CUBIST
PHARMACEUTICALS

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June 25, 2001

Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Dear Messrs/Madams:

Cubist Pharmaceuticals has reviewed "Reference Docket No. 00N-1269 (Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics: Requirements for Prescription Drug Product Labels)". This proposal to remove information related to the potency of an anti-infective from the package insert represents a dramatic change. The suppression of validated medical information is unlikely to improve prescription practice or decrease the incidence of bacterial resistance. The likely result of this proposal is an increase in appropriate usage of antibiotics as physicians are forced to choose therapies without specific potency information. Cubist Pharmaceuticals strongly believes that in vitro MIC data should be retained in antibiotic package inserts. The following specific comments are offered:

The current wording in drug package insert (i.e., "The following *in vitro* data are available, but their clinical significance is unknown... However, the safety and efficacy of [drug] have not been established in adequate and well-controlled clinical trials.") clearly communicates the limitations of the data. Bacterial MIC values are included in the *in vitro* section of an anti-infective's package insert (PI) only if (1) they are associated with an infection that appears in the "approved indications" section of the PI; and (2) at least 90% of the strains tested were susceptible *in vitro*, using the approved interpretive breakpoints. These breakpoints are developed and approved based on susceptibility population studies, pharmacokinetic and pharmacodynamic studies, and drug resistance studies. These data should be included in the package insert.

Cubist Pharmaceuticals supports the proposal wording of the change proposed by Dr. F. Marsik and H. Silver in their January 19, 2001 comments to the docket. The new wording appears to be to be even more useful in educating physicians about how to interpret the "*in vitro*" section:

00N-1269 C59

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"The pharmacological parameters and *in vitro* susceptibility data for the drug *suggest in vivo* activity against the following organisms for infection occurring at those sites indicated under "Indications and Usage". This has not been proven clinically."

Many antimicrobial therapies must be initiated with incomplete knowledge of the pathogen(s). The precise species is almost never known when empiric therapy is started. Knowledge of the spectrum of activity for an antibiotic is essential to both the selection of the most appropriate drug and the adjustment of therapy in the case of apparent failure.

Removal of the *in vitro* section of an anti-infective package insert will effectively remove a large amount of information needed by physicians to determine proper course of action at initiation and during therapy.

Many pathogens do not occur frequently enough in clinical trials to be included in the "indicated uses" section. However, these pathogens are often both susceptible to antibiotics and cause infections in body sites for which the antibiotics are approved. Excluding these organisms from the "*in vitro*" section of drug package insert will make it more difficult to physicians to know proper treatments for infections caused by those particular species.

In summary, Cubist Pharmaceuticals believes that bacterial susceptibility data should be included in the package insert for all pathogens in which 90% of the isolates are susceptible under approved breakpoints. This will require no change and will allow for valuable information to continue to be disseminated to physicians. While Cubist Pharmaceuticals desires to combat the spread of drug resistance, the exclusion of potency information from the package insert is unlikely to decrease the standard of medical care without producing a reduction in incidence of drug resistance.

Sincerely,

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