DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

Our STN: BLA 103663/5069

APPROVAL
July 2, 2010

Three Rivers Pharmaceuticals, LLC
Attention: Paul F. Fagan, J.D., C.P.A.
Executive Vice President and General Counsel
119 Commonwealth Drive
Warrendale, PA 15086

Dear Mr. Fagan

Please refer to your supplement to your biologics license application (BLA), dated June 30, 2008, received July 2, 2008, submitted under section 351 of the Public Health Service Act for Infergen® (interferon alfacon-1).

We acknowledge receipt of your amendments to this supplement dated July 25, 2008, July 29, 2008, August 22, 2008, September 23, 2008, October 3, 2008, October 15, 2008, October 28, 2008, October 29, 2008, November 12, 2008, December 2, 2008, December 9, 2008, December 16, 2008, January 13, 2009, January 19, 2009, January 28, 2009, January 30, 2009, March 2, 2009, March 17, 2009, March 19, 2009, October 16, 2009, December 30, 2009, January 12, 2010, January 22, 2010, February 26, 2010, April 9, 2010, April 21, 2010, May 27, 2010, June 15, 2010, and June 22, 2010. The December 30, 2009, submission constituted a complete response to our May 1, 2009, action letter. We also acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment and your proposed REMS modification, dated June 15, 2010.

Your request to supplement your BLA for Infergen® (interferon alfacon-1), to update the package insert with the results of the DIRECT trials and to include information on combination therapy with weight-based dosing of ribavirin in the Medication Guide, has been approved. The labeling changes include revisions to:

1) Indications and Usage section to include information describing when patients are unlikely to benefit from retreatment;

2) Dosage and Administration section to include dose recommendations for retreatment in combination with weight-based dosing of ribavirin for the treatment of chronic hepatitis C;

3) Clinical Studies and Adverse Reactions section to include information regarding study IRHC-001/IRHC-002; and

4) To update the Contraindications, Warnings and Precautions and Animal Toxicology and/or Pharmacology sections.

In addition, the package insert was converted to PLR format.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because there is evidence strongly suggesting that the biological product fails to represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is unlikely to be used in a substantial number of pediatric patients. After review of the adult clinical trials data, we find no clinical advantage to use of Infergen® (interferon alfacon-1), and it requires more frequent injections than current standard of care therapy.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Infergen® (interferon alfacon-1) was originally approved on August 7, 2009, and consists of a Medication Guide and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of revisions to the Medication Guide to provide an accurate description of the risks associated with Infergen® (interferon alfacon-1) therapy.

Your proposed modified REMS, submitted on June 15, 2010, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS and the REMS assessment plan will remain the same as that approved on August 7, 2009.

We remind you that the requirements for assessments of an approved REMS under section 505-1(g)(3)(B) and (C) include requirements for information on the status of any post approval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such post approval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

BLA 103663 REMS ASSESSMENT

NEW SUPPLEMENT for BLA 103663
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 103663
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send five copies of REMS-related submissions.

CONTENT OF LABELING

Within 14 days of the date of this letter, submit content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm that is identical in content to the enclosed labeling text. The content of labeling should be submitted by updating your applications by referencing the SPL file submitted to the drug establishment registration and drug listing system. To do this, place a link in your application submissions that directs FDA to your SPL file. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 103663/5069.**" In addition, within 14 days of the date of this letter, amend any pending supplement for this BLA with content of labeling in SPL format to include the changes approved in this supplement. For additional information on submitting labeling to drug establishment registration and drug listing and to applications, see the FDA guidances at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072339.pdf and http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4) to the following address or by facsimile at 301-847-8444:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

In addition, as required under 21 CFR 601.12(f)(4), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

If you have any questions, call Myung-Joo Patricia Hong, Regulatory Project Manager, at (301) 796-0807.

Sincerely,

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: Content of Labeling
Modified REMS