Aventis Pasteur

03 December 2003

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

Re: Docket No. 2003D-0385; Draft Guidance for Industry on Comparability Protocols—Protein Drug Products and Biological Products—Chemistry, Manufacturing, and Controls Information [68 Federal Register 52776, September 5, 2003]

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Pennsylvania thanks the Food and Drug Administration (FDA) for the opportunity to comment on the above-referenced draft guidance for industry entitled, "Comparability Protocols—Protein Drug Products and Biological Products—Chemistry, Manufacturing, and Controls Information." 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.

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Aventis Pasteur Inc. · Discovery Drive · Swiftwater PA 18370 · www.aventis.com
Telephone 570-839-7187

I. Introduction

Line 30. "This guidance also applies to new drug applications (NDAs), abbreviated new drug applications (ANDAs), new animal drug applications (NADAs), abbreviated new animal drug applications (ANADAs), or supplements to these applications for protein drug products, and not sufficiently characterizable peptide products (e.g., complex mixture of small peptides)."

We are unclear as to why this reference to ANDAs is provided in this guidance as there currently is no provision for the approval of so-called generic biologics. Further, comparability protocols are developed to support manufacturing changes made by a manufacturer for products licensed by that manufacturer. We therefore request that FDA revise this section of the document accordingly.

III. What to Consider in Planning a Comparability Protocol

B. When Might a Comparability Protocol Be Useful for a CMC Change?

Line 207. "Degree of product heterogeneity"

It is unclear what exactly FDA's expectation is in proposing this product-specific, process-specific attribute as criteria for deciding whether or not to develop a comparability protocol. As FDA accurately acknowledges in this document, many biologics are heterogeneous in nature and we therefore believe FDA should provide a bit more of an explanation as to this proposal.

III. What to Consider in Planning a Comparability Protocol

B. When Might a Comparability Protocol Be Useful for a CMC Change?

Line 211. "*Rigorousness* of the manufacturing process controls (i.e., the ability of the manufacturing process controls to ensure that the product remains unaffected by changes)."

We believe it would be more appropriate to use the word *effectiveness* or *robustness* here in place of rigorousness.

V. Content of a Comparability Protocol

E. Does FDA Have Specific Concerns About Changing Manufacturing Facilities That Should Be Addressed in a Comparability Protocol?

Line 653. "The introduction of additional product(s) into an approved product-dedicated manufacturing area of a facility where containment is a concern (e.g., live virus manufacturing operations such as replication competent gene therapy vector propagation, or live attenuated viral vaccine finishing operations)."

Comparability protocols are useful to us for the purpose of introducing additional products into an approved dedicated area in a facility. The current draft guidance document is very general in discussing this topic, while recognizing the utility. It would be helpful if the FDA could expand this section to describe their expectations in a little more detail when this involves, for example, a biological product licensed by the FDA in a different facility or area. Aventis Pasteur would like FDA to consider adding additional clarity around this topic in the final document.

On behalf of Aventis Pasteur Inc., 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 Kenneth P. Guito, Global Head, Regulatory Policy and Intelligence, by telephone at (570) 839-4212, or by email at ken.guito@aventis.com.

Sincerely,

for Luc Kuykens, MD, MPH, DTM
Vice President, Regulatory Affairs, North America
and Authorized Official

LK/KPG/kh