NDA 20-955

R & D Laboratories, Incorporated
Attention: Rhoda Makoff, Ph.D.
President and CEO
4640 Admiralty Way, Suite 710
Marina del Rey, CA 90292

Dear Dr. Makoff:

Please refer to your new drug application (NDA) dated December 30, 1997, received December 30, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ferrlecit® (sodium ferric gluconate complex in sucrose injection) .

We acknowledge receipt of your submissions dated July 9 and 20, August 19, October 6 and 30, December 28, 29, 30, and 31, 1998, January 4, 6, and 25, and February 4 and 8, 1999.

This new drug application provides for the use of Ferrlecit® (sodium ferric gluconate complex in sucrose injection) for treatment of iron deficiency anemia in patients undergoing chronic hemodialysis who are receiving supplemental erythropoetin therapy.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) as well as the immediate container, foil-on-tray, and carton labeling submitted August 19, 1998 . Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-955." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submissions dated December 30, 1998 and February 8, 1999. These commitments, along with any completion dates agreed upon, are listed below.

1. Conduct a Segment I fertility and reproductive performance study in the rat. You have committed to complete the study and submit the Final Study Report not later than January 31, 2000.

2. Conduct a 13-week subchronic toxicity study in the dog. You have committed to

complete the study and submit the Final Study Report not later than February 29, 2000.

3. Conduct a pilot human pharmacokinetic study of Ferrlecit®. You have committed to complete the study not later than July 31, 1999 and submit the Final Study Report not later than October 31, 1999.

4. Conduct a study to determine the optimal dosing regimen for patients requiring repeated courses of Ferrlecit® for the achievement of iron repletion and for the maintenance of iron repletion. You have committed to complete the study not later than November 30, 2000 and submit the Final Study Report not later than July 31, 2001.

5. Conduct studies to determine the safe and effective dosage regimens in the pediatric population. You have committed to complete a study in children aged 2 years to 12 years not later than 28 months following the submission of the interim analysis from Study FER 9803 entitled, "Crossover, Randomized, Blinded, Prospective, Multicenter Clinical Evaluation of the Rate of Adverse Effects to Ferrlecit® in Hemodialysis Patients as Compared to Placebo". In addition, you have committed to submit the Final Study Report not later than six months after study completion. You have committed to complete a study in adolescents aged 12 years to less than 16 years not later than May 30, 2000 and submit the Final Study Report not later than August 31, 2000. Our request for this commitment does not constitute a Written Request to conduct pediatric studies that could qualify for pediatric exclusivity. If you wish to pursue a Written Request, we recommend that you continue your discussions with this Division.

6. Conduct a study to provide additional safety data (e.g., incidence of allergic or anaphylactic reactions, cross-reactivity with other parenteral iron preparations). You have committed to complete the study not later than November 5, 1999 and submit the Final Study Report not later than April 5, 2000.

7. Conduct a study to evaluate the possibly increased risk of allergic/anaphylactic reactions in patients receiving angiotensin converting enzyme inhibitor therapy and Ferrlecit® concurrently. You have committed to complete the study not later than August 5, 2000 and submit the Final Study Report not later than January 5, 2001.

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Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since

the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

As per our agreement of September 22, 1998, Ferrlecit® may not be promoted as being safer than iron dextran or other parenteral iron drug products without adequate supporting data that the Agency has reviewed and found acceptable. Please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Gastrointestinal and Coagulation Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Brian Strongin, Project Manager, at (301) 827-7310.

Sincerely,

Victor F. Raczkowski, M.D., M.S.
Acting Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research