DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-227/S-007

Merck Research Laboratories
Attention: Tamra Goodrow, Ph.D.
Director, Regulatory Affairs
P.O. Box 4
West Point, PA 19486

Dear Dr. Goodrow:

Please refer to your supplemental new drug application dated March 6, 2002, received March 7, 2002, submitted under section 505(b) pursuant to the Federal Food, Drug, and Cosmetic Act for Cancidas® (caspofungin acetate) For Injection.

We acknowledge receipt of your submissions dated below:

April 18, 2002
May 2, 2002
May 7, 2002
May 17, 2002
June 5, 2002 (2)
June 21, 2002 (2)
June 27, 2002
July 18, 2002
July 19, 2002
July 22, 2002
July 24, 2002
July 26, 2002
July 31, 2002
August 2, 2002
September 9, 2002
September 16, 2002
September 30, 2002
October 2, 2002
October 16, 2002
October 17, 2002
October 22, 2002
October 25, 2002
November 19, 2002
December 11, 2002
December 13, 2002
December 18, 2002
December 19, 2002 (3)
December 23, 2002 (2)
December 27, 2002
January 3, 2003 (2)
January 6, 2003

This supplemental new drug application provides for the use of Cancidas® (caspofungin acetate) For Injection for the treatment of candidemia and the following *Candida* infections: intra-abdominal abscesses, peritonitis and pleural space infections.

We completed our review of this application, as amended. This application is approved, effective of 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 submitted January 6, 2003). 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 the FPL electronically 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, 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 supplement of NDA 21-227/S-007". Approval of this submission by FDA is not required before the labeling is used.

The text in italics below addresses the application of FDA's Pediatric Rule at 21 CFR 314.55 to this supplemental new drug application. FDA's Pediatric Rule at 21 CFR 314.55 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. Although the government decided not to pursue an appeal in the courts, it will work with Congress in an effort to enact legislation requiring pharmaceutical manufacturers to conduct appropriate pediatric clinical trials. In addition, third party interveners have decided to appeal the court's decision striking down the rule. Therefore, we encourage you to submit a pediatric plan that describes development of your product in the pediatric population where it may be used. Please be aware that whether or not this pediatric plan and subsequent submission of pediatric data will be required depends upon passage of legislation or the success of the third party appeal. In any event, we hope you will decide to submit a pediatric plan and conduct the appropriate pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens must contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (21 CFR 314.55).

Based on information submitted, we conclude the following:

For the treatment of candidemia and the following Candida infections: intra-abdominal abscesses, peritonitis and pleural space infections.

- *We are deferring submission of pediatric studies for pediatric patients ages 0-16 years until December 31, 2008.*

The pediatric exclusivity provisions of FDAMA as reauthorized by the Best Pharmaceuticals for Children Act are not affected by the court's ruling.

As you continue your development program for Cancidas®, please consider addressing some of the following issues of interest:

(1) Continue to evaluate the efficacy and safety of Cancidas® in patients with candidemia and other candida infections, particularly in patients with azole-resistant *Candida albicans* and non-albicans species of Candida, including but not limited to *C. glabrata*, *C. krusei*, and *C. parapsilosis*, some of which are also azole-resistant.

(2) Continue to evaluate the in vitro activity of Cancidas® and establish breakpoints for Candida species.

(3) Evaluate the efficacy of Cancidas® in neutropenic patients with candidemia and invasive candidiasis, including endophthalmitis, endocarditis, osteomyelitis, and meningitis.

(4) Evaluate the efficacy of Cancidas® in a randomized study comparing Cancidas® to fluconazole in patients with candidemia and invasive candidiasis.

In addition, submit three copies of the introductory promotional materials that you propose to use for Cancidas® (caspofungin acetate) For Injection for this new indication. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the reviewing Division 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

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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, please call Christina H. Chi, Ph.D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure: Package Insert Labeling

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

/s/

Renata Albrecht
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NDA 21-227/S-007