

COVINGTON & BURLING

1201 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004-2401
TEL 202.662.6000
FAX 202.662.6291
WWW.COV.COM

WASHINGTON
NEW YORK
SAN FRANCISCO
LONDON
BRUSSELS

March 16, 2006

VIA FEDERAL EXPRESS

Dockets Management Branch (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket Number 2003P-0064

Ladies and Gentlemen:

The undersigned submit this letter to you on behalf of sanofi-aventis US LLC, successor-in-interest to Aventis Pharmaceuticals, Inc. ("sanofi-aventis"). Sanofi-aventis is the manufacturer of Lovenox[®] (enoxaparin sodium), a low molecular weight heparin ("LMWH"). On February 19, 2003, sanofi-aventis filed a citizen petition to the above-referenced docket number (the "Citizen Petition") arguing that FDA should not approve a generic version of enoxaparin sodium until the conditions set forth in the Citizen Petition are satisfied.¹ Since that initial submission, sanofi-aventis has submitted several supplements and comments, providing additional scientific data and responding to arguments raised by various entities that have submitted comments to the docket.

This letter provides additional information for FDA's consideration in ruling on the Citizen Petition. Attached hereto as Attachment A, is a copy of FDA's October 25, 2005 rejection of a citizen petition filed by ISTA Pharmaceuticals, Inc. ("ISTA"), regarding ISTA's

¹ FDA Docket Number 2003P-0064(CP1).

2003P-0064

C9

March 16, 2006

Page 2

hyaluronidase product, Vitrase.² ISTA had requested that FDA reverse its previous decision to grant Vitrase 5-year new chemical entity marketing exclusivity rather than 3-year exclusivity.

In rejecting ISTA's request, FDA relied heavily on the fact that hyaluronidase is not fully characterized. FDA's letter states that because hyaluronidase is not fully characterized, "the Agency does not know whether [hyaluronidase] products, in fact, contain any previously approved active moieties."³ FDA went on to note that "[g]enerally, if the Agency has insufficient information to know whether a product contains a previously approved active moiety, the applicant would be required to submit an NDA containing substantial clinical safety and efficacy data."⁴

FDA's rejection of ISTA's citizen petition has relevance to FDA's consideration of applications for generic enoxaparin products. As sanofi-aventis has pointed out in its Citizen Petition and Supplements, enoxaparin cannot be fully characterized (by direct analysis) due to limitations on current analytical technology.⁵ As FDA itself stated in its letter to ISTA, if an active moiety is not fully characterized, FDA cannot determine if it is the same as another active moiety contained in another product. Thus, because enoxaparin is not fully characterized (by direct analysis), there is no way for FDA to determine if the active ingredient specified in an ANDA for generic enoxaparin is "the same as" enoxaparin, as required by section 505(j) of the Federal Food, Drug, and Cosmetic Act.⁶

² See Letter from FDA to Marvin J. Garrett, Vice President, ISTA Pharmaceuticals, Inc., regarding Docket Number 2005P-0134/CP1 (October 25, 2005).

³ *Id.* at 2.

⁴ *Id.* at 9.

⁵ See, e.g., Citizen Petition, at 18-19.

⁶ 21 U.S.C. § 355(j).

COVINGTON & BURLING

March 16, 2006

Page 3

FDA's rejection of ISTA's citizen petition provides an additional ground for FDA to withhold approval of proposed generic versions of enoxaparin. Sanofi-aventis requests that FDA give this precedent significant consideration in its evaluation of the issues raised by the Citizen Petition.

Respectfully submitted,



Peter O. Safir
Scott L. Cunningham
Attorneys for sanofi-aventis US LLC

Covington & Burling
1201 Pennsylvania Ave., N.W.
Washington, D.C. 20004-2401

Attachment

cc (w/attachment): Mr. Gary Buehler
FDA: Office of Generic Drugs (HFD-600)