DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-749/SLR-002
NDA 21-751/SLR-002

Hameln Pharmaceuticals GmbH
c/o B & H Consulting Services, Inc.
Attention: Elizabeth N. Dupras
Associate Project Manager
55 North Gaston Avenue
Somerville, NJ 08876

Dear Ms. Dupras:

Please refer to your supplemental new drug applications dated February 24, 2005, received February 26, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pentetate zinc trisodium and Pentetate calcium trisodium injection.

These "Changes Being Effected in 30 days" supplemental new drug applications propose to change the package insert to include the Patient Data Treatment form.

We completed our review of these applications, as amended. These applications are 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 submitted labeling (package insert submitted February 24, 2005).

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 these submissions "**FPL for approved supplement NDA 21-749/SLR-002, NDA 21-751/SLR-002**." Approval of these submissions by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated August 10, 2004. Please note that in the NDA approval letter dated August 11, 2004, the first commitment was incorrectly cited to be a required study under section 2 of the Pediatric Research Equity Act (PREA). The Ca and Zn DTPA have been granted orphan status and therefore, do not trigger PREA. Although not required under PREA, you are still required to fulfill the first commitment along with other postmarketing commitments listed in your August 10, 2004, submission. These commitments are listed below.

1. Human pharmacokinetic study in pediatric subjects to compare and evaluate the absorption, distribution and elimination of Ca and Zn-DTPA via inhalation using a commonly available jet type nebulizer (FDA approved model to be selected by the sponsor) with the intravenous route.

Data/information on dose delivered and the particle size distribution obtained from the specified nebulizer shall be provided.

a. Protocol submission: Within 6 months of the date of final approval of these applications
b. Study start: Within 6 months of agreement to the protocol
c. Final study report submission: Within 12 months of initiation of the study.

2. Longitudinal studies involving follow up of Patient Treatment Data Forms and placement of data into a registry for periodic analyses related to post-marketing drug safety and uses.
   a. Protocol submission: Within 6 months of the date of final approval of these applications
   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
   c. Agree to submit annual reports of ongoing longitudinal studies beginning one year from study initiation.

3. Human pharmacokinetic study in adult subjects to compare and evaluate the absorption, distribution and elimination of Ca and Zn-DTPA via inhalation using a commonly available jet type nebulizer (FDA approved model to be selected by the sponsor) with the intravenous route. Data/information on dose delivered and the particle size distribution obtained from the specified nebulizer shall be provided.
   a. Protocol submission: Within 6 months of the date of final approval of these applications
   b. Study start: Within 6 months of agreement to the protocol
   c. Final study report submission: Within 12 months of initiation of the study.

Submit clinical protocols to an IND for these products. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your NDAs. 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 your NDAs. 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**."

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. 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

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).

If you have any questions, call Lynn Henley, Regulatory Project Manager, at (301) 827-6312.

Sincerely,

{See appended electronic signature page}

George Q. Mills, M.D., M.B.A.
Director
Division of Medical Imaging and Hematology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Kyong Kang
8/4/05 04:07:02 PM
Signing for George Mills, M.D.