





April 19, 1995

Food and Drug Administration  
Rockville MD 20857

Approved NDA 50-573  
Approved NDA 50-574  
Approved NDA 50-625  
Pending NDA 50-715  
Pending NDA 50-716

Thomas P. Koestler, Ph.D.  
Vice President, Corporate Head  
Drug Registration and Regulatory Affairs  
Sandoz Pharmaceuticals Corporation  
59 Route Ten  
East Hanover, New Jersey 07936-1080

Dear Dr. Koestler,

On October 14, 1994 and February 28, 1995 you wrote letters to the Center for Drug Evaluation and Research (CDER) requesting that your applications for SANDIMMUNE (cyclosporine) and NEORAL (cyclosporine, microemulsion) be reclassified as drugs under section 505(b) of the Federal Food, Drug, and Cosmetic Act (the Act). Presently they are classified as antibiotics under section 507 of the Act.

After reviewing the information submitted by Sandoz to support this request, I am now able to inform you that CDER intends to continue to regulate these products under section 507 of the Act.

As we both agree, the manufacture of cyclosporine involves a fermentative process employing a microorganism, and, as such, it meets the first part of the statutory definition of an antibiotic. Thus, the crux of the classification decision rests on whether cyclosporine has the capacity to inhibit or destroy microorganisms in dilute solution . . . (21 U.S.C. 357).

We do find, based on the information we presently have, that cyclosporine can indeed inhibit or kill certain human pathogens *in vitro* at concentrations that are relevant to those found in the human body when cyclosporine is used clinically as described in its approved or proposed labeling. For your convenience, I have appended to this letter, a copy of the microbiologist's report from HFD-530 summarizing our analysis of cyclosporine's antimicrobial capacity. Cyclosporine meets both parts of the statutory definition of products that must be regulated under section 507.

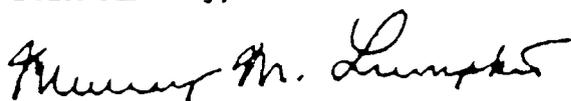
Approved NDA 50-573  
Approved NDA 50-574  
Approved NDA 50-625  
Pending NDA 50-715  
Pending NDA 50-716

Page 2

In our review of the legislative history of section 507 of the Act, we found no Congressional reference as to how the term "inhibits or destroys microorganisms in dilute solution" should be interpreted. However, we believe our findings are consistent with the ordinary meaning of the words in the statute and with Congressional intent to single out those drugs, such as cyclosporine, which are produced by a fermentative process. In addition, the FDA has a strong history of interpreting section 507 without reference to whether the product is used clinically as an antibiotic. Several anti-neoplastic agents have been classified as Section 507 products because they meet the legal definition of an "antibiotic drug".

I realize that the classification of cyclosporine is of significant importance to Sandoz. Thus, if you or your staff believe we have misinterpreted the scientific information you submitted or that we have misinterpreted the intent of the law, please do not hesitate to let me know. I would be happy to facilitate a meeting with the scientific and legal staff of the Center to discuss this further if you feel such would be helpful.

Yours sincerely,



Murray M. Lumpkin, M.D.  
Deputy Center Director (Review Management)  
Center for Drug Evaluation and Research

cc: Janet Woodcock, M.D.  
Amanda Pedersen, J.D.  
Ann Wion, J.D.  
David Fox, J.D.  
David Falgal, M.D.  
James Bilstad, M.D.  
Jane Axelrad, J.D.