarizes the results of Example 1 and shows that, as the concentration of citric acid increases from 0 to 100 mM, the bioavailability and plasma concentration of salmon calcitonin also increases. (PMX 6 (Kwan Decl.) para. 21.)

Example 3 of the '392 patent examines the effect of citric acid concentration on the stability of salmon calcitonin stored for varying periods of time at a temperature of 50 (deg.) C (PMX 1 ('392 Patent), col. 5, line 66-col. 6, line 1.) Table 3 of the '392 patent summarizes the results of Example 3 and indicates that:

in the absence of citric acid, the amount [of] sCT in the formulation decreased steadily between 0 and 9 days after the study was begun. In the presence of citric acid (10-50 mM) the rate of disappearance of sCT decreased significantly, however, as the concentration of citric acid was further increased, the rate of sCT disappearance from vials stored at 50 (deg.) C increased in proportion to the amount of buffered citric acid in the formulation.

(Id., col. 6, lines 8-15.)

The specification also discloses two specific pharmaceutical compositions. The first is "a liquid pharmaceutical composition comprising about 2,200 MRC units of salmon calcitonin, about 10 mM citric acid, about 0.2% phenylethyl alchohol, about 0.5% benzyl alcohol, and about 0.1% TWEEN(R) 80 [(polyoxyethylene(20) sorbitan monooleate)]." (Id., col. 1, ll. 55-60.) The second is "a liquid pharmaceutical composition comprising about 2,200 MRC units of salmon calcitonin, about 20 mM citric acid, about 0.2% phenylethyl alchohol, about 0.5% benzyl alcohol, and about 0.1% TWEEN(R) 80 [(polyoxyethylene(20) sorbitan monooleate)]." (Id., col. 1, ll. 61-65.)

B. The Relevant File History

During the prosecution of the '392 patent, the PTO examiner Mina Haghighatian rejected certain claims, including claim 19, as obvious pursuant to 35 U.S.C. s. 103(a) and therefore unpatentable over the prior art. FN3 In the PTO office action dated December 2, 2001, the examiner stated: "Claims 1-4, 6-14 and 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mardente et al (6,149,893) in view of Cho et al (5,665,700)." (DX-1-H at 3). In response, the inventor William Stern submitted an amendment dated March 20, 2002 to overcome the obviousness rejection. His amendment stated:

FN3. The examiner also rejected certain claims including claim 19 for use of the trademark TWEEN(R) 80.

Mardente does not disclose citric acid concentrations in the claimed range. In fact, Mardente discloses citric acid amounts between 0.4 g per liter and 0.7 g per liter and for sodium citrate to between 0.4 g per liter and 0.7 g per liter. Thus, the maximum molar concentration for citric acid and/or its salt disclosed by Mardente is about 6.1 mM outside the claimed range. There is nothing in Mardente or in Cho or Dua alone or in combination that discloses or suggest [sic] the use of 10 to 50 mM citric acid or a salt thereof to stabilize a liquid nasal calcitonin formulation.
(DX-1-I at 3.)
On May 28, 2002, the examiner issued a Notice of Allowability (i.e., the PTO communication indicating that a patent will issue if the required fee is paid). The notice contained an examiner's amendment, which provided, "Please delete the term 'about' before '10' in claims 1, 18, 22 and 23." (DX-1-J at 2.) The examiner noted, "Authorization for this examiner's amendment was given in a telephone interview with Mr. Charles C. Achkar," the inventor's attorney, "on 05/28/02." (*Id.*) The examiner gave the following statement of reasons for allowance: "the prior art does not teach or suggest a liquid pharmaceutical composition containing calcitonin or an acid addition salt thereof and citric acid and/or salt thereof in a concentration from 10 to about 50 mM in a form suitable for nasal administration." (*Id.*) The examiner further stated that "[a]ny comments considered necessary by the applicant must be submitted no later than the payment of the issue fee." (*Id.*) There is no record of any comments submitted by the inventor on the statement of reasons for allowance.

When the '392 patent issued on August 27, 2002, the word "about" preceding the figure "10" had been removed from claims 1, 22, and 23 in the phrase "adding citric acid or a salt thereof in a concentration from about 10 to about 50 mM." The word "about" had not been removed, however, from claim 18 in the phrase "about 10 mM citric acid." (*See* PMX 1, cols. 6, 7, 8.) Claim 18 was issued as follows:

A liquid pharmaceutical composition comprising about 2,200 MRC units of salmon calcitonin, about 10 mM

citric acid, about 0.2% phenylethyl alcohol, about 0.5% benzyl alcohol, and about 0.1% polyoxyethylene(20) sorbitan monooleate.

(PMX 1, col. 7, ll. 16-20.)

On July 30, 2008, subsequent to the claim construction hearing before this Court, the inventor submitted a supplemental amendment to the PTO regarding his reissue patent application filed on February 5, 2004. (Defs.' Letter Br. dated Aug. 4, 2008, Attach. A.) Among many other items, the inventor requested an amendment to claim 18 to delete the word "about" preceding "10 mM citric acid." (Id. at 10.) The remarks attached to the amendment explained that "claim 18 is amended to reflect an examiners [sic] amendment that accompanied the notice of allowance mailed June 4, 2002 during the original prosecution that matured into the original patent number 6,440,392." (Id. at 14.)

DISCUSSION

A. Law on Claim Construction

Claim construction is a question of law to be decided by the court. Markman v. Westview Instruments, Inc., 52 F.3d 967, 970-71 (Fed.Cir.1995). The court "must construe 'only those [claim] terms ... that are in controversy, and only to the extent necessary to resolve the controversy.' " McNeil-PPC, Inc. v. Perrigo Co., 443 F.Supp.2d 492, 501 (S.D.N.Y.2006) (quoting Vivid Techs., Inc. v. Am. Science & Eng'g, Inc., 200 F.3d 795, 803 (Fed.Cir.1999)). Claim terms "are generally given their ordinary and customary meaning," which is the meaning they would have to a person of ordinary skill in the art at the time of the invention. Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd., 476 F.3d 1321, 1326 (Fed.Cir.2007); *see also Philips v. AHW* Corp., 415 F.3d 1303, 1312-13 (Fed.Cir.2005). In this case, the time of the claimed invention is February 4, 2000, the filing date of the provisional application on which the '392 patent is based. (PMX 1 ('392 patent) at 1; DX-2 (Klibanov Decl.) para. 31.)

In construing a claim, the court looks first to "the intrinsic evidence of record, i.e., the patent itself, including the claim, the specification and, if in evidence, the prosecution history." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996) (citing Markman, 52 F.3d at 979). The court first must review "the words of the claims themselves, both asserted and nonasserted." *Id.;* Interactive Gift Express, Inc. v. Compuserve, Inc., 256 F.3d 1323, 1331 (Fed.Cir.2001) (stating that the court's "analytical focus must begin and remain centered on the language of the claims themselves"). A disputed claim term must be construed in a "manner consistent with the scientific and technical context in which it is used in the patent." AFG Indus. Inc. v. Cardinal JG Co., 239 F.3d 1239, 1248 (Fed.Cir.2001). Typically, the "ordinary and customary meaning" of the term as understood by a person of ordinary skill in the art is controlling, Johnson Worldwide Assoc., Inc. v. Zebco Corp., 175 F.3d 985, 989 (Fed.Cir.1999), unless it is clear from the patent, specification, and file history that the inventor used the term with a special meaning. Vitronics, 90 F.3d. at 1582; *accord* Texas Digital Sys., Inc. v. Telegenix, Inc., 308 F.3d 1193, 1204 (Fed.Cir.2002).

In that regard, the court next must review "the specification to determine whether the inventor has used any terms in a manner inconsistent with their ordinary meaning." Vitronics, 90 F.3d. at 1582. In doing so, the court must take care to avoid "import[ing] into the claims [any] limitations that were unintended by the patentee." Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1325 (Fed.Cir.2003).

Finally, if in evidence, the court may examine the prosecution history of the patent, which contains the "complete record of all the proceedings before the Patent and Trademark Office, including any express

representations made by the applicant regarding the scope of the claims." *Id*. Statements of the applicant "regarding the meaning of a claim term are relevant to the interpretation of that term in every claim of the patent absent a clear indication to the contrary." CVI/Beta Ventures, Inc. v. Tura LP, 112 F.3d 1146, 1155 (Fed.Cir.1997). The file history of a reissue application may also be considered as intrinsic evidence in construing the meaning of a claim. *See* Ortho-McNeil Pharm., Inc., 476 F.3d at 1324-25 (affirming the district court's claim construction which relied in part on the file history of the reissue application that was pending during claim construction).

If an analysis of the intrinsic evidence alone resolves the ambiguity in a disputed claim term, it is improper for the court to rely on extrinsic evidence. Vitronics, 90 F.3d at 1583; *see also* Interactive Gift Express, 256 F.3d at 1332. The policy behind this limitation is that the patent, specification, and file history constitute the public record on which competitors are entitled to rely in "ascertain[ing] the scope of the patentee's claimed invention and ... design[ing] around the claimed invention. Vitronics, 90 F.3d at 1583. "Allowing the public record to be altered or changed by extrinsic evidence introduced at trial, such as expert testimony, would make this right meaningless." *Id*. Extrinsic evidence includes expert testimony, inventor testimony, dictionaries, and learned treatises. *See* Key Pharm. v. Hercon Lab. Corp., 161 F.3d 709, 716 (Fed.Cir.1998); Vitronics, 90 F.3d at 1584; Markman, 52 F.3d at 980.

B. Construction of "About 20 mM citric acid"

The '392 patent uses the word "about" to modify several different quantities, including millimolar concentration of citric acid in claims 1, 18, 19, 22, and 23. The parties agree that the ordinary and customary meaning of "about" is "approximately," and that a person of ordinary skill in the art as of February 4, 2000, would have understood the term "about 20 mM citric acid" to mean "approximately 20 mM citric acid." (Pls.' Opening Br. at 13; Defs.' Claim Construction Mem. Law at 12; PMX 6 (Kwan Decl.) para.para. 30, 49; DX-2 (Klibanov Decl.) para.para. 36-37; Tr. (Kwan) at 91:8-10; Tr. (Klibanov) at 195:4-6.) This construction is consistent with way the word "about" is used in all the claims to indicate an approximate measurement of a substance. It is also consistent with ordinary English meaning of the word "about," which dictionaries define as "approximately." (PMX 6 (Kwan Decl.) para.para. 30, 49-50; DX-2 (Klibanov Decl.) para. 36.) Given that nothing in the patent specification contradicts this ordinary and customary meaning, the Court agrees that "about" is correctly construed as "approximately" in the term "about 20 mM citric acid."

Although both parties construe the term "about 20 mM citric acid" to mean "approximately 20 mM citric acid," they disagree as to the numerical limits imparted by the term. Plaintiffs propose the construction that "about 20 mM citric acid" means "approximately 20 mM citric acid and would encompass a reasonable variation of (plus-or-minus sign) 10% in the concentration of 20 mM of citric acid." (Pls.' Opening Br. at 13; PMX 6 (Kwan Decl.) para. 50.) In support of this construction, Plaintiffs' expert Henry Kwan testified that a person of ordinary skill in the art would understand "about 20 mM citric acid" to encompass a variation of (plus-or-minus sign) 10% after taking into consideration Tables 1 and 3 of the ' 392 patent, in particular the sensitivity of bioavailability to citric acid concentration within the 10 to 25 mM range, and the ordinary English meaning of the word "approximately," which would reasonably allow a variation of (plus-or-minus sign) 10%. (PMX 7 (Kwan Reply Decl.) para.para. 11, 13-23.) Specifically, Table 3 demonstrates that changes in citric acid concentration produce relatively small effects on the stability of salmon calcitonin within this range (overall an 8% increase in recovery of sCT from 10 mM to 25 mM FN4), while Table 1 demonstrates that changes in citric acid concentration produce relatively large effects on the bioavailability of salmon calcitonin within this range (overall an 82% increase FN5 in bioavailability of sCT from 10 to 25

mM). (Tr. (Kwan) at 93:17-23, 94:5-10.) In Dr. Kwan's opinion, considering the two tables together in addition to the ' 392 patent's goal of maximizing both stability and bioavailability, a person of ordinary skill in the art would adopt a variation around 20 mM citric acid that maximizes the citric acid concentration as much as possible without resulting in a lower limit too low to achieve the desired enhancement of bioavailability levels. (PMX 7 (Kwan Reply Decl.) para.para. 22-23; Tr. (Kwan) at 104:24-106:20.) In Dr. Kwan's expert opinion, plus/minus ten percent is "a reasonable compromise." (Tr. (Kwan) at 106:18-19.)

FN4. In the '392 patent as issued, Table 3 contains a typographical error: the column heading "20 mM" should read "25 mM." To amend this error, the applicant submitted an amendment dated September 7, 2007 to the PTO in connection with his reissue application. (DX-1-L at 8, 16.) Dr. Kwan revised his declarations at the *Markman* hearing to conform to the data in Table 3 as amended.

FN5. In the '392 patent as issued, Table 1 also contains typographical errors in the reported figures for bioavailability: the table should report a bioavailability of 3.57% (plus-or-minus sign)1.39 at a citric acid concentration of 10 mM and 6.49% (plus-or-minus sign)2.93 at a citric acid concentration of 25 mM. The applicant called to the attention of the PTO examiner in his amendment dated September 7, 2007. (DX-1-L at 6.) Dr. Kwan revised his declarations at the *Markman* hearing to conform to the data in Table 1 as amended.

Defendants, on the other hand, propose the construction that "about 20 mM citric acid" means "approximately 20 mM citric acid, encompassing a range of concentrations greater than or equal to 15 mM citric acid to less than 25 mM citric acid." (Defs.' Claim Construction Mem. Law at 20-21; DX-2 (Klibanov Decl.) para. 42.) Defendants' expert Alexander M. Klibanov testified that to construe "about 20 mM," a person of ordinary skill in the art would rely on conventional rounding to determine the range of concentrations that would round off to 20 mM. (DX-2 (Klibanov Decl.) para. 41.) Having determined that 20 mM has one significant figure, the person of ordinary skill in the art would understand that "about 20 mM" encompasses a range of concentrations greater than or equal to 15 mM to less than 25 mM. (*Id.* para.para. 41-42.) In support of his rounding methodology, Dr. Klibanov cited the *Chemist's Companion: A Handbook of Practical Data, Techniques, and References,* specifically its discussion of the use of significant figures and rounding in chemistry. (DX-2 (Klibanov Decl.) para. 44 (citing DX-2, Attach. 2 at 481).)

The Federal Circuit has repeatedly observed that "[t]he use of the word 'about[ ]' avoids a strict numerical boundary to the specified parameter. Its range must be interpreted in its technological and stylistic context." Central Admixture Pharmacy Servs., Inc. v. Advanced Cardiac Solutions, P.C., 482 F.3d 1347, 1355-56 (Fed.Cir.2007) (construing the term "osmolality ... of between about 400-500 mOsmol"); Ortho-McNeil, 476 F.3d at 1326 (internal quotation marks omitted) (construing the disputed claim limitation "about 1:5"): Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1217-18 (Fed.Cir.1995) (construing the scope of "about 5:1 to about 7:1"). The Court must therefore examine how the word "about" was used in the other claims, specification, and file history of the patent-in-suit. In particular, the Court must focus on "the criticality" of the 20 mM concentration to the invention in claim 19 of the '392 patent. Ortho-McNeil, 476 F.3d at 1327.

The intrinsic evidence indicates that the term "about 20 mM citric acid" in claim must not be construed as encompassing a broad range of concentrations because the inventor selected a single concentration. By contrast to claim 19, in claims 1, 22, and 23, the inventor specified a range "from 10 to about 50 mM" citric

acid or a salt thereof. (PMX 1 ('392 Patent), col. 6, l. 37; col. 8, ll. 13-14, 19.) Similarly, in claims 8 through 13 and 15, the inventor specified ranges for measurements such as MRC units/ml (e.g., "about 1,000 to about 2,500 MRC units/ml"), pH level (e.g., "a pH of from about 3 to about 5"), and osmotic pressure (e.g., "osmotic pressure of from about 250 to about 350 mOsm/liter"), while in claims 14, 18 and 19, he selected distinct figures for pH levels and MRC units/ml of salmon calcitonin. (Id., col. 6, l. 54-col. 7, l. 7.) The inventor's selective use of distinct figures demonstrates the relative criticality of the measurement "about 20 mM citric acid" to the claimed invention. It also "leads to a conclusion that one of ordinary skill in the art would understand the inventor[ ] intended a range when [he] claimed one and something more precise when [he] did not." Ortho-McNeil, 476 F.3d at 1327. Defendants' proposed construction of "about 20 mM citric acid" encompassing a range as wide as 15 mM to 25 mM is at odds with this conclusion.

The criticality of "about 20 mM citric acid" to the claimed invention is also supported in the patent specification. The specification suggests that when a claim uses a distinct figure to claim a quantity, that quantity is "most preferable" or optimal to achieve the desired effects of the '392 patent. For example, when teaching the suitable total composition quantities to be administered at each nasal application, the specification states,

Compositions for use in accordance with the invention accordingly suitably comprise from about 150 to about 8,000, preferably from about 500 to about 4,000, more preferably from about 500 to about 3,000, yet again more preferably from about 1,000 to about 2,500, and *most preferably about 2,200 MRC units of calcitonin per ml*.

(PMX 1, col. 3, ll. 59-64 (emphasis added).) When describing the amount of surfactant that should be present in the compositions of the invention, the specification states that "the amount present will be of the order of from about 0.1 mg/ml to about 10 mg/ml, preferably about 0.5 mg/ml to 5 mg/ml and *most preferably about 1 mg/ml*." (Id., col. 3, ll. 28-30 (emphasis added).) When describing the suitable pH levels, the specification states, "Preferably the compositions of the invention have a pH of from about 3 to 5, more preferably from about 3.5 to 3.9 and *most preferably 3.7*." (PMX 1, col. 3, ll. 9-14 (emphasis added).) The specification thus supports the conclusion by a person of ordinary skill in the art that "about 20 mM citric acid" is a concentration selected by the inventor because of its criticality to the claimed invention and its significance in achieving the desired effects of the '392 patent. The specification supports a narrower construction of "about 20 mM citric acid" than the range proposed by Defendants.

The observations a person of ordinary skill in the art would make with respect to Tables 1 and 3 of the patent specification are consistent with the conclusions drawn above. As Dr. Kwan testified, a person of ordinary skill in the art would observe that from 10 mM to 25 mM citric acid, changes in concentration produce relatively small effects on the stability of salmon calcitonin and relatively large effects on the bioavailability of salmon calcitonin. (Tr. (Kwan) at 93:17-23, 94:5-10.) The Federal Circuit has instructed that when considering how to construe the term "about" in the context of a particular patent, "[i]t is appropriate to consider the effects of varying that parameter, for the inventor's intended meaning is relevant." Ortho-McNeil, 476 F.3d at 1326 (quoting Pall Corp., 66 F.3d at 1217). If the parameter of "about 20 mM citric acid" were to encompass a range as wide as 15 mM to 25 mM, then a composition of the invention comprising a citric acid concentration at the low end of the range could fall short of the "high standards of stability and bioavailability required for nasal application" that the '392 patent claims. (PMX 1, col. 2, ll. 24-25.)

Defendant relies on the file history of the patent prosecution and the reissue application as intrinsic

evidence. Defendants contend that the deletion of the word "about" before "10 mM citric acid" in claim 18 is relevant to the construction of "about" in regard to "20 mM citric acid" in claim 19. According to Defendants' interpretation of the inventor's amendment dated March 20, 2002 in conjunction with the examiner's amendment in the Notice of Allowability dated May 28, 2002, the deletion of the word "about" in claim 18 is an acknowledgement by the inventor that 6.1 mM (almost 4 mM less than 10 mM) fell within the range of "about 10 mM." (DX-2 (Klibanov Decl.) para. 63; Defs.' Letter Br. dated Aug. 4, 2008, at 3-4; Defs.' Claim Construction Br. at 19; Tr. (Klibanov) at 221:1-12.) Citing Superior Fireplace Co. v. Majestic Products Co., 270 F.3d 1358 (Fed.Cir.2001), Defendants maintain that the examiner, with authorization from the inventor's attorney, deleted the word "about" from claim 18 to overcome prior art, specifically the Mardente patent. They point to the July 30, 2008 amendment in connection with Plaintiffs' reissue application as confirmation that the examiner and the applicant's attorney agreed to delete the term "about" before "10 mM citric acid" in claim 18. Defendants argue that in view of the inventor's acquiescence to the examiner's amendment to claim 18, the disputed claim term "about 20 mM citric acid" in claim 19 must be construed to encompass at least a (plus-or-minus sign) 4 mM variation to remain consistent with this evidence.

In the Court's view, however, the file history on which Defendants rely does not shed any light on the construction of "about 20 mM citric acid" in claim 19. Defendants focus on the following statement from the inventor's amendment dated March 20, 2002:

Mardente does not disclose citric acid concentrations in the claimed range. In fact, Mardente discloses citric acid amounts between 0.4 g per liter and 0.7 g per liter and for sodium citrate to between 0.4 g per liter and 0.7 g per liter. Thus, the maximum molar concentration for citric acid and/or its salt disclosed by Mardente is about 6.1 mM outside the claimed range.

(DX-1-I at 3.) No useful conclusions can be drawn from this statement, however, because the last sentence is ambiguous. Courts have "consistently rejected prosecution statements too vague or ambiguous to qualify as a disavowal of claim scope." Omega Eng'g v. Raytek Corp., 334 F.3d 1314, 1325 (Fed.Cir.2003). Alleged disavowing statements must be "so clear as to show reasonable clarity and deliberateness" and "so unmistakable as to be unambiguous evidence of disclaimer." *Id*. That standard is not met here. FN6 Moreover, as Plaintiffs point out, the same examiner stated in an office action mailed on October 21, 2005, in connection with the reissue application, "The term 'ABOUT' is a relative term and there is no standard for ascertaining the requisite degree." (PMX 3, Office Action mailed 10/21/05, at 7.)

FN6. Defendants read the last sentence as though there is a comma or dash between "about 6.1 mM" and "outside the claimed range," so that the inventor seems to claim that the concentration of 6.1 mM is outside (i.e., not within) the claimed range of "about 10 mM." Another perhaps more plausible reading is that the concentration disclosed by the Mardente patent is 6.1 mM outside of (or away from) the claimed range of "about 10 mM."

In view of the claims, the specification, and the file history, the Court rejects the testimony of Defendants' expert Dr. Klibanov that a person of ordinary skill in the art would use the rounding approach to determine the range of concentrations claimed in claim 19.FN7 A construction of "about 20 mM citric acid" that encompasses a range of 15 mM to 25 mM citric acid "is clearly at odds with the claim construction mandated by the claims themselves." Phillips v. AWH Corp., 415 F.3d 1303, 1318 (Fed.Cir.2005). It is also at odds with the ordinary meaning of the word "approximate," which is defined as "nearly correct or exact,"

or "located close together." Webster's Seventh New Collegiate Dictionary (7th ed.1969). Moreover, Defendants' rounding approach leads to erratic and unreasonable results when applied to the other claim terms modified by the word "about." (*See* PMX 7 (Kwan Reply Decl.), tbl.B.)

FN7. Contrary to Defendants' assertion, the Federal Circuit has not endorsed the rounding approach. In U.S. Philips Corp. v. Iwasaki Electric Co., 505 F.3d 1371 (Fed.Cir.2007), the Federal Circuit affirmed the district court's construction of the halogen concentration range "between 10^{-6} and 10^{-4} "mu"mol/mm ^{3}" as meaning "between 1×10^{-6} and 1×10^{-4} "mu"mol/mm ^{3}," having rejected the plaintiff's argument that the claim expressed a range of orders of magnitude rather than a range more precise numbers. Id. at 1376. The plaintiff had argued before the district court that a lamp with a halogen concentration somewhat outside the elaimed range might still be infringing due to rounding at either end of the range, but the district court disagreed and held that the question of whether and how to apply rounding should be treated as a claim construction issue, not an issue of fact for the jury. Id. at 1377. The Federal Circuit expressly declined to address the question of rounding and whether or not it should have been presented to a jury. *Id*. The court did note that "[b]ecause '10^{-6}' and '10^{-4}' are simply the numbers 0.000001 and 0.0001 expressed as powers of ten, the claim language provides no basis for inferring any level of precision beyond the single digit '1.' " *Id*. at 1377. In any event, this case is not instructive because the claim term did not contain the modifier "about."

The Court also rejects the expert testimony of Plaintiffs' expert Dr. Kwan that a person of ordinary skill in art would understand "about 20 mM citric acid" to encompass a reasonable variation of (plus-or-minus sign) 10%. While Dr. Kwan sought to justify his selection of the number 10% by analyzing the patent specification, he admitted that he "could easily have selected a number like eight percent or perhaps 11.5 percent. But unfortunately, as a pharmaceutical development scientist, we like to think in terms of round numbers." (Tr. (Kwan) at 102:10-21.) FN8 The selection of a variation of (plus-or-minus sign) 10%, which was admittedly "not easy" (*id*. at 100:6-7), appears to be an unsupported opinion. The unreliability of this expert's construction due to its arbitrariness is exacerbated by the inherent unreliability of expert testimony "generated at the time of and for the purpose of litigation." Phillips v. AWH Corp., 415 F.3d 1303, 1318 (Fed.Cir.2005).

FN8. Adding to the possible numbers one could select, Dr. Kwan indicated that regulatory agencies use 5% as the allowable range for the active ingredient when approving pharmaceutical products for marketing. (Tr. (Kwan) at 101:20-102:11.)

Without evidence, either intrinsic or extrinsic, that would provide a basis for construing the numerical limits of the term "about 20 mM citric acid" in claim 19 of the '392 patent, the Court gives the word "about" its ordinary meaning of "approximately" and construes the claim term no further. *See* Biopolymer Eng'g Inc. v. Immunocorp., Nos. 05-536, 05-2972, 2007 U.S. Dist. LEXIS 94207, at *27-31, 2007 WL 4562592 (D.Minn. Dec. 21, 2007) (rejecting the defendant's application of general rounding principles and giving the word "about" its ordinary meaning of "approximately," resulting in the construction of the term "less than about one percent, by weight, protein" to mean "less than approximately one percent, by weight, protein").

CONCLUSION

Having held a claim construction hearing and reviewed the parties' briefs (Doc. Nos.74, 76, 82), the Court

hereby construes the term "about 20 mM citric acid" in claim 19 of the patent-in-suit as "approximately 20 mM citric acid."

IT IS SO ORDERED.

S.D.N.Y.,2008.
Unigene Laboratories, Inc. v. Apotex Inc.

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