



Schering-Plough

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April 10, 2003

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

Re: Docket No. 03D-0001; Draft Guidance for Industry on Nonclinical Safety  
Evaluation of Pediatric Drug Products

Dear Sir/Madam:

Schering-Plough has reviewed the Draft Guidance for Industry on Nonclinical Safety  
Evaluation of Pediatric Drug Products, and we offer the following comments for your  
consideration.

With regard to Table E (Immune System) in Section VI, it would be helpful if rat  
timelines are provided, rather than mouse timelines. The rat is a more appropriate species  
to assess effects on pediatric immune systems for the following reasons.

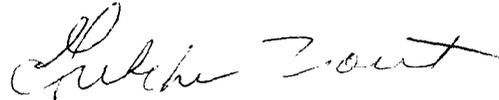
1. In drug development programs, toxicity and exposure are usually more  
thoroughly characterized in the rat than in the mouse. Selection of appropriate  
doses and interpretation of data related to changes in immune system parameters  
would be handicapped if mice were used to assess pediatric immunotoxicity.
2. Although the tools available to assess the immune system are more limited in  
young rats than in adult rats, as pointed out in the guidance, they are extremely  
limited in mice because of sample size restrictions. Functional assessments are  
not feasible, and it is also not possible to assess multiple parameters (chemistry,  
hematology, exposure, FACS analysis) in an individual mouse because of sample  
size restrictions. This latter constraint may hamper interpretive power for the  
parameters which are obtainable.
3. The use of juvenile mice for only the immunotoxicity assessment adds animals,  
studies, time, cost, and effort to a program without adding value. Inclusion of  
immunotox assessment in the same species used to assess toxicities to other  
systems is better science and less wasteful.

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Schering-Plough appreciates the opportunity to comment on this guidance document, and we hope that you will take our comments under consideration.

Sincerely,

A handwritten signature in cursive script, appearing to read "Gretchen Trout".

Gretchen Trout  
Director, Regulatory Relations and Policy  
Worldwide Regulatory Affairs