DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

NOV 22 2000

Robert J. McCormack, Ph.D.
Senior Vice President, Development
Cubist Pharmaceuticals, Inc.
24 Emily Street
Cambridge, MA 02139

RE: IND #[redacted]
Daptomycin
MACMIS ID # 9486

Dear Dr. McCormack:

As a part of the Division of Drug Marketing, Advertising, and Communications' (DDMAC) routine surveillance, we have reviewed the website for Cubist Pharmaceuticals, Inc. (Cubist)[1], press releases, and printed materials disseminated by Cubist representatives at the Infectious Diseases Society of America (IDSA) 2000 annual meeting in New Orleans. We find the website, press releases, and disseminated print materials in violation of the Federal Food, Drug, and Cosmetic Act and its applicable regulations because they promote the safe or effective use of the unapproved drug, daptomycin. Specifically, we object to the following:

Pre-Approval Promotion

- Daptomycin is an investigational new drug. Cubist has promoted daptomycin as safe or effective prior to FDA approval for the treatment of several indications including: complicated skin and soft tissue infections, bacteremia, endocarditis, osteomyelitis, complicated urinary tract infection (cUTI), intra-abdominal infection, pneumonia, and several bacterial pathogens including: *vancomycin resistant enterococcus* (VRE), *methicillin resistant staphylococcus aureus* (MRSA), and all bacterial gram positive strains, including drug resistant strains. The website contains press releases dated, March 6, 2000, April 12, 2000, July 27, 2000, and September 19, 2000, that make conclusions about the safety or efficacy of daptomycin prior to FDA approval. Examples of violative statements in the press releases include, but are not limited to:

[1] www.cubist.com, 9/27/00.

The observed advantages of daptomycin to date include its rapidly bactericidal activity and effectiveness in vitro against all clinically relevant gram-positive bacterial strains, including drug resistant strains. Daptomycin has a favorable side effect profile and will be administered as a once-a-day therapy.

All signs point to Cidecin as a most promising answer to today's critical need for new therapies for serious and life-threatening infections.

No serious adverse events were attributable to the use of daptomycin in any patients at any of the doses studied.

Daptomycin also had a favorable safety profile similar to the comparator agents.

Cidecin is the first in a new class...developed to treat serious and life-threatening infections, including those resistant to current therapies.

We feel that the name Cidecin best conveys the potent, bactericidal nature of daptomycin.

Daptomycin...has demonstrated potent bactericidal activity in vitro against Gram-positive bacteria including methicillin resistant staphylococci (MRSA), vancomycin resistant enterococci (VRE), and glycopeptide intermediate resistant staphylococci (GISA).

Daptomycin appears to be safe and well-tolerated, with no trends in drug-related local or systemic adverse events.

In addition to the website information, Cubist representatives promoted its daptomycin product in the commercial exhibit hall at the IDSA meeting prior to FDA approval by disseminating a booklet that contained 14 abstracts of clinical studies, a published review article entitled, "Daptomycin: a novel agent for Gram-positive infections", and an abstract promoting the use of daptomycin for *Bacillus anthracis* bacterial strains. These promotional materials also make conclusions about the safety or efficacy of daptomycin prior to FDA approval.

Failure to Present Material Facts

- Cubist presents misleading information on their website that fail to disclose facts that are material in light of the representations made about daptomycin. Specifically, Cubist fails to disclose important risk information about daptomycin. For example, Cubist fails to present that there have been cases of reversible muscle toxicity at lower doses and irreversible muscle toxicity at higher doses of daptomycin.

Requested Action

We request that Cubist immediately cease dissemination of all materials and activities that contain these and similar representations and conclusions concerning the safety or efficacy of daptomycin. In addition, we request that Cubist submit a written response on or before December 5, 2000, describing its intent and plans to comply with the above. The response should include a list of materials discontinued and the date on which these materials were discontinued.

You should direct your response to the undersigned by facsimile by at (301) 594-6759, or to the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm 17-B-20, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 9486 in addition to the IND number.

Sincerely,

/S/

James R. Rogers, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications