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June 14, 1999

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane  
Rm. 1061  
Rockville, MD 20852

Re: [Docket No. 98D-0362] Site Specific Stability Data for Drug and Biologic Applications; Public Meeting; Request for Comment

Dear Madam or Sir:

Pfizer Inc appreciates the opportunity to provide comments on FDA's revised site-specific stability proposal presented at the public meeting held on March 31, 1999 in Bethesda, MD. FDA is commended for organizing the public meeting in response to requests from several organizations. Pfizer Inc's position on site-specific stability remains the same as expressed in our December 7, 1998 response to the June 1998 Stability Draft Guidance. We question the scientific rationale for site-specific stability testing. Contemporary process validation practice, coupled with effective technology transfer, assures equivalent products are made at multiple sites. FDA may evaluate these activities through the GMP inspection program. This combination obviates the need for site-specific stability testing.

At the March 31, 1999 meeting, FDA distributed and discussed a "Revised Proposal on Site-Specific Stability Data". Pfizer has several comments concerning this revised proposal.

- Process validation and technology transfer assure equivalent products between sites. The new proposal addresses the timing of presenting site-specific data based upon classifications of major, moderate, and minor potential for adverse effects on stability. Site specific stability information should not be required as part of the NDA approval process. The revised proposal should require only the current "standard stability commitment" with data reported in annual reports. The field alert system would assure that potential stability issues are addressed.

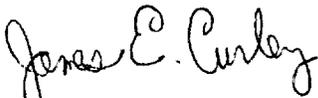
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- The drug substance table classifies potential adverse effects as major, moderate and minor. The process for categorizing a site-change as major, moderate or minor is unclear. In the example for major potential adverse effects, particle size and polymorphic changes of the drug substance are cited. Particle size and polymorphic form would be controlled during manufacture and drug substance testing. Additional stability testing should be unnecessary if previous studies indicated the attributes were not expected to change on storage. In addition, even if changes were occurring, where these have been demonstrated to have no affect upon quality, safety or efficacy of the dosage form, additional stability testing is unnecessary.
- The drug product table also classifies potential adverse effects as major, moderate and minor. The rationale for classification is not clear. For example, sterile solutions are classified in the moderate category, but non-sterile are classified as minor. Whether a solution were sterile or not should not be expected to effect its stability characteristics.
- If the concept of 'adverse effect' category is retained for drug product and drug substance, consideration should be given to having only two categories. If no adverse effect is anticipated, then the standard stability commitment should be sufficient. If an adverse effect is anticipated, then a single batch of drug substance or drug product should be tested for stability, followed by the standard stability commitment.
- Alternate approaches are discussed in Section III. This section includes the use of process validation and technology transfer as an alternate to site specific stability. This alternate should be retained in the final text of the stability guideline.

We appreciate the opportunity to comment on this important guidance.

Sincerely,



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