DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-572

Cubist Pharmaceuticals, Inc.
Attention: David H. Schubert
Vice President, Regulatory Affairs and Quality
65 Hayden Avenue
Lexington, MA 02421

Dear Mr. Schubert:

Please refer to your new drug application (NDA) dated December 19, 2002, received December 20, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cubicin™ (daptomycin for injection) Intravenous Injection.

We acknowledge receipt of your submissions dated January 23, February 4, March 12, 17 (2), 26, 27, and 31, April 7, 9, 11, 16, 21, and 22, May 8, 12, 14 (2), 15, 16, 19, 20, 28 (2), 29, and 30, June 16, 19, and 30, July 3, 15, 18, 23, and 30, August 5 (2), 7, and 8, September 3 (2), 10, 11, and 12, 2003.

This new drug application provides for the use of Cubicin™ (daptomycin for injection) for the treatment of complicated skin and skin structure infections caused by susceptible strains of the following Gram-positive microorganisms: *Staphylococcus aureus* (including methicillin-resistant strains), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae* subsp. *equisimilis* and *Enterococcus faecalis* (vancomycin-susceptible strains only).

We have 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, immediate container and carton label). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and 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 21-572**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitment agreed to in your submission dated September 11, 2003. This commitment is listed below.

COMMITMENT #1

Description:	Conduct a clinical study to assess the safety, efficacy, and pharmacokinetics of daptomycin in renal impairment patients (inclusive of patients with foot and decubitus ulcers complicated by diabetes) with complicated skin and skin structure infections. Enrollment into the study should be limited to patients with an estimated (via the Cockcroft and Gault equation using actual body weight) creatinine clearance ≤50 mL/min and an attempt should be made to enroll an equal number of patients into the following categories: CL_{CR} 30-50 mL/min, CL_{CR} <30 mL/min, hemodialysis patients, and CAPD patients.
Protocol Submission:	Within 3 months of this letter
Study Start:	Within 6 months of this letter
Final Report:	Within 24 months of this letter

Submit clinical protocols to your IND for this product. Submit all study 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."**

As you pursue additional development of daptomycin, we strongly encourage you to investigate potential risk factors for development of muscle toxicity due to daptomycin. These could include effects of altered fluid/electrolyte and metabolic states (e.g., diabetes, thyroid disease, altered hormonal status).

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. 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.

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 this 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

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

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 LTJG Raquel Peat, Regulatory Health Project Manager, at (301) 827-2125.

Sincerely,

{See appended electronic signature page}

Mark J. Goldberger, M.D., M.P.H.
Director
Office of Drug Evaluation IV, HFD-104
Center for Drug Evaluation and Research

Enclosure: package insert, immediate container, and carton label

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

/s/

Mark Goldberger

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