IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ELAN PHARMA INTERNATIONAL LIMITED, Plaintiff, v. ABRAXIS BIOSCIENCE, INC., Defendant.	)	Case No. 06-438-GMS

PLAINTIFF ELAN PHARMA INTERNATIONAL LIMITED'S BRIEF IN SUPPORT OF MOTION FOR CLARIFICATION OF ORDER CONSTRUING THE TERMS OF U.S. PATENT NO. 5,834,025

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I. Introduction

Plaintiff Elan Pharma International Limited ("Elan") respectfully submits this brief in support of its concurrently-filed Motion For Clarification Of Order Construing The Terms Of U.S. Patent No. 5,834,025 (the "Motion"). Elan files the Motion to request clarification regarding one unclear aspect in the Court's Order Construing The Claims Of U.S. Patent Nos. 5,399,363 and 5,384,025 (the "Order"), issued on August 17, 2007 in this matter. Specifically, Elan is uncertain as to the specific meaning the Court ascribed to one of the claim terms of U.S. Patent No. 5,834,025. Concerned that its own uncertainty might be shared by a jury at a trial of this matter, Elan seeks clarification of the Court's Order so as to avoid any future confusion.

II. Nature And Stage Of Proceedings

On July 19, 2006, Plaintiff Elan Pharma International Limited ("Elan") filed suit alleging that Abraxis BioScience, Inc. ("Abraxis") infringes U.S. Patent Nos. 5,399,363 (the "'363 Patent") and 5,834,025 (the "'025 Patent") (collectively, the "Patents-In-Suit"). Elan's '363 Patent is directed to a nanoparticulate anticancer drug composition; and Elan's '025 Patent is directed to an intravenous method of administering a nanoparticulate drug composition so as to avoid eliciting adverse hemodynamic effects. The accused product, Abraxane®, is a nanoparticulate anticancer drug composition, which is intravenously administered.

On July 24, 2007, the parties presented their respective positions regarding the construction of certain claim terms in the Patents-In-Suit; and, on August 17, 2007, the Court issued its Order construing the contested claims. *See* D.I. 271, Order Construing The Terms Of U.S. Patent Nos. 5,399,363 and 5,834,025, August 17, 2007. Among other terms, the Court construed the claim term "at an infusion rate not exceeding 10 mg/min," which appears in independent claims 1 and 13 of the '025 Patent. The Order states that: "The term 'at an infusion

rate not exceeding 10 mg/min' is construed to mean 'intravenously administering the composition at a rate not exceeding 10 milligrams per minute.'" D.I. 271 at ¶ 9. Elan seeks clarification and amplification as to what specifically the "mg" in "10 mg/min" refers to, as employed in the Court's construction, so as to avoid there being any ambiguity or scientifically-inconsistent understanding of this term.

III. Summary Of Argument And Relief Requested

Motions for clarification are properly granted when there has been a misapprehension of law or fact. Elan thus seeks clarification as to what the "mg" in 10 mg/min refers to as employed by the Court in its construction of the '025 Patent claim term "at an infusion rate not exceeding 10 mg/min." In a footnote, the Court made clear that "composition" refers to a "nanoparticulate drug composition," which includes more than the nanoparticles alone. What is less clear is whether the "mg" in the Court's construction refers to: (a) the "nanoparticulate drug composition;" (b) only the active pharmaceutical ingredient, i.e. the nanoparticulate drug compound; or (c) the stabilized nanoparticles, i.e. the drug and the surface modifier. Elan believes, and Abraxis's own documentation as well as prevailing scientific understanding establish, that this ambiguity needs to be resolved.

Specifically, it should be clear that the term "mg" is most reasonably understood in context as including only the active pharmaceutical ingredient. Saline or sterile water dilutants are not pharmaceutically active, and their mass would not be relevant to administration of effective quantities of active drugs.

Abraxis's own product documentation shows, and the scientific record confirms, that those skilled in the art would unequivocally recognize that a measure expressed in units of mass (i.e. milligrams) as used in an infusion rate must refer to the active pharmaceutical ingredient alone, and exclude dilutants or carriers. Indeed, the directions accompanying every

pharmaceutical product of which Elan is aware refer to infusion rate in terms of the weight or mass of the active pharmaceutical ingredient to be administered over time. For example, the package insert for the accused product, Abraxane® provides that it is to be administered at a rate of 260mg/m^2 over a 30 minute period. *See* Exh. 1[1] at 17. The insert expressly states that the "mg/m^{2}" refers to the active pharmaceutical ingredient, paclitaxel. Indeed, the United States Food And Drug Administration ("FDA") requires that infusion rates be provided in terms of the weight and mass of the active pharmaceutical ingredients on any pharmaceutical labeling. *See* 21 C.F.R. § 201.57(j).

Elan thus understands the Court's use of the term "nanoparticulate drug composition" in its construction of the '025 Patent claim term "at an infusion rate not exceeding 10 mg/min" to refer to the mass of active pharmaceutical ingredient infused, and to exclude the mass of inert dilutant in which the nanoparticles, i.e. active pharmaceutical agent and surface modifier are carried. To avoid any potential future confusion, however, Elan respectfully requests that the Court confirm that Elan's understanding of the Order is correct.

IV. Statement Of Facts

On July 24, 2007, the parties appeared before the Court to present their respective interpretations of contested claim terms in the '363 and '025 Patents. With regard to the '025 Patent, Elan argued that the term "at an infusion rate not exceeding 10 mg/min" referred to the rate at which the nanoparticles are infused into a subject. Abraxis, on the other hand, urged that the term referred to the infusion of the nanoparticulate composition including (a) the drug, (b) surface modifier, and (c) the liquid carrier in which it was diluted.

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[1] Citations herein to "Exh. ___" refer to the respective Exhibits of the Declaration Of Lisa A. Chiarini, submitted concurrently herewith in support of the Motion.

On August 17, 2007, the Court issued its Order construing the contested claims of the Patents-In-Suit, including the following:

> "[A]t an infusion rate not exceeding 10 mg/min" is construed to mean "intravenously administering the composition at a rate not exceeding 10 milligrams per minute."

D.I. 271 at ¶ 9.

In a footnote to its construction, the Court commented that:

> In making its ruling, the Court concludes that the plain meaning of the claim states that it is the nanoparticulate drug composition that is administered, not only the nanoparticles.

Id. at n.9.

Elan understands that not only the nanoparticles are administered to a patient and further that the "nanoparticulate drug composition," i.e. the active pharmaceutical agent and the adhered surface modifiers, suspended in a liquid carrier are administered. Elan further understands that although the entire nanoparticulate composition is administered to a patient, the 10 mg/min parameter refers to the amount of the active pharmaceutical agent, or drug, that is infused during that administration. To avoid any confusion, and to ensure that the Court's construction of the term "at an infusion rate not exceeding 10 mg/min" is properly honored, Elan seeks clarification of the Order on this issue alone.

V. Argument and Authorities

A. Elan Seeks Clarification To Avoid Potential Future Confusion

Motions for clarification and/or reconsideration are "the 'functional equivalent' of a Rule 59(e) motion to alter or amend a judgment." *See Jones v. Pittsburgh Nat'l Corp.*, 899 F.2d 1350, 1352 (3d Cir. 1990) (citing *Federal Kemper Ins. Co. v. Rauscher*, 807 F.2d 345, 348 (3d Cir. 1986)). The purpose of such motions "is to correct manifest errors of law or fact or to present newly discovered evidence." *Max's Seafood Cafe ex rel Lou-Ann, Inc. v. Quinteros*, 176

F.3d 669, 677 (3d Cir. 1999). Accordingly, a court may alter or amend its judgment if the movant demonstrates at least one of the following:: (1) a change in the controlling law; (2) the availability of new evidence; or (3) a need to correct a clear error of law or fact or to prevent manifest injustice. *See Glendon Energy Co. v. Borough of Glendon*, 836 F. Supp. 1109, 1122 (E.D. Pa. 1993).

Reconsideration may be appropriate when "the Court has patently misunderstood a party, or has made a decision outside the adversarial issues presented to the Court by the parties, or has made an error not of reasoning but of apprehension." *Brambles USA, Inc. v. Blocker*, 735 F. Supp. 1239, 1241 (D. Del. 1990). In the context of a patent claim construction, any definition of a claim term that would controvert or create ambiguity vis à vis "the ordinary and customary meaning of a claim term," which "is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application," would be ripe for clarification so as to ensure compliance with the governing law as to the proper sources for and conducting of claim construction. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (*en banc*).

Elan does not contend that there has been a change in controlling law or that new and compelling evidence has recently become available, either of which would support a motion for reconsideration. Nor does Elan believe that the Order is erroneous as such. Rather, Elan understands the Court's construction of the '025 Patent claim term "at an infusion rate not exceeding 10 mg/min" to mean that although the nanoparticulate drug composition is administered to a patent, the "mg" refers to only the mass of active pharmaceutical ingredient that is infused in a given time period, and desires that its understanding be confirmed.[2] Absent

[2] Elan could ignore this issue for the moment and make the tactical decision simply to argue its clarified interpretation of "at an infusion rate not exceeding 10 mg/min" to a jury. However, taking such a position would

confirmation of this open-ended and possibly ambiguous point in the Order, confusion could develop and the parties could waste time and effort attempting to resolve the ambiguity, such that the lack of clarification or completeness in the definition would serve as effectively a significant error by omission.

B. One Skilled In The Art Would Recognize That Infusion Rates Refer To The Weight Or Mass Of The Active Pharmaceutical Ingredient Only.

In construing the term "at an infusion rate not exceeding 10 mg/min," the Court noted that the claim term refers to the "nanoparticulate drug composition that is administered, not only the nanoparticles." D.I. 271 at n.9. One of ordinary skill in the art would interpret the phrase "10 mg/min" as referring only to the active pharmaceutical ingredient because it is well known that infusion rates refer only to the mass or weight of the active pharmaceutical ingredient (or drug) in a given formulation, and not to the carrier in which it is diluted.

Not all drugs can be administered in their pure form. Rather, some drugs have to be formulated with other non-therapeutic ingredients and/or carriers to permit their administration to patients. In any active pharmaceutical compound or drug, the therapeutic activity comes from the drug itself, not from the non-therapeutic ingredients. Therefore, the rate at which formulated drugs are administered is provided in terms of the weight or mass of the active pharmaceutical ingredient, without reference to the non-therapeutic dilutant in which it is carried.

As further support for the logic of this conclusion, it is well-known in science and the pharmaceutical industry that metric units of mass or weight (milligrams or mg) are typically used to measure the mass of solids (*e.g.*, a solid active pharmaceutical ingredient), but that when

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frustrate the very purpose of the *Markman* briefing process and *Markman* Order, which is to provide a comprehensive definition of claim terms as a meaning of law, such that the jury has clear guidance in applying the claim terms, does not struggle with ambiguous rival interpretations of the *Markman* Order, and is not bombarded by the parties with additional claim construction arguments.

a quantity of liquid (*e.g.*, a saline suspension of a drug) is to be characterized, metric units of volume (milliliters or ml) are in almost every instance what is used. This is the common-sense reason that no one speaks of buying a pound of cola, or a quart of sugar. And conversely, if one were to describe a quantity of an unknown substance in terms of pounds, or milligrams, no one would reasonably infer, on either a common sense or scientific basis, that he was making reference to a fluid suspension, or indeed to anything but a net quantity of solid substance.

In every example of instructions for administering a drug of which Elan is aware, the rate of administration is determined from the dose of the active pharmaceutical ingredient over the time of administration.

For example, the 2007 package insert to Abraxane® provides a prime example of how the rate of administration is determined from the dose of the active pharmaceutical ingredient over the time of administration. Abraxis itself recommends that Abraxane® be infused at a rate of 260mg/m^2 over 30 minutes. *See* Exh. 1, Abraxane® package insert at 17. In the package insert, Abraxis instructs that "[d]ose levels of mg/m2 refer to mg of paclitaxel in ABRAXANE." *See id.* at 2. Thus, the rate at which Abraxane® is administered is measured solely by the mass or weight of the active pharmaceutical ingredient, paclitaxel, and not by the mass or weight of an inert fluid carrier such as saline or sterile water (which would more readily be described in terms of fluid volume in milliliters). Abraxis can hardly gainsay an understanding of what "mg/min." means that comports exactly with Abraxis's own usage of this term in its instructions on how to administer its flagship drug, the accused product Abraxane®.

A person of ordinary skill in the art, such as a prescribing physician, would clearly share Abraxis's understanding that dosages and infusion rates are measured in terms of

milligrams of active pharmaceutical ingredient. Indeed, this understanding is mandated by Food and Drug Administration Rules for prescription drug labels.

> (iv) This section must also contain specific direction on dilution, preparation (including the strength of the final dosage solution, when prepared according to instructions, ***in terms of milligrams of active ingredient*** per milliliter of reconstituted solution, unless another measure of the strength is more appropriate), and administration of the dosage form, if needed (*e.g.*, the ***rate of administration of parenteral drug in milligrams per minute***; storage conditions for stability of the reconstituted drug, when important; essential information on drug incompatibilities if the drug is mixed in vitro with other drugs or diluents; and the following verbatim statement for parenterals: "Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.")

21 C.F.R. § 201.57(j) (2007) (emphasis supplied).

Further confirmation that those of skill in the pharmaceutical industry apply just such an understanding of "mg/min." comes from, for instance, the package insert for the anti-fungal drug AmBisome®, which instructs that 3-5 milligrams of the active pharmaceutical ingredient, amphotericin B, may be administered per each kilogram of body weight, each day, for the treatment of systemic fungal infections. *See e.g.,* Exh. 2, AmBisome® package insert, Dosage and Administration at 26. The package insert instructs how to reconstitute 50 milligrams of amphotericin B with 12 milliliters of sterile water to yield a preparation that contains 4 milligrams of amphotericin B per milliliter, which would be the midrange dose of AmBisome recommended to treat a fungal infection. *See id.*

Another good example of this concept comes from considering a tablet form of a drug, which is prepared, prescribed, and dispensed to the patient based on the mass or weight of active pharmaceutical ingredient in the tablet. For example, aspirin tablets come in stated strengths of 81 mg and 325 mg of aspirin, yet the total tablet weight in each case may be in

excess of 500 mg. The tablets are prescribed and dispensed based on the aspirin content, not the total tablet weight including excipients or carriers.

Thus, Elan understands the Court's construction to mean that the nanoparticulate composition is administered to a patient, but the "mg" in "not exceeding 10 mg/min refers to the active pharmaceutical agent contained within the nanoparticulate composition.

VI. Conclusion

Accordingly, Elan respectfully requests that the Court clarify its construction of the term "at an infusion rate not exceeding 10 mg/min" by modifying the interpretive language in its Order to the following:

> "[A]t an infusion rate not exceeding 10 mg/min" is construed to mean "intravenously administering the nanoparticulate composition at a rate not exceeding 10 milligrams of active pharmaceutical agent per minute."

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