Schering-Plough

Schering-Plough Therapeutics Group, Inc.
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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Re: Docket No. 03D-0001; Draft Guidance for Industry on Nonclinical Safety Evaluation of Pediatric Drug Products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Schering-Plough has reviewed the Draft Guidance for Industry on Nonclinical Safety Evaluation of Pediatric Drug Products, and we offer the following comments for your consideration.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,

Gretchen Trout
Director, Regulatory Relations and Policy
Worldwide Regulatory Affairs