

Aventis Pasteur



2883 5 AUG -4 18:14

3 August 2005

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

Re: Docket No. 2005D-0155; Draft Guidance for Industry on Toxicity Grading Scale for Healthy Adults and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials [70 Federal Register 22664, May 2, 2005]

Dear Sir/Madam,

Aventis Pasteur Inc. of Swiftwater, Pennsylvania thanks the Food and Drug Administration (FDA) for the opportunity to comment on the above-referenced draft guidance for industry entitled, "Toxicity Grading Scale for Healthy Adults and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials." Aventis Pasteur Inc. is part of the Aventis Pasteur family of companies, which consists of the parent firm Aventis Pasteur SA, headquartered in Lyon, France, Aventis Pasteur Inc., and other subsidiaries (collectively Aventis Pasteur). In turn, Aventis Pasteur SA is a subsidiary of Aventis SA.

Aventis Pasteur is a world leader in vaccines and produces more than one billion doses of vaccines every year to immunize 400 million people around the world. Aventis Pasteur, in close consultation with the US public health establishment, including the FDA, and Centers for Disease Control and Prevention (CDC), strives to alleviate the suffering and death of vaccine-preventable diseases.

We offer the following comments for your consideration concerning the FDA's solicitation of responses as they apply to the Biologics (Vaccine) industry.

2005D-0155

C6

General Comment

We applaud the Food and Drug Administration’s (FDA) effort for the development of this Draft Guidance Document for toxicity grading scales for healthy adults and adolescents enrolled in prophylactic vaccine clinical trials. We agree with the FDA acknowledgement, however, that clinical laboratory tests are rarely if ever applied during the course of prophylactic vaccine trials. Further, laboratory tests should only be utilized in clinical trials when results from preclinical testing of the vaccine under development suggest doing so would be appropriate, and following discussion with Center for Biologics Evaluation and Review (CBER) staff. The laboratory tests included in the clinical trial(s) should only be those relevant to the vaccine being studied. As FDA has noted, the laboratory values provided in this Guidance would serve only as a guideline and would be dependent upon institutional normal parameters. The Sponsor would be required to demonstrate that institutional normal reference ranges are then appropriate.

Aventis Pasteur also takes this opportunity to remind FDA of the importance of global harmonization when establishing criteria for adverse events that may occur during vaccine clinical trials. As we and other manufacturers often conduct clinical trials on a global scale, applying a set of evaluation criteria that meet global regulatory standards is critical to optimizing costly clinical development.

Specific Comments

Section III A – Tables for Clinical Abnormalities

Under “Local Reaction to Injectable Product”:

- “Tenderness” appears to be redundant to “Pain”.
- Use same grade or classification for “Erythema/Redness”.
- Although we recognize the usefulness of a functional scale for “Swelling”, we believe it should not be combined with a measurement scale.

Under “Vital Signs”:

- For “Tachycardia” and “Bradycardia”, replace “for arrhythmia” with “for this condition”.
- For “Hypertension” (systolic and diastolic), replace “for malignant hypertension” with “for this condition”.

Under "Systemic (General)"

- For "Nausea/vomiting", nausea and vomiting should not be bundled together, i.e., that episode should only refer to vomiting.

Section III B – Tables for Laboratory Abnormalities

Under "Hematology"

- For "PT" and "PTT", it is unusual that the upper limit of the normal range is considered as "Mild (Grade 1)".

On behalf of Aventis Pasteur we appreciate the opportunity to comment on this draft guidance and thank you for your consideration of these responses. Should you wish to discuss any of our comments or concerns further, please address inquiries directly to Denise Rieker, Deputy Director, Regulatory Policy and Intelligence, by telephone at (570) 895-3465, or me directly at 570-839-4212.

Sincerely,

A handwritten signature in cursive script that reads "Kenneth P. Guito".

Kenneth P. Guito
Sr. Director, Regulatory Policy and Intelligence

KPG/DR/kh