

Wyeth Pharmaceuticals Inc.
P.O. Box 8299
Philadelphia, PA 19101-8299

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March 20, 2006

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

RE: Docket No. 2005D-0286, January 17, 2006 (71 FR, 2552-2554)

Dear Sir/Madam:

Wyeth Pharmaceuticals is submitting the following comments on the FDA's draft Guidance for Industry entitled, "INDs - Approaches to Complying with CGMP during Phase 1".

Wyeth is one of the largest research based pharmaceutical and healthcare products companies and is a leading developer, manufacturer, and marketer of prescription drugs, biopharmaceuticals, vaccines, and over the counter medications. Wyeth appreciates the opportunity to comment on the above mentioned draft guidance; our comments are provided below.

In general, Wyeth supports the development of this FDA guidance, as we believe there is currently a general consensus within Industry that there should be an incremental application of CGMP expectations throughout clinical development as a product approaches commercialization. However, we believe that the guidance is vague in several sections and recommend clarification of those sections.

Clarification of "adequately controlled"

Clarification is requested regarding the interpretation of "adequately controlled". The document recommends in Section V (Recommendations for Complying with the Statute) that adherence to QC procedures during Phase 1 development occurs largely through (among other factors) having "Equipment that is adequately controlled" (Line 170). While the document states (Line 173) that "producers may have acceptable alternative ways of meeting the objectives", this section does not include examples of how "adequately controlled" should be interpreted. However, Section V. C. Facility and Equipment (Lines 263-265) recommends the use of "appropriate equipment that will not contaminate the product or otherwise be reactive, additive, or absorptive with the products and that is properly

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maintained, calibrated, cleaned, and sanitized at appropriate intervals following written procedures.”

We recommend that the description from Lines 263-265 be included in Line 173 to help define “adequately controlled,” or that a cross-reference to lines 263-265 be inserted.

Clarification of “QC plan”

Clarification is requested regarding the interpretation of “QC plan” as used in Line 226, which states, “We recommend that every producer establish a QC plan and document that plan in writing.” Based on the examples provided, it appears that the “QC plan” is specifically related to the Quality Control/Quality Assurance roles and responsibilities.

We recommend that Line 226 be revised to, “We recommend that every producer establish written procedures that delineate the roles and responsibilities of the Quality Control/Assurance functions....”

Clarification of “equipment qualification”

Clarification is requested regarding the interpretation of “qualifying” equipment with respect to the recommendations in this guidance. This term is used in several sections but the document does not include examples to clarify how ‘equipment qualification’ should be interpreted.

We recommend that the Glossary (Line 555) be revised to include a definition for “Equipment Qualification” including specific examples of how this may be interpreted for Phase 1 development.

We recommend that Lines 184-185 (Section V. Recommendations for Complying with the Statue) be revised to add an example to clarify how “qualifying” should be interpreted in this section. This clarification may also be accomplished by including examples in the Glossary within a new “Equipment Qualification” definition.

We recommend that Line 538 (Section VI. D. Sterile Products/Aseptically Processed Products) be revised to add an example to clarify what is meant by “qualifying” in this section. This clarification may also be accomplished by including examples in the Glossary within a new “Equipment Qualification” definition.

Clarification of “internal performance reviews”

Clarification is requested regarding the interpretation of “internal performance reviews” as used in Section VI.C.4 Lines 498-499, “When producing multiple batches of the same investigational product, we recommend that producers periodically conduct and document internal performance reviews.” Examples are

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provided to provide clarification on the type of information that should be assessed however, it is unclear if this is intended to mean the same as "annual product reviews", as these are typically not performed on investigational products, especially at Phase 1 development. Moreover, the rationale for recommended internal performance reviews should be provided because in most cases only a small number of batches are produced for phase 1 clinical studies.

Please confirm, "internal performance reviews" are not intended to mean the same as "annual product reviews".

Guidance on segregation of live biological, viral or attenuated type products

Additional guidance is requested for the manufacture of live biological, viral or attenuated type products. While Section VI.C addresses many considerations for biological and biotechnical products it does not include guidance on adequate segregation of live biological, viral or attenuated type products.

We recommend the addition of specific guidance on the expectations for segregation of live biological, viral or attenuated type products during production of investigational materials for phase 1 studies, for example addition of the statement "there shall be adequate segregation of materials and intermediates which are part of the manufacture of live biological, viral or attenuated organism type products" into Lines 462-465.

We are submitting the above comments in duplicate. Wyeth appreciates the opportunity to comment on the above mentioned draft guidance and trusts that the Agency will take these comments into consideration.

Sincerely,



Roy J. Baranello
Assistant Vice President
Regulatory Policy and Operations
Worldwide Regulatory Affairs