IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

**AMPHASTAR PHARMACEUTICALS, INC.**
**11570 Sixth Street**
**Rancho Cucamonga, California 91730**

**Plaintiff,**

**v.**

**FOOD AND DRUG ADMINISTRATION**
**10903 New Hampshire Avenue**
**Silver Spring, Maryland 20993;**

**MARGARET A. HAMBURG, M.D.**
**Commissioner of Food and Drugs**
**Food and Drug Administration**
**10903 New Hampshire Avenue**
**Silver Spring, Maryland 20993;**

**and**

**KATHLEEN SEBELIUS**
**Secretary of Health and Human Services**
**U.S. Department of Health and Human Services**
**200 Independence Avenue, S.W.**
**Washington, D.C. 20201**

**Defendants.**

Case: 1:10-cv-01800
Assigned To : Urbina, Ricardo M.
Assign. Date : 10/25/2010
Description: TRO/PI

## COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiff Amphastar Pharmaceuticals, Inc. ("Amphastar"), by and through undersigned counsel, brings this Complaint against the Food and Drug Administration ("FDA"); the Commissioner of Food and Drugs, Margaret A. Hamburg, M.D.; and the Secretary of Health and Human Services, Kathleen Sebelius. In support thereof, Amphastar avers and alleges as follows:

## NATURE OF THE ACTION

1. Amphastar brings this action for declaratory judgment and injunctive relief requiring the FDA to cease its unlawful detention of two shipments of raw materials, which will

be used for the development of starting materials, that will then be used for an Active Pharmaceutical Ingredient ("API") of a pending Abbreviated New Drug Application ("ANDA").

2. The FDA has never provided adequate justification for its continued detention of Amphastar's raw materials, but nonetheless continues to detain the materials, in contravention of applicable law and regulations.

3. The FDA lacks jurisdiction or other statutory or regulatory authority for its detainment of Amphastar's raw materials because the import of the raw materials is a transfer between wholly owned subsidiaries of the same parent company.

4. The FDA's actions against Amphastar are part of a broader pattern of arbitrary, capricious and vindictive behavior posing a serious threat to Amphastar's business. This pattern of behavior includes numerous unwarranted inspections apparently designed to harass Amphastar and persistent refusal to respond to written inquiries from Amphastar.

5. To prevent any further irreparable harm to Amphastar, the Court should declare the FDA's actions unlawful and enjoin the FDA from continuing to detain Amphastar's raw materials.

6. The relief Amphastar seeks would present no threat whatsoever to the drug consuming public because the materials involved are not part of any consumed drug. Amphastar merely seeks access to the raw materials required for scientific, process development, and regulatory qualification purposes.

## PARTIES

7. Plaintiff Amphastar is a corporation incorporated, organized and existing under the laws of the State of Delaware, with its principal place of business at 11570 Sixth Street, Rancho Cucamonga, California 91730.

8. Defendant FDA is an agency of the United States Government within the Department of Health and Human Services, with offices at 200 C Street, S.W., Washington, D.C. 20201, and 10903 New Hampshire Avenue, Silver Spring, Maryland 20993. The Secretary of Health and Human Services, the official responsible by law for administering the Federal Food, Drug, and Cosmetic Act ("FDCA"), has delegated to the FDA the authority to administer the relevant provisions of the FDCA.

9. Defendant Margaret A. Hamburg, M.D., is Commissioner of Food and Drugs and is the senior official of the FDA. She is sued in her official capacity. Dr. Hamburg maintains offices at 200 C Street, S.W., Washington, D.C. 20201, and 10903 New Hampshire Avenue, Silver Spring, Maryland 20993.

10. Defendant Kathleen Sebelius is Secretary of Health and Human Services and the official charged by law with administering the FDCA. She is sued in her official capacity. Secretary Sebelius maintains an office at 200 Independence Avenue, S.W., Washington D.C. 20201.

## JURISDICTION AND VENUE

11. This Court has jurisdiction pursuant to 5 U.S.C. § 706 and 28 U.S.C. §§ 1331, 1361, and 2201-2202.

12. There exists an actual and justiciable controversy between Amphastar and Defendants requiring resolution by this Court. Amphastar has no adequate remedy at law.

13. Venue is proper in this district pursuant to 28 U.S.C. § 1391(e).

## STATEMENT OF FACTS

### Background

14. Amphastar, established in 1996, is a specialty and generic pharmaceutical company focusing on injectable, inhalation, and other categories of pharmaceutical products and active pharmaceutical ingredients ("API").

15. International Medication Systems, Ltd. ("IMS") is a wholly-owned subsidiary of Amphastar Pharmaceuticals, Inc., located in South El Monte, California. IMS is a registered pharmaceutical manufacturer of sterile injectable drug product and API. Amphastar Nanjing Pharmaceuticals, Inc. ("ANP") is a wholly-owned subsidiary of Amphastar Pharmaceuticals, Inc., located in Nanjing, People's Republic of China. ANP produces raw materials for Amphastar products. ANP's production facility is registered with the FDA.

16. Amphastar applied for FDA approval to market Enoxaparin Sodium injection in March 2003. This application remains pending due to arbitrary and capricious actions by the FDA.

17. Heparin is the required starting material, as specified by the United States Pharmacopeia ("USP") for production of enoxaparin sodium API. The raw material that has been improperly detained for more than five months is "semi-purified heparin" produced by ANP. This raw material will not enter commerce or be used for human clinical studies. Rather, the material is critical for Amphastar to perform its proof of process development and validation studies necessary to qualify ANP with the FDA as a supplier of the raw material. The qualification documents will subsequently be filed with the FDA for its review and approval.

18. The semi-purified heparin at issue in this case is an intermediate raw material. Using this intermediate raw material, IMS can develop the process to produce Heparin USP and be qualified by Amphastar as one of its suppliers of Heparin USP. Heparin USP from IMS

would then be qualified as the starting material for the API of Amphastar's pending enoxaparin Abbreviated New Drug Application. The qualification documents will be filed with the FDA for its review and approval.

19. Heparin is an anticoagulant, which prevents the formation or growth of blood clots. It is used to treat several serious and potentially fatal conditions, including deep vein thrombosis, atrial fibrillation (abnormal heart beat), and acute coronary syndrome (decreased blood flow to the heart). It also plays an important role during heart surgery in facilitating cardiac bypass (a technique that maintains the circulation of blood and oxygen in the body).

20. On March 3, 2003, Amphastar was the first company to file an application for generic enoxaparin with the FDA.

21. The FDA's improper detention of raw materials needed to secure the company's supply chain, especially for this critical application, causes irreparable harm to Amphastar.

22. Abbreviated New Drug Application approval is required prior to the marketing and sale of generic pharmaceuticals in the United States.

23. Amphastar's enoxaparin Abbreviated New Drug Application remains pending despite reaching "sameness" (a prerequisite for FDA generic drug approval) on November 2, 2007; the FDA's improper detention of Amphastar's raw materials represents an obstacle, insurmountable without Court intervention, to Amphastar bringing an important product to the American public.

24. Amphastar's Abbreviated New Drug Application currently has named Qingdao Jiulong Biopharmaceuticals Co. Limited ("QJBC") as its starting material (Heparin USP) supplier.

25. Pharmaceutical companies like Amphastar (and, as Amphastar's subsidiary, IMS) regularly secure raw materials from multiple sources. In accordance with this practice, Amphastar established ANP in January 2009 as a wholly-owned subsidiary. ANP allows Amphstar to strengthen its supply chain and provides greater control over both quality and availability. In addition, shipping from ANP to IMS is completely within the same umbrella of corporate entities owned by Amphastar.

26. Amphastar seeks to bring the raw materials at issue in this case into the United States for process development so that Amphastar can document the submission package for the FDA regarding the qualification of IMS's Heparin USP (the starting material of enoxaparin API) using ANP's raw materials.

27. Unless it can complete the qualification of IMS's Heparin USP using ANP's raw materials, Amphastar cannot continue its normal business operations.

28. Enoxaparin is a cornerstone of Amphastar's pharmaceutical product pipeline.

**The FDA's Improper Detention of Amphastar's Raw Materials**

29. The FDA has improperly detained two shipments of raw materials, which Amphastar, through its subsidiary IMS, is attempting to import into the United States from its subsidiary ANP.

30. The FDA's unlawful detention of these shipments of raw materials has rendered them currently unusable by Amphastar.

31. The raw heparin (semi-purified heparin) in question is not intended for commercialization, or clinical studies, or any other type of human or animal consumption.

32. Instead, the semi-purified heparin from ANP is intended for – and necessary for – IMS to perform process development and regulatory qualification studies needed for Amphastar

to qualify with the FDA Heparin USP from Amphastar's subsidiary IMS, that is itself based on raw material from ANP. Amphastar has registered ANP with the FDA as the supplier of the raw material.

**Entry 1: No. E4K-0053715-4**

33. The first shipment of raw materials improperly detained by the FDA contained 2.44 kilograms of Semi-Purified Heparin Sodium (FDA Entry No. E4K-0053715-4) ("Entry 1"). Entry 1 arrived at Los Angeles International Airport from ANP on or about May 16, 2010, and was received at IMS on or about May 21, 2010.

34. Approximately 30 days after Entry 1 was conditionally released pursuant to 19 C.F.R. § 141.113(c), Amphastar commenced processing a portion of Entry 1 into heparin sodium USP in a process development experiment not intended for human or animal use.

35. On or about June 23, 2010, more than 30 days after Entry 1 was conditionally released pursuant to 19 C.F.R. § 141.113(c), Amphastar received notice of a pending review by the FDA.

36. On or about June 25, 2010, an FDA investigator arrived at IMS and sought to test a sample of the Semi-Purified Heparin Sodium. The FDA investigator did not present a copy of FDA Form 482, as required by 21 U.S.C. § 374.

37. Despite the FDA's failure to follow the statute and its own regulations, and although the FDA lacks jurisdiction over Entry 1, pursuant to 21 C.F.R. § 207.3(a)(5), Amphastar permitted a sample to be taken of the Semi-Purified Heparin Sodium that had not been processed into heparin sodium USP, while noting its objections to the FDA's action.

38. No contamination was found in the sample taken by the FDA.

39. On or about July 14, 2010, the FDA issued a Notice of FDA Action releasing Entry 1 to IMS.

40. On or about July 22, 2010, Amphastar's customs broker reported that an FDA Compliance Officer had telephoned him, stating that the July 14, 2010 Notice of FDA Action releasing Entry 1 had been issued in error.

41. On or about July 29, 2010, Amphastar received a Notice of FDA Action, dated July 26, 2010 notifying Amphastar that the release had been rescinded.

42. On or about August 5, 2010, Amphastar received notice that the FDA's investigation of Entry 1 had again been reopened and that Entry 1 had been detained due to "misbranding," in violation of FDCA §§ 502(o) and 801(a)(3). This time, the notice stated that "[t]he foreign manufacturer has not registered as required by section 510(i)(1)."

43. This statement was incorrect because ANP is, in fact, registered with the FDA.

44. On or about August 9, 2010, Amphastar received notice that the FDA's investigation of Entry 1 had been reopened and that Entry 1 had been detained due to "misbranding," in violation of FDCA §§ 502(f)(1) and 801(a)(3). The notice stated that "[t]he article appears to lack adequate directions for use, and the article does not appear to be exempt from such requirements."

45. FDCA § 502 applies to drugs, as defined in FDCA § 201(g)(1). Under that definition, the raw materials contained in the detained shipment are not drugs and therefore do not require "adequate directions for use."

46. Even if the raw material could be construed as a drug for the purposes of requiring "directions for use" in accordance with 21 C.F.R. § 201.5, the shipment would fall under 21 C.F.R. § 201.122, which exempts from the "adequate directions for use" requirement in

FDCA § 502(f)(1) a drug in a bulk package, except tablets, capsules, or other dosage unit forms, intended for processing, repacking, or use in the manufacture of another drug, provided certain labeling requirements are met.

47. Despite the FDA's lack of authority and failure to follow the statute and its own regulations, in a demonstration of good faith, Amphastar labeled its shipments with the statements required to qualify for the exemption under 21 C.F.R. § 201.122(c). Amphastar notified the FDA of this action on or about August 12, 2010.

48. The remaining, unprocessed portion of Entry 1 has been held in quarantine at IMS since July 22, 2010.

**Entry 2: No. E4K-0053980-4**

49. The second shipment of raw materials improperly detained by the FDA contained 46.5 kilograms of Semi-Purified Heparin Sodium (FDA Entry No. E4K-0053775-8) ("Entry 2"). Entry 2 arrived at Los Angeles International Airport from ANP on or about May 27, 2010 and was received at IMS on or about June 4, 2010.

50. On or about June 25, 2010, an FDA investigator arrived at IMS and sought to test a sample of the Semi-Purified Heparin Sodium. The FDA investigator did not present a copy of FDA Form 482, as required by 21 U.S.C. § 374.

51. Despite the FDA's failure to follow the statute and its own regulations, and although the FDA lacks jurisdiction over Entry 2, pursuant to 21 C.F.R. § 207.3(a)(5), Amphastar permitted documentary samples to be taken of Entry 2 while noting its objections.

52. The documentary samples taken included nuclear magnetic resonance testing results demonstrating that Entry 2 was free of oversulfated chondroitin sulfate (an indicator of contamination) and a certificate of analysis for Entry 2.

53. Following the FDA's collection of samples, Entry 2 remained in quarantine.

54. On or about June 29, 2010, an FDA investigator again arrived at IMS and again sought to test a sample of the Semi-Purified Heparin Sodium.

55. Despite the FDA's failure to follow the statute and its own regulations, and although the FDA lacks jurisdiction over Entry 2, pursuant to 21 C.F.R. § 207.3(a)(5), Amphastar permitted a sample to be taken of the Semi-Purified Heparin Sodium, again noting its objections to the FDA's action.

56. On or about July 14, 2010, the FDA issued a Notice of FDA Action releasing Entry 2 to IMS.

57. Following the July 14, 2010 release of Entry 2, Amphastar's subsidiary IMS processed two of the three lots of semi-purified heparin contained in Entry 2 into Heparin Sodium USP.

58. To date, no test results for the samples taken by the FDA have been provided to IMS or Amphastar.

59. On or about July 22, 2010, Amphastar's customs broker reported that an FDA Compliance Officer had telephoned him, stating that the July 14, 2010 Notice of FDA Action releasing Entry 2 had been issued in error.

60. On or about July 26, 2010, the FDA issued a Notice of FDA Action stating that the previous release of Entry 2 had been rescinded.

61. On or about August 5, 2010, Amphastar received notice that the FDA's investigation of Entry 2 had been reopened and that Entry 2 had been detained due to "misbranding," in violation of the FDCA §§ 502(o) and 801(a)(3). The notice stated that "[t]he foreign manufacturer has not registered as required by section 510(i)(1)."

62. This statement was incorrect because ANP is, in fact, registered with the FDA.

63. On or about August 9, 2010, Amphastar received notice that the FDA's investigation of Entry 2 had been reopened and that Entry 2 had been detained due to "misbranding," in violation of FDCA §§ 502(f)(1) and 801(a)(3). The notice stated that "[t]he article appears to lack adequate directions for use, and the article does not appear to be exempt from such requirements."

64. FDCA § 502 applies to drugs, as defined in FDCA § 201(g)(1). Under that definition, the raw materials contained in the detained shipment are not drugs and therefore do not require "adequate directions for use."

65. Even if the raw materials could be construed as a drug for the purposes of requiring "directions for use" in accordance with 21 C.F.R. § 201.5, the shipment would fall under 21 C.F.R. § 201.122, which exempts from the "adequate directions for use" requirement in FDCA § 502(f)(1) a drug in a bulk package, except tablets, capsules, or other dosage unit forms, intended for processing, repacking, or use in the manufacture of another drug, provided certain labeling requirements are met.

66. Despite the FDA's lack of authority and failure to follow the statute and its own regulations, in a demonstration of good faith, Amphastar labeled its shipments with the statements required to qualify for the exemption under 21 C.F.R. § 201.122(c). Amphastar notified the FDA of this action on August 12, 2010.

67. Both the remaining Heparin Sodium USP processed from Entry 2 and the unprocessed portion of Entry 2 have been held in quarantine at IMS since July 22, 2010.

68. On or about September 30, 2010, an FDA investigator arrived at IMS and took physical samples of the heparin sodium USP processed from Entry 2 and the remaining

unprocessed portion of Entry 2. The FDA investigator did not present a copy of FDA Form 482, as required by 21 U.S.C. § 374.

69. In an e-mail dated October 18, 2010, an FDA Compliance Officer denied Amphastar's request to meet with the FDA's District Director of Los Angeles. The FDA Compliance Officer claimed that the FDA's June 29, 2010 sample of Entry 2 was still being processed and that the testing would not be completed until November 17, 2010.

70. Upon information and belief, no other sample taken from Amphastar or its competitors has taken nearly five months to complete testing.

**Harm Suffered by Amphastar**

71. The FDA's actions with respect to Amphastar stand in stark contrast to the FDA's treatment of Amphastar's competitors, who regularly import raw materials from China, including raw heparin.

72. Without raw heparin, Amphastar cannot begin the qualification procedure for ANP as a supplier of raw material related enoxaparin.

73. Qualification of ANP is crucial in order to maintain Amphastar's economic viability.

74. Amphastar has repeatedly sought information from the FDA on the agency's detentions of Entries 1 and 2, but the FDA has provided only pretextual justifications for the detentions.

75. Amphastar, on multiple occasions, via letter and e-mail, has provided the FDA with written explanations of any claimed deficiencies in the labeling of the raw materials contained in Entries 1 and 2.

76. In addition, Amphastar has repeatedly sought to present its case orally to the FDA officials but has been denied the opportunity to do so. Since the detentions began, Amphastar has communicated with the FDA more than twenty times concerning this matter.

77. Upon information and belief, the FDA's claimed justification for refusing to grant Amphastar a hearing is without merit or basis in law or regulation and was created to further delay Amphastar's ability to conduct scientific testing necessary to its business.

78. The FDA's actions with respect to Amphastar reflect a broader pattern of arbitrary, capricious, and vindictive behavior against Amphastar by the FDA.

79. For example, between February 2008 and December 2009, the FDA – using what appeared to be only pretextual justifications – inspected Amphastar facilities approximately fifteen times within the span of ninety-four working days, using nineteen different FDA investigators, and without finding anything more than extremely minor deficiencies with Amphastar.

80. In addition, Amphastar has sent approximately forty letters to the FDA and has attempted in-person or telephonic engagement of FDA officials with respect to Amphastar's treatment by the FDA, but these efforts have been fruitless. Further efforts by Amphastar to resolve this dispute without Court intervention would be futile.

81. In light of the FDA's intransigence, Amphastar has concluded that seeking Court intervention is the Company's only recourse for relief from the FDA's improper actions.

82. Thus, Amphastar has exhausted any administrative remedies available to it. Alternatively, any additional pursuit of administrative relief from the FDA would be futile and would only result in further delay and harm to Amphastar.

## COUNT I

### Violation of the FDCA and Federal Regulations

83. The allegations set forth in the foregoing paragraphs are incorporated by reference as if fully set forth herein.

84. The FDA has demanded inspection of Amphastar's raw materials without statutory or regulatory authority to do so.

85. The FDA has refused to release Entries 1and 2 without evidence that the contents of those Entries violate the FDCA or applicable regulations.

86. The FDA has provided no adequate justification for its decision, despite repeated requests from Amphastar.

87. The FDA's decision refusing to release Entries 1 and 2 is arbitrary and capricious; an abuse of discretion; in excess of statutory jurisdiction, authority, or limitations, or short of statutory right; and not in accordance with the law.

88. Amphastar has been harmed and is experiencing harm directly and proximately caused by Defendants' failure to follow applicable statutes and regulations.

89. The FDA's unlawful conduct is ongoing and immediate. As a result of the FDA's conduct, Amphastar has been harmed and is being harmed. The FDA's actions make it impossible for Amphastar to complete its enoxaparin Abbreviated New Drug Application.

## COUNT II

### Violation of the Administrative Procedure Act

90. The allegations set forth in the foregoing paragraphs are incorporated by reference as if fully set forth herein.

91. The FDA has demanded inspection of Amphastar's raw materials without statutory or regulatory authority to do so.

92. The FDA has failed to follow the procedures required of it by statute and regulation for inspections, testing, and detention of regulated materials, as well as the procedures required for resolution of detention questions.

93. The FDA has refused to release Entries 1and 2 without evidence that the contents of those Entries violate the FDCA.

94. The FDA has provided no justification for its decision, despite repeated requests from Amphastar.

95. While refusing to release Amphastar's raw materials, the FDA has allowed Amphastar's competitors to import substantially identical materials without interference.

96. The FDA's decision refusing to release Entries 1and 2 is arbitrary, capricious, an abuse of discretion, not in accordance with the law, and in excess of statutory authority, and therefore violates 5 U.S.C. §§ 706(2)(A) and 706(2)(C).

97. Amphastar has been harmed and is experiencing harm directly and proximately caused by Defendants' failure to follow the law.

98. The FDA's unlawful conduct is ongoing and immediate. As a result of the FDA's conduct, Amphastar has been harmed and is being harmed. The FDA's actions make it impossible for Amphastar to complete its Abbreviated New Drug Application for enoxaparin.

## COUNT III

## Declaratory Judgment

99. The allegations set forth in the foregoing paragraphs are incorporated by reference as if fully set forth herein.

100. Defendants' actions are in violation of federal statute and regulations.

101. Amphastar is suffering harm due to Defendants' failure to follow the law.

102. The FDA's unlawful conduct is ongoing and immediate. As a result of the FDA's conduct, Amphastar has been directly and proximately harmed and is being harmed. The FDA's actions make it impossible for Amphastar to complete its enoxaparin Abbreviated New Drug Application.

103. Pursuant to 28 U.S.C. § 2201 *et seq.*, Amphastar respectfully requests that the Court: (a) declare the FDA's actions as set forth in this Complaint are contrary to federal law and regulations; (b) declare that the FDA has acted arbitrarily and capriciously in its application of federal law and regulations; (c) preliminarily and permanent enjoin the FDA from continuing to improperly detain Entries 1 and 2; and (d) enter judgment in favor of Amphastar.

## PRAYER FOR RELIEF

WHEREFORE, Amphastar requests that the Court enter judgment in its favor and against Defendants and award the following relief:

a. A temporary restraining order and/or a preliminary injunction, pending a decision on the merits, that enjoins Defendants from continuing to detain Entries 1 and 2;

b. A declaratory judgment that Defendants acted unlawfully in detaining Entries 1 and 2;

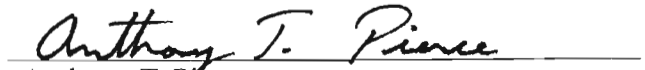
c. A permanent injunction directing Defendants to cease their improper detention of Entries 1 and 2 immediately;

d. A permanent injunction directing Defendants to cease their improper interference with the shipment of raw materials between ANP and IMS/Amphastar; and

e. Such other and further relief as the Court may deem just and proper.

Dated: October 25, 2010

Respectfully submitted,



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# United States District Court
# For the District of Columbia

AMPHASTAR PHARMACEUTICALS, INC.

Plaintiff

vs

FOOD AND DRUG ADMINISTRATION, et al.

Defendant

Case: 1:10-cv-01800
Assigned To : Urbina, Ricardo M.
Assign. Date : 10/25/2010
Description: TRO/PI

**CERTIFICATE RULE LCvR 7.1**

I, the undersigned, counsel of record for Amphastar Pharmaceuticals, Inc. certify that to the best of my knowledge and belief, the following are parent companies, subsidiaries or affiliates of Amphastar Pharmaceuticals, Inc. which have any outstanding securities in the hands of the public:

None.

These representations are made in order that judges of this court may determine the need for recusal.

Attorney of Record

Signature

D.C. Bar No. 415263
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