

HOGAN & HARTSON

L.L.P.

DAVID M. FOX
PARTNER
(202) 637-5878
DMFOX@HHLAW.COM

COLUMBIA SQUARE
555 THIRTEENTH STREET, NW
WASHINGTON, DC 20004-1109
TEL (202) 637-5600
FAX (202) 637-5910
WWW.HHLAW.COM

July 29, 2003

BY HAND DELIVERY

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

Re: *Citizen Petition, Supplement No. 1*
Docket Number 2003P-0321

Dear Sir or Madam:

The undersigned, on behalf of ICN Pharmaceuticals, Inc. and Ribapharm Inc. (together "ICN/Ribapharm"), submits the following additional information to supplement the record in support of the citizen petition submitted by ICN/Ribapharm on July 16, 2003. Specifically, we are submitting information regarding the contractual relationship between Schering-Plough Corporation ("Schering"), the sponsor of PEG-Intron, and three sponsors of proposed generic ribavirin products, Geneva Pharmaceuticals, Inc. ("Geneva"), Teva Pharmaceuticals USA, Inc. ("Teva"), and Three Rivers Pharmaceuticals, LLC ("Three Rivers").

As shown in our petition, Rebetol® (ribavirin, USP) and PEG-Intron™ (peginterferon alfa-2b) are approved for use as a combination product for the treatment of hepatitis C. The labeling of the products fit hand-in-glove. Indeed, the labeling of PEG-Intron is replete with references to "PEG-Intron/Rebetol Combination Therapy." See, e.g., *ICN/Ribapharm Petition*, Tab 3 at 4. Even the black box warning in the labeling for PEG-Intron includes information on "Use with ribavirin." *Id.* at 1. The Medication Guide for PEG-Intron likewise instructs patients who are taking PEG-Intron/Rebetol combination therapy to read the Medication Guide for Rebetol. *ICN/Ribapharm Petition*, Tab 6 at 1. The textual

2003P-0321

SUP 1

BERLIN BRUSSELS LONDON PARIS BUDAPEST PRAGUE WARSAW MOSCOW TOKYO

NEW YORK BALTIMORE McLEAN MIAMI DENVER BOULDER COLORADO SPRINGS LOS ANGELES

July 29, 2003

Page 2

relationship between the labeling of the two products is so strong that, even if the sponsor of a generic Rebetol product were to “disclaim” any use with PEG-Intron, the labeling of PEG-Intron would still render the generic product unlawful. *ICN/Ribapharm Petition* at 10-12; *see generally Kordel v. United States*, 335 U.S. 345 (1948) (if written material supplements, explains, or is otherwise textually related to an FDA-regulated product, the material is deemed to accompany the product for purposes of section 201(m) of the Food, Drug, and Cosmetic Act).

The fact that FDA approved Rebetol and PEG-Intron as a combination product, and the fact that the products share – as they must – mutually conforming labeling, is sufficient in itself to require the agency to grant ICN/Ribapharm’s petition. However, should there be any doubt, we are providing in this supplement additional evidence in support of the necessary relationship between the labeling of generic Rebetol products and the labeling of Schering’s PEG-Intron.

Specifically, Schering and three generic manufacturers (Geneva, Teva, and Three Rivers) have entered into a contractual relationship under which Schering has agreed to license its U.S. patents to each of the generics. In return for the license, each of the generic manufacturers must pay Schering a royalty based on net sales of their ribavirin products. *See* Tab 1, Schering Press Release, “Schering-Plough in Licensing Agreements with Geneva Pharmaceuticals and Teva Pharmaceuticals to Resolve U.S. Ribavirin Patent Disputes” (Mar. 26, 2003); Tab 2, Schering Press Release, “Schering-Plough in Licensing Agreement with Three Rivers Pharmaceuticals to Resolve U.S. Ribavirin Patent Dispute” (Feb. 7, 2003); Tab 3, Par Pharmaceutical, Inc. Press Release, “Settlement is Reached with Schering Regarding Ribavirin (Rebetol)” (Feb. 7, 2003).

Further, Schering has confirmed that the licensing agreements include the use of the generic ribavirin with PEG-Intron. According to documents filed by Schering with the Securities and Exchange Commission in February 2003, describing the contract with Three Rivers:

July 29, 2003

Page 3

What patents are covered by this licensing agreement? Does this agreement include rights to Schering-Plough's patents covering ribavirin in combination with interferon or peginterferon?

The licensing agreement includes all of Schering-Plough's U.S. patents relating to ribavirin and its use in treating hepatitis C, *including its use in combination with interferon or peginterferon.*

Tab 4, Schering SEC Form 8-K (Feb. 7, 2003) Exh. 99.2 (emphasis added). We have no reason to believe that the agreements with Geneva and Teva are materially different from the agreement with Three Rivers.^{1/}

The financial relationship between the generics and Schering, centered on sales of ribavirin, lends even more support to ICN/Ribapharm's core argument – that intended uses of ribavirin, as set forth in the labeling for PEG-Intron, also must be regarded as intended uses of the proposed generic products. By entering into these agreements, the generic sponsors cannot separate themselves from labeling and marketing of PEG-Intron. The generic sponsors are, in effect, paying Schering based on sales of ribavirin and, in doing so, the generics have further integrated the marketing of their products with the marketing of PEG-Intron.

In short, Geneva, Teva, and Three Rivers have entered into licensing agreements with Schering, under which Schering is eligible to collect a royalty based on the sale of generic ribavirin. The agreements include Schering's patent rights to the PEG-Intron/Rebetol combination. Schering, in turn, will be distributing labeling that makes specific claims about the use of ribavirin in combination with PEG-Intron. Under these circumstances, and given the

^{1/} The press releases make clear that the terms of these agreements have not been disclosed to the public.

HOGAN & HARTSON L.L.P.

July 29, 2003

Page 4

overwhelming textual relationship between the labeling of PEG-Intron and Rebetol, any generic Rebetol product marketed by Geneva, Teva, and Three Rivers must include labeling for use with PEG-Intron.

Respectfully submitted,



David M. Fox
Hogan & Hartson LLP
555 Thirteenth Street, NW
Washington, DC 20004
(202) 637-5678

Enclosures