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Wyeth

August 19, 2004

Food and Drug Administration
Division of Dockets Management
5630 Fishers Lane; Room 1061
Rockville, MD 20852

**RE: Docket No. 2004N-0194, Proposed Rule on Definition of
Primary Mode of Action of a Combination Product, 69 FR
25527-33, May 7, 2004**

Dear Sir/Madam:

Wyeth Pharmaceuticals is one of the world's largest research-based pharmaceutical and healthcare products companies and is a leading developer, manufacturer and marketer of prescription drugs, vaccines, biopharmaceuticals, and other health care products. We are hereby providing comments on the above-referenced proposed rule to modify the combination product regulations found at 21 CFR Part 3.

Wyeth agrees with the basic objectives of the proposed rule and with many of the proposed changes to 21 CFR Part 3. However, Wyeth has the following comments on certain aspects of the proposed rule.

Clarification That Previously-Assigned Products Will Not Be Affected By the Newly-Defined Assignment Algorithm

FDA stated that the proposed rule merely clarifies and codifies principles the agency is already using to assign products. Given this, we do not believe it is the agency's intent to re-assign products based on the assignment algorithm FDA is proposing to codify. Such reassignment would be very disruptive to the development of these novel products; this is true from both the sponsor's and the agency's perspectives.

Therefore, Wyeth requests that FDA clarify, either in the final regulations or in the preamble accompanying the final rule, that the newly codified assignment algorithm is not to be applied retroactively to previously assigned combination products unless so requested by a Sponsor.

2004N-0194

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The Need to Maintain Due Consideration of the Sponsor's Viewpoints in the Assignment of Combination Products

Request for Designation submissions are typically made very early in a product's development; at this early point, the sponsor will normally have the greatest understanding of the mechanism(s) of action of their products. This factor, among others, led the agency to grant significant weight to sponsors' viewpoints on the assignment of their products (e.g., refer to the extant regulations at 21 CFR Part 3.7(c)(3), 3.8(b), and 3.8(c)).

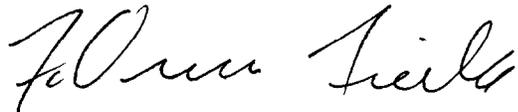
It is also important to note that the assignment of combination products to an agency component often has significant practical implications for sponsors. Most drug and device companies have made major human resource, information system, and other investments in order to be able to efficiently comply with regulatory requirements and procedures during the investigational period (IDE vs. IND phase), approval period (PMA vs. NDA/BLA review), and post-marketing period (Quality System Regulations vs. cGMPs and drug vs. device adverse event reporting). The drug and device regulatory procedures share the same basic objectives; however, for historical, legal, and practical reasons the regulatory procedures for these product types are different. Some business practices in the drug and device industries also differ. Given this, product jurisdiction assignments can result in drug or device companies having to follow unfamiliar regulatory and business practices. The resulting need to adapt company systems and procedures to unfamiliar regulatory and business procedures could be predicted to cause delays in the development, approval, and availability of potentially important new medical products.

Such considerations must clearly be subordinated to ensuring the optimal scientific review of medical products. However, for some highly novel products the agency's proposed algorithm may not lead to a clear rationale for assignment to a given agency component. In such cases, we believe that the viewpoints of the sponsor on the assignment of their product should be given considerable weight. We realize that 21 CFR 3.8(b) (which defaults jurisdictional assignments to the sponsor's recommendation if the Agency has not made a determination in 60 days) will remain in the regulations. However, we also believe that the proposed rule is inadequate in that it lacks a reliable mechanism for incorporating the sponsor's views into the decision algorithm.

Wyeth

Please contact the undersigned at 484-865-3733 if there are any questions on these comments.

Sincerely,

A handwritten signature in black ink that reads "F. Owen Fields". The signature is written in a cursive style with a large initial "F" and a long, sweeping underline.

F. Owen Fields, Ph.D.

Director

Worldwide Regulatory Affairs