# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**21-626**

# APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-626

Heyl Chemisch-pharmazeutische Fabrik GmbH & Co. KG
c/o Heyltex Corporation
Attention: Robert Martin, Vice President of Operations
925 South Mason Road
PMB # 242
Katy, TX 77450

Dear Mr. Martin:

Please refer to your new drug application (NDA) dated March 10, 2003, received March 13, 2003, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Radiogardase™ (insoluble Prussian blue) 0.5gm capsules.

We acknowledge receipt of your submissions dated March 27, April 22 and 28, May 5 and 13, July 30, August 13 and 28, September 1, 5, 10, 11, 12, 18 and 29, and October 2, 2003.

This new drug application provides for the use of Radiogardase™ (insoluble Prussian blue) capsules for treatment of patients with known or suspected internal contamination with radioactive cesium and/or radioactive or non-radioactive thallium to increase their rates of elimination.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the Patient Treatment Data Forms) and submitted labeling (immediate container and carton labels submitted September 18, 2003). Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-626.**" Approval of this submission by FDA is not required before the labeling is used.

We remind you of your agreements in your September 10 and 11, 2003 submissions, and in the September 10 and 11, 2003 teleconferences with the Division to provide chemistry information.

We also remind you of your postmarketing study commitments in your submission dated September 29, 2003. These commitments are listed below.

1. Longitudinal studies involving follow up on case report forms and placement of data into a database for periodic analyses to determine length of treatment, safety profile, and other factors related to drug effectiveness.

   a. Protocol submission: Within 6 months of the date of this letter
   b. Study start (i.e. the date the database will be ready to accept patient data, should it be necessary): Within 6 months of agreement to the protocol

   We also remind you of your agreement to provide annual reports of ongoing studies beginning one year from study initiation.

2. Pediatric studies

   a. Develop appropriate dosage form for use in younger children.

      i. Submission of plan to develop pediatric formulation: Within 6 months of the date of this letter
      ii. Begin development: Within 6 months of agreement to plan
      iii. Completion of formulation development: Within 18 months of initiation of development

   b. Studies to determine dosing for neonates to 2 years of age (based on human extrapolation and/or animal models).

      i. Protocol submission: Within 6 months of the date of this letter
      ii. Study start: Within 6 months of agreement to the protocol
      iii. Final study report submission: Within 12 months of initiation of the study

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

FDA's Pediatric Rule [at 21 CFR 314.55/21 CFR 601.27] was challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. The pediatric exclusivity provisions of FDAMA as reauthorized by the Best

Pharmaceuticals for Children Act are not affected by the court's ruling. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products. You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request". FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Medical Imaging and Radiopharmaceutical Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Lynn Panholzer, Pharm.D., Regulatory Project Manager, at (301) 827-3132.

Sincerely,

*{See appended electronic signature page}*

Florence Houn, M.D., M.P.H.
Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures