United States District Court
District of Massachusetts

MOMENTA PHARMACEUTICALS, INC., SANDOZ INC., Plaintiffs,	)	
v.	)	**Civil Action No. 11-11681-NMG**
AMPHASTAR PHARMACEUTICALS, INC., INTERNATIONAL MEDICATION SYSTEMS, LTD., WATSON PHARMACEUTICALS, INC., Defendants.	)	

MEMORANDUM & ORDER

GORTON, J.

Plaintiffs Momenta Pharmaceuticals, Inc. ("Momenta") and Sandoz Inc. (collectively, "the plaintiffs") bring suit against Amphastar Pharmaceuticals, Inc. ("Amphastar"), International Medication Systems, Ltd. ("IMS") and Watson Pharmaceuticals, Inc. ("Watson") (collectively, "the defendants") for patent infringement.

The plaintiffs have moved for a preliminary injunction to enjoin the defendants from launching their allegedly infringing product. This Court issued a temporary restraining order ("TRO") on October 7, 2011. It now considers plaintiffs' pending motion for a preliminary injunction.

I. Factual Background

In July, 2010, plaintiffs began to market the first generic enoxaparin sodium product in the United States. Enoxaparin is an anticoagulant used to prevent blood clots in the legs and other parts of the body. It is a kind of low molecular weight heparin ("LMWH") manufactured by cleaving raw heparin, which consists of sugar chains (saccharides) of various lengths and composition, into smaller sugar chains. Heparin is also an anticoagulent, but the therapeutic effects of LWMH are more lasting and predictable than heparin.

To obtain approval from the United States Food and Drug Administration ("FDA") to market its generic enoxaparin product, Momenta submitted an Abbreviated New Drug Application ("ANDA") to the FDA. In an ANDA, a manufacturer must show that its generic drug includes the same active ingredients as, and is bioequivalent of, the drug it is copying.

In the case of enoxaparin, that showing is particularly challenging due to the biochemical complexities of the product. Generic enoxaparin sodium must have the same active ingredient as Lovenox, its brand-name counterpart. Unlike most traditional drugs that have relatively simple chemical structures that are easily characterized, it is much more difficult to demonstrate the "sameness" of a generic enoxaparin product. Given those complexities, Sanofi-Aventis, the manufacturer of Lovenox,

submitted a Citizen Petition to the FDA requesting that the FDA withhold approval of any ANDA for a generic version of the drug until enoxaparin had been fully characterized unless the applicant was able to demonstrate 1) that its manufacturing process was the equivalent of Sanofi's own manufacturing process or 2) equivalent safety and effectiveness through clinical testing.

The FDA denied Sanofi's request but recognized the complicated scientific and regulatory issues attendant to approval of generic enoxaparin. It concluded that an ANDA applicant for enoxaparin can establish sameness by meeting five criteria: 1) the physical and chemical characteristics of enoxaparin, 2) the nature of the source material and the method used to break up the polysaccharide chains into smaller fragments, 3) the nature and arrangement of components that constitute enoxaparin, 4) certain laboratory measurements of anticoagulant activity and 5) certain aspects of the drug's effect in humans.

To satisfy the third criterion, Momenta developed a set of manufacturing control processes to ensure that each batch of its generic product included the individual sugar chains characteristic of enoxaparin. Momenta is the assignee of two patents which are directed to those processes, U.S. Patent No. 7,575,886 ("the '886 patent"), issued in August, 2009, and U.S.

Patent No. 7,790,466 ("the '466 patent"), issued in September, 2010. A particular batch of enoxaparin will not be finalized and approved for sale until those processes confirm that the batch contains a certain percentage of the unique sugars.

Plaintiffs filed the instant action two days after the FDA approved defendant Amphastar's ANDA for generic enoxaparin and Watson issued a press release announcing that the companies would launch the product in the fourth quarter of 2011 (which began October 1, 2011).

II. Procedural History

On September 21, 2011, the plaintiffs filed their complaint. After service of process was returned executed by all defendants, plaintiffs moved for a TRO and preliminary injunction to keep the defendants from launching their allegedly infringing product. Plaintiffs initially relied on publicly available information to allege that there is a strong likelihood that defendants' manufacturing process infringes the '466 and '886 patents. They also moved for limited, expedited discovery of documents pertaining to the defendants' ANDA.

After a hearing on October 7, 2011, the Court entered a TRO enjoining defendants from advertising, offering for sale or selling a generic enoxaparin product that allegedly infringes one or more of the patents issued to Momenta Pharmaceuticals, Inc. until the Court could conduct a preliminary injunction hearing on

October 20, 2011. Moreover, at the hearing itself, the Court instructed plaintiffs to submit a short memorandum that further narrowed their discovery request.

Five days after the TRO was entered, the defendants submitted an emergency motion to modify or dissolve it.[1] The Court denied that motion following a hearing on October 14, 2011. Also on that date, the Court allowed plaintiffs' request for limited, expedited discovery as modified in their supplemental memorandum. After obtaining such discovery, plaintiffs opted not to pursue their claim of infringement with respect to the '466 patent.

Before the Court is plaintiffs' motion for preliminary injunction based on alleged infringement of the '886 patent. The Court heard oral argument on the motion on October 20, 2011. The following day, it extended the TRO for seven additional days in order to review the issues in more depth. Extensive briefing has been submitted with respect to the motion, including an opposition, reply and sur-reply briefs and five-page supplemental memoranda submitted by each side on a discrete claim construction issue.

[1] Defendants also moved to dismiss or transfer the case. Plaintiffs have opposed the motion to dismiss and have filed an amended complaint which adds Watson Pharma, Inc., a subsidiary of Watson, as a defendant.

III. Analysis

A. Motion for Preliminary Injunction

The decision to allow or deny a preliminary injunction is a matter of discretion for the Court. LeBeau v. Spirito, 703 F.2d 639, 642 (1st Cir. 1983). To obtain injunctive relief, the plaintiffs bear the burden of demonstrating:

> 1) a substantial likelihood of success on the merits, 2) a significant risk of irreparable harm if the injunction is withheld, 3) a favorable balance of hardships and 4) a fit (or lack of friction) between the injunction and the public interest.

Nieves-Márquez v. Puerto Rico, 353 F.3d 108, 120 (1st Cir. 2003) (citation omitted). No individual factor is dispositive. Amazon.com, Inc. v. Barnesandnoble.com, Inc., 239 F.3d 1343, 1350 (Fed. Cir. 2001). Instead, the court "must weigh and measure each factor against the other factors and against the form and magnitude of the relief requested." Id.

1. Likelihood of success on the merits

To establish likelihood of success on the merits, a patentee must demonstrate that it will likely prove that its patent was infringed and is valid. See AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1050 (Fed. Cir. 2010) (citing Amazon.com, Inc. v. Barnesandnoble.com, Inc., 239 F.3d 1343, 1350-51 (Fed. Cir. 2001)). If an accused infringer raises a "substantial question" regarding infringement or validity that the patentee has not shown lacks "substantial merit", a preliminary injunction should

not issue. Id.

Defendants argue that plaintiffs have not demonstrated a likelihood of success on the merits because: 1) defendants do not infringe the '886 patent, 2) there are substantial questions as to the validity of that patent, 3) plaintiffs' claims are barred by the safe harbor provision of the Hatch-Waxman Act, 35 U.S.C. § 271(e)(1), and 4) there are serious questions regarding personal jurisdiction and venue (as raised in defendants' motion to dismiss). Each of these arguments will be considered in turn.

a. Infringement

Determining infringement requires the Court to conduct a two-step analysis 1) to determine the meaning and scope of the asserted patent claims and 2) to compare the properly construed claims to the process accused of infringing. Purdue Pharma L.P. v. Boehringer Ingelheim GMBH, 237 F.3d 1359, 1363 (Fed. Cir. 2001). At the preliminary injunction stage, a district court need not conclusively and finally interpret the claims at issue. See id. Its conclusions at this juncture are subject to change upon the ultimate trial on the merits. Id.

The patented methods in the '886 patent involve identification of a non-naturally occurring sugar that arises when enoxaparin is made. Specifically, the sugar arises when a sample is "exhaustively digested" (broken down into small sub-chains) by using two or more heparin-degrading enzymes. The

sugar includes a signature 1,6-anhydro ring structure that does not normally exist in heparin. A manufacturer of enoxaparin must be able to identify that structure and determine its quantity in a given sample to ensure that the sample is, in fact, enoxaparin that conforms to the requisite standards. A reference standard for enoxaparin is set by the U.S. Pharmacopia ("USP") Monograph and enforced by the FDA. It requires that between 15% and 25% of the sugar chains in a batch of enoxaparin include, at their reducing ends, a sugar containing the 1,6-anhydro ring structure.

Claims 6, 15 and 53 of the '886 patent describe how to analyze a sample of enoxaparin to ensure its conformity to the USP Monograph standard. The process involves, first, determining the presence and amount of a non-naturally occurring sugar in the batch and, second, comparing the amount of non-naturally occurring sugar in the sample to the USP Monograph reference standard. Claims 6, 15 and 53 include the following limitations: 1) providing an enoxaparin sample that has been exhaustively digested with two or more heparin degrading enzymes, 2) using a separation method to determine the presence of a structural signature associated with the non-naturally occurring sugar associated with peak 9 of Fig. 1, 3) making a determination about the enoxaparin sample by comparing the information gathered to the USP reference standard in order to 4) assess the quality of the sample (Claim 6), assess the level of non-naturally occurring

sugar in the sample (Claim 15) or select an appropriate batch (Claim 53).

Whether defendants infringe the second limitation of these claims is the essence of the parties' dispute. That alleged infringement, in turn, depends on how broadly the claim term "separation method" is construed. The parties agree that the ordinary meaning of the term to a person skilled in the art would include two separation techniques known as Capillary Electrophoresis ("CE") and High Pressure Liquid Chromatography ("HPLC"), among others. Plaintiffs contend the ordinary meaning should control, whereas defendants contend that the context of the patent makes clear that the term has a more limited meaning and refers only to CE.

The construction of the term is crucial to the infringement issue because defendants' testing process uses HPLC but otherwise performs all the steps of the disputed claims. The parties agree that if the separation method in claims 6, 15 and 53 does not cover HPLC, there is no infringement of the '886 patent by the defendants. Thus, the Court will proceed to construe the term conditionally, mindful that a construction at this preliminary stage is subject to revision later in the litigation. See Jack Guttman, Inc. v. Kopykake Enters., Inc., 302 F.3d 1352, 1361 (Fed. Cir. 2002).

For the reasons stated below, the Court concludes that "a

separation method" includes both CE and HPLC and that defendants have failed to raise a substantial question regarding the validity of the '886 patent. Thus, the plaintiffs have succeeded in showing a likelihood of success on the merits.

i. Principles of Claim Construction

Claim construction is a question of law for the court. Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1997) (en banc), aff'd, 517 U.S. 370 (1996). The objective of claim construction is to ascertain the meaning that a person of ordinary skill in the art would give to the terms in dispute at the time of the filing of the patent application. Wiener v. NEC Elec., Inc., 102 F.3d 534, 539 (Fed. Cir. 1996) (abrogated on other grounds). The meaning of the terms are initially discerned from three sources of intrinsic evidence: (1) the claims themselves, (2) the specification and (3) the prosecution history of the patent. See Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582-83 (Fed. Cir. 1996). If the intrinsic evidence is inadequate to resolve the meaning of a disputed term, the Court should consider extrinsic evidence such as inventor and expert testimony, treatises and technical writings. Phillips v. AWK Corp., 415 F.3d 1303, 1314 (Fed. Cir. 2005) (en banc).

The patent claims themselves define the scope of the patented invention. See Philips, 415 F.3d at 1312 ("It is a bedrock principle of patent law that the claims of a patent

define the invention to which the patentee is entitled the right to exclude." (internal quotation omitted)). Claim terms are generally given their "ordinary and customary meaning", which is the meaning that a person skilled in the art would attribute to the claim term. See id. at 1312-13. Even if a particular term has an ordinary and customary meaning, however, a court may need to examine the patent as a whole to determine if that meaning controls. Id. at 1313 ("[A] person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification."); see also Medrad, Inc. v. MRI Devices Corp., 401 F.3d 1313, 1319 (Fed. Cir. 2005) (noting that a court cannot construe the ordinary meaning of a term "in a vacuum"). Ultimately, the correct construction will be one that "stays true to the claim language and most naturally aligns with the patent's description of the invention ...." Id. at 1316 (citation omitted).

ii. "Separation Method"

As an initial matter, the Court notes that the "separation method" in each of Claims 6, 15 and 53 is

> to determine ... the presence of a structural signature associated with the non-naturally occurring sugar associated with peak 9 of FIG. 1.

Figure 1 is a CE electropherogram of an enoxaparin sample. Its various peaks correspond to different structures of the sample.

The unique 1,6-anhydro ring structure is what the method is intended to detect. The patent does not explicitly identify that structure because it was unknown at the time the patent application was filed. Instead, the patent identifies that structure by its association with peak 9 of Fig. 1.

According to the defendants, the claims are limited, by their own terms, to a CE separation method due to the "associated with peak 9 of Fig. 1" limitation. Defendants contend that identifying and separating a sugar that is only known by its association with peak 9 requires literal reproduction of figure 1, which was generated via CE. An HPLC chromatogram of enoxaparin, they contend, would not yield peak 9. One skilled in the art thus could not necessarily verify that a sugar associated with a particular HPLC peak was the same as the sugar associated with peak 9 of figure 1.

The Court finds defendants' arguments unpersuasive. The manner in which the patent identifies the pertinent structural signature does not limit the term "separation method" to CE. A person skilled in the art would understand that the structural signature is "associated" with peak 9 insofar as the peak indicates the structure is present. That relationship is the focus of the description, not the method of analysis that was used to arrive at peak 9. A person skilled in the art would understand that he or she could detect a similar anomolous peak

by a parallel analysis using a different but similar separation technique such as HPLC, a technique that is in fact discussed in the patent.

The Court agrees with plaintiffs that the doctrine of claim construction undermines defendants' contention that the term should be construed more narrowly than its ordinary meaning would suggest. Under that doctrine, there is a rebuttable presumption that different claims in a patent are different in scope. See Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1326 (Fed. Cir. 2003). When analyzing independent and dependent claims, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." Enzo Biochem, Inc. v. Applera Corp., 599 F.3d 1325, 1342 (Fed. Cir. 2010) (internal citation omitted); see also Sunrace Roots Enter. Co. v. SRAM Corp., 336 F.3d 1298, 1303 (Fed. Cir. 2003). That presumption is especially strong "where the limitation that is sought to be 'read into' an independent claim already appears in a dependent claim." Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 910 (Fed. Cir. 2004).

Plaintiffs state that claims 54 and 56, both of which depend on claim 6, require the use of HPLC and CE, respectively, to

determine the presence of the claimed structural signature.[2] Given the presumption that a dependent claim is narrower than the claim upon which it depends, they argue that CE is merely a sub-category of the claimed separation method. Plaintiffs add that limiting "a separation method" to CE would render claim 56 superfluous and redundant. See Manchak v. Chem. Waste Mgmt., Inc., No. 98-cv-1530, 1999 WL 1103364, at *4 (Fed. Cir. Dec. 6, 1999) ("Under the doctrine of claim differentiation, a claim should not ordinarily be construed in such a manner that would render a related dependent claim superfluous.").

As defendants point out, however, there appears to be some inconsistency between the meaning of the term "is determined" in the dependent claims and the term "to determine" in the independent claims. In dependent claims 54, 56 and 59, the structural signature "is determined" using a separation technique. In dependent claims 55, 57, 58 and 60, however, the structural signature "is determined" through NMR or other mass spectrometry techniques which are not separation methods. Those

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[2] Those claims are as follows:

> 54. The method of claims 1, 3, 6, 7, 8, 10, 11, 14, 20 or 43, wherein the structural signature is determined using ... [HPLC].
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> ...
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> 56. The method of claims 1, 3, 6, 7, 8, 10, 11, 14, 15, 20, 43, 49 or 53, wherein the structural signature is determined using CE.

'886 patent, 70:30-32 and 36-38.

techniques could be used to analyze a structural signature only in an already-separated sample and are described in the specification as techniques that may be used in combination with a separation technique to derive additional structural information or to corroborate findings with respect to the structural signature. See, e.g., '886 patent, 7:55-60; 34:5-14; 47:62-65.

Despite the inconsistency, the Court finds that a person skilled in the art would understand that dependent claims 54, 56 and 59 provide specific examples of technology that may be used to perform the "separation method" in the independent claims upon which they depend. The use of the word "wherein" in the dependent claims indicates that they are further qualifications of "a separation method" rather than different or additional steps. Syntactically, the specific techniques claimed could only refer back to the phrase "using a separation method to determine ... the presence of a structural signature ...." If the techniques in dependent claims 55, 57, 58 and 60 cannot, in fact, function as a "separate method," those claims may be invalid on their own terms.

Defendants further contend that their proposed limited construction aligns with the patent's written description which not only states that CE is the method of a preferred embodiment but repeatedly distinguishes CE as a superior separation method

to HPLC. See, e.g., '886 patent, 4:32-48 (stating that HPLC is often insufficient for analyzing heparins); 33:53-34:24 (listing several reasons why CE is superior to HPLC in oligosaccharide analysis); 47:40-48:9 (stating that HPLC is often insufficient for analyzing heparins and discussing advantages of CE). On the basis of plaintiffs' expressed preference, defendants argue that the Court should construe the patented separation method to exclude HPLC. See Phillips, 415 F.3d at 1316 ("[T]he specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor.").

The Court is not convinced that the language in the specification amounts to a disclaimer of HPLC as a separation method. The ordinary meaning of "a separation method" includes HPLC and the patentee specifically claims HPLC as a separation method in dependent claim 54. Although the discussion in the specification of HPLC vis-á-vis CE makes clear that CE is the preferred separation method, there is no assertion that HPLC cannot be used to perform the claimed methods. On the contrary, a preferred embodiment includes use of that method to determine the structural signature. See '886 patent, 7:55-67. The written description, therefore, neither limits the scope of the claims as defendants suggest nor amounts to an express disclaimer of HPLC. See Epistar Corp. v. Int'l Trade Comm'n, 566 F.3d 1321, 1335-36 (Fed. Cir. 2009) ("[A] discussion of the shortcomings of certain

techniques is not a disavowal of the use of those techniques in a manner consistent with the claimed invention.").

Finally, defendants argue that the plaintiffs are estopped from claiming that a "separation method" includes HPLC due to the prosecution history of the patent. Defendants contend that the addition of the "associated with peak 9 of FIG 1" limitation was included to overcome the examiner's rejection of the claim on the grounds of the Linhardt et al. ("Linhardt") prior art, which disclosed HPLC, but not the Desai et al. ("Desai") prior art, which disclosed CE.

That argument is tenuous, at best, and is not compelling. The PTO did not discuss its decision to withdraw its rejection based upon the Linhardt reference. Rather, it stated that plaintiffs' arguments regarding its rejection based on that reference had been considered but were moot in light of new grounds of rejection. Plaintiffs' arguments had focused on how the prior art, including Linhardt, did not suggest the very existence of the non-naturally occurring sugar associated with peak 9 that the various analytical methods should look for in a given enoxaparin sample. At no point did plaintiffs claim that the patent was limited to a single separation method or that it did not use HPLC as claimed in Linhardt.

At this juncture, therefore, the Court concludes that "a separation method" includes both HPLC and CE. Because

defendants' testing process uses HPLC and otherwise performs all the steps of the disputed claims, the plaintiffs have established a likelihood of infringement.

b. Validity

Defendants have alleged that the two patents-in-suit are invalid for obviousness and indefiniteness. At the preliminary injunction stage, the Court need not resolve the validity question but rather must assess "the persuasiveness of the challenger's evidence, recognizing that it is doing so without all evidence that may come out at trial." See Titan Tire Corp. v. Case New Holland, Inc., 566 F.3d 1372, 1376 (Fed. Cir. 2009). If the alleged infringer successfully raises a "substantial question" regarding a patent's validity, the patentee must persuade the court that, despite the challenge presented to validity, it is nevertheless likely to succeed at trial on the validity issue. Id.

i. Obviousness

An invention is invalid for obviousness under 35 U.S.C. § 103(a)

> if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art ....

To assess whether an invention is obvious, a court must consider: (1) the scope and content of the prior art, (2) the differences

between the prior art and the claims at issue, (3) the level of ordinary skill in the art and (4) any relevant secondary considerations, including commercial success, long felt but unsolved needs and the failure of others to invent. Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966).

Defendants assert that Claims 6, 15 and 53 of the '886 patent are invalid as obvious on the basis of two prior art references, Desai et al. (1993) and Sasisekharan et al. (1990), both of which were considered by the patent examiner during prosecution. The examiner initially rejected Claim 331, which encompassed most of Claims 6, 15 and 53, as anticipated and obvious in light of those references. That rejection was eventually overcome when plaintiffs added certain limitations directed at the practical uses of their invention taught by the patent, including: determining the quality of the sample (Claim 6), determining the level of non-naturally occurring sugar in the sample (Claim 15) and selecting an appropriate batch (Claim 53). Defendants contend that those added limitations would have been obvious to a person skilled in the art because, as enoxaparin is an FDA controlled drug, anyone skilled in the art would know to use such standard tests for quality-control purposes.

Defendants' arguments are largely conclusory and fail to raise a substantial question relative to validity. The Court notes that the burden of showing invalidity is "especially

difficult" when "the infringer attempts to rely on prior art that was before the patent examiner during prosecution." Glaxo Grp. Ltd. v. Apotex, Inc., 376 F.3d 1339, 1348 (Fed. Cir. 2004). As discussed previously, the plaintiffs overcame many of the examiner's objections by emphasizing that the prior art did not disclose identifying the presence of a non-naturally occurring sugar characteristic of enoxaparin that is not found in raw heparin or other LMWHs. Furthermore, the prior art did not suggest incorporating use of the final limitations of each claim which are directed to use of the methods in a manufacturing process. Indeed, at the time the patent application was filed in 2003, no standard analytical test was in place. Defendants' evidence of obviousness is therefore insufficient to contradict the findings of the examiner.

ii. Indefiniteness

Defendants also argue that the claims are invalid for indefiniteness. A claim is definite if one skilled in the art would understand the bounds of the claim when read in light of the specification. See 35 U.S.C. § 112. A claim is indefinite if a claim is "insolubly ambiguous" such that "reasonable efforts at claim construction prove futile." Exxon Research & Eng'g Co. v. United States, 265 F.3d 1371, 1375 (Fed. Cir. 2010). On the other hand,

> Even if it is a formidable task to understand a claim, and the result not unanimously accepted, as long as the

> boundaries of a claim may be understood it is sufficiently clear to avoid invalidity for indefiniteness.

Invitogen Corp. v. Biocrest Mfg., L.P., 424 F.3d 1374, 1383 (Fed. Cir. 2005) (internal quotation omitted).

Defendants' arguments of indefiniteness echo their claim construction arguments which the Court has already rejected. In defendants' view, the disputed claims are indefinite because, although each includes the limitation "a non-naturally occurring sugar associated with peak 9 of FIG 1", the patent nowhere specifies how to reproduce Fig. 1. The defendants add that if, as plaintiffs contend, the claims are broad enough to cover an HPLC separation method, they are "hopelessly indefinite" because Fig. 1 is a CE, not an HPLC, spectrograph.

As stated previously, one skilled in the art would understand the scope of the relevant claim limitation. He or she would understand that the sugar associated with peak 9 of Figure 1 corresponds to a different anomolous peak in a graph generated under a parallel analysis, whether that graph was generated by CE or a different but similar separation method such as HPLC (a method discussed in the patent and the prior art). See generally '886 patent, 6:57-10:27; see also Epistar Corp. v. Int'l Trade Comm'n, 566 F.3d 1321, 1336 (Fed. Cir. 2009) ("[A]n applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention."). Furthermore, the specification, and the prior art references incorporated

therein, provide sufficient instruction on how to reproduce the specific CE test that resulted in Figure 1 of the patent. See '886 patent, 27:26-31; 33:9-17; 47:54-65; 48:50-49:20; 62:47-60. Thus, defendants have failed to raise a substantial question that the patent is invalid for indefiniteness.

c. Safe Harbor Provision of Hatch-Waxman

Defendants contend that, even if they were deemed to infringe the '886 patent, their allegedly infringing activity falls squarely within the safe harbor provision of the Hatch-Waxman Act, 35 U.S.C. § 271(e)(1). That provision provides:

> It shall not be an act of infringement to make, use, offer to sell or sell ... a patented invention ... solely for uses reasonably related to the development and submission of information under a federal law which regulates the manufacture, use or sale of drugs ....

35 U.S.C. § 271(e)(1).

The Supreme Court has held that the provision protects the use of patented inventions so long as the use is "reasonably related to the development and submission of any information" under the Federal Food, Drug, and Cosmetic Act. Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 201 (2005). The Court has stated that there is

> no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included.

Id.

Defendants contend that, if they did use Momenta's patented

testing methods, it would be 1) to meet FDA requirements and 2) to provide the FDA with documentation of after-market approval quality control testing. Compiling data to submit to the FDA using the claimed testing methods, they assert, would be reasonably related to developing and submitting information to the FDA and therefore not infringing under the safe harbor provision.

Defendants' argument is unavailing because, although the safe harbor provision permits otherwise infringing activity that is conducted to obtain regulatory approval of a product, it does not permit a generic manufacturer to continue in that otherwise infringing activity after obtaining such approval:

> [T]he only activity which will be permitted by the [provision] is a limited amount of testing so that generic manufacturers can establish the bioequivalency of a generic substitute .... [T]he generic manufacturer is not permitted to market the patented drug during the life of the patent; all that the generic can do is test the drug for purposes of submitting data to the FDA for approval.

See Classen Immunotherapies, Inc. v. Biogen IDEC, 2011 WL 3835409, at *12-13 (Fed. Cir. Aug. 31, 2011) (quoting H.R. Rep. No. 98-857, at 8 (1984)).

Here, the alleged infringing activity involves use of plaintiffs' patented quality control testing methods on each commercial batch of enoxaparin that will be sold after FDA approval. Thus, it is not exempted under § 271(e)(1).

d. Jurisdictional issues

The jurisdictional questions that defendants' raise in their motion to dismiss are not so substantial as to affect the Court's analysis of the motion for a preliminary injunction. Defendants market their product to the national pharmaceutical market, and certain defendants have subsidiaries located in Massachusetts. It appears likely that the Court has either general or specific personal jurisdiction over defendants in this matter. The Court will entertain the defendants' jurisdictional arguments in more depth at a later time.

2. Irreparable Harm

A finding of irreparable harm is dependent upon whether a patent owner has an adequate remedy at law if a preliminary injunction is not granted. "[A] presumption of irreparable harm arises when a patentee makes a clear showing that a patent is valid and that it is infringed." High Tech Med. Instrumentation, Inc. v. New Image Indus., Inc., 49 F.3d 1551, 1556 (Fed. Cir. 1995). Absent such a showing, however, that presumption is unavailable and a patent holder must offer specific evidence of irreparable harm. See id.

In view of plaintiffs' showing of infringement and validity, the Court applies the presumption of irreparable harm in this case. Even in the absence of such a showing, however, plaintiffs have submitted sufficient evidence to demonstrate that the

marketing of defendants' product will cause them immediate and long-term irreparable harm. That harm would likely involve price erosion, lost market share, loss of market capitalization, reputational injury and threats to both the funding of ongoing research development and the hiring and retention of critical scientific talent.

Sandoz currently markets the only generic enoxaparin. It competes for sales only with Sanofi-Aventis, the maker of the brand-name product, Lovenox. Plaintiffs contend that market entry by defendants would cause an immediate and significant reduction in the price Sandoz can charge for enoxaparin which, in turn, would permanently alter customers' price expectations. See Polymer Techs., Inc. v. Bridwell, 103 F.3d 970, 976 (Fed. Cir. 1996) ("Requiring purchasers to pay higher prices after years of paying lower prices to infringers is not a reliable business option.").

Plaintiffs add that under the plaintiffs' collaboration agreement, entry of a competing product into the market would mean that Momenta's royalty on the Sandoz profits from the sale of generic enoxaparin would be drastically reduced. The decline in prices and market share coupled with the contractual limitation would purportedly have a devastating impact on Momenta's revenues. That, in turn, would cripple Momenta's long-term ability to continue funding ongoing research efforts and to

retain or recruit top scientific talent.

Finally, plaintiffs contend that generic enoxaparin is Momenta's only product and the cornerstone of its success and reputation as an innovator. The harm that would ensue if defendant's product is introduced to the market is not, plaintiffs assert, merely speculative: just the announcement that the FDA had approved Amphastar's generic enoxaparin ANDA apparently caused Momenta's stock price to decline by more than 30%. Plaintiffs allege that the investment community reacted by downgrading its analysis of Momenta and questioning the inherent value of its core technology. Defendant's launch, they contend, would place further pressure on Momenta's stock price and further damage Momenta's standing in the investment community.

Defendants respond that plaintiffs' harms are entirely calculable and compensable by money damages. They contend that plaintiffs' own pleadings demonstrate that the losses are quantifiable, even if somewhat difficult to measure, insofar as plaintiffs calculate the impact on company revenues of 1) stock price decline, 2) lost royalties and 3) loss of market share. They further contend that inability to reinvest profits in research and development is not irreparable harm and cannot justify injunctive relief.

Although some of plaintiffs' potential for harm is quantifiable, its allegations of price erosion, reputational

injury and loss of goodwill likely are not. Defendants have failed to rebut the presumption of irreparable harm and plaintiffs have demonstrated the sort of market loss and reputational harm that constitute evidence of irreparable harm. See, e.g., Abbott Labs. v. Sandoz, Inc., 544 F.3d 1341, 1361-62 (Fed. Cir. 2008) (likelihood of market share and revenue loss upon competitor's entry into market supported finding of irreparable harm); Glaxo Grp., 64 Fed. Appx. at 756 (likelihood that generic entry "would affect not only price and profit but also cause a significant loss in market share" supported finding of irreparable harm); Bio-Tech. Gen. Corp. v. Genentech, Inc., 80 F.3d 1553, 1566 (Fed. Cir. 1996) (likelihood of loss of revenue, goodwill, and research and development activity upon competitor's entry into market supported finding of irreparable harm). But see Eli Lilly & Co. v. American Cyanamid Co., 82 F.3d 1568, 1578-79 (Fed. Cir. 1996) (finding no irreparable harm where money damages was a sufficient remedy and "calculating lost profits would be a relatively simple task").

3. Balance of Hardships

To assess the balance of hardships, the Court must determine whether the threatened injury to the patent owner, in light of the strength of the showing of likelihood of success on the merits, outweighs the harm that a preliminary injunction may inflict on the accused infringer. Holmes Prods. Corp. v.

Catalina Lighting, Inc., 67 F. Supp. 2d 10, 14 (D. Mass. 1999) (citing H.H. Robertson, Co. v. United Steel Deck, Inc., 820 F.2d 384, 390 (Fed. Cir. 1987)).

Plaintiffs have alleged that the defendants are large, multi-product companies that will face only monetary harm if enjoined. By contrast, plaintiffs assert that they are a single product company whose potential harm, as discussed above, is far broader and more serious.

Defendants counter that Amphastar and IMS are "far from being the large multi-product companies that plaintiffs disingenuously claim them to be." Enoxaparin is not one of a portfolio of many products but rather a product upon which Amphastar's success depends. They have invested heavily to develop and introduce this product to the marketplace, and "every penny of revenue is required to make the company secure and assure its future." The TRO alone purportedly cost the defendants millions of dollars in lost sales, lost contractual opportunities and reputational harm. In a market with three participants, defendants contend, a preliminary injunction would cost Amphastar an estimated average of $7 million per week.

Defendants add that each defendant's reputation is also at stake. Amphastar has allegedly already "fielded questions from potential customers" regarding its ability to supply enoxaparin in light of the instant lawsuit. Meanwhile, Watson's reputation

as "a consistent and timely supplier" in the pharmaceutical industry is in jeopardy.

Given plaintiffs' showing of likelihood of success on the merits, the balance of hardship tips in their favor. While defendants' harm appears almost entirely monetary (albeit, with very substantial sums at stake), plaintiffs face significant damage in the form of price erosion and loss of customer good-will, as noted above. Those kinds of harm cannot be fully compensated by money damages. See Glaxo Grp., 64 Fed. Appx. at 756 (finding balance of harms in patent holder's favor after comparing patentee's potential for lost patent value and generic competitor's inability to enter the market and begin earning profits). Defendants' loss of profits can be secured by the posting of a significant bond to protect defendants in the event the patent is later found to be invalid or otherwise not infringed.

4. Public Interest

Finally, the Court must consider whether the granting of a preliminary injunction will serve or disserve the public interest. Protecting rights secured by valid patents is an important public interest, Smith Int'l, Inc. v. Hughes Tool Co., 718 F.2d 1573, 1581 (Fed. Cir. 1983), but the focus of the Court's inquiry is whether "there exists some critical public interest that would be injured by the grant of preliminary

relief." Holmes Prods., 67 F. Supp. 2d at 14 (internal quotation and citation omitted).

Defendants cite the general public benefit of lower drug costs, particularly at a time of drug shortages and rising health care costs. That benefit does not, however, outweigh protection of plaintiffs' patent rights, in which they have invested talent, time and money. Abbott Labs., 544 F.3d at 1363 (patent law promotes significant public interest in drug development by offering inventors incentives "to risk the often enormous costs in terms of time, research, and development"). Granting preliminary injunctive relief in this matter will serve the public interest and will not unduly stifle competition.

ORDER

In accordance with the foregoing, plaintiffs' motion for preliminary injunction (Docket No. 18) is **ALLOWED**, and defendants are enjoined according to the terms of the Preliminary Injunction filed concurrently with this Order.

So ordered.

/s/ Nathaniel M. Gorton
Nathaniel M. Gorton
United States District Judge

Dated October 28, 2011