PRODUCT JURISDICTION – NEW DEVELOPMENTS

PRIMARY MODE OF ACTION FINAL RULE

On August 25, 2005, FDA issued a final rule amending its combination product regulations to define "mode of action" and "primary mode of action" (PMOA) to be used in assigning a combination product to an agency component, i.e., CDER, CBER, or CDRH. 70 Fed. Reg. 49,848. The final rule also sets forth a two-tiered assignment algorithm to be used to determine assignment when FDA cannot determine with reasonable certainty which mode of action of a combination product provides the most important therapeutic action of the product.

"Mode of action" is defined as "the means by which a product achieves its intended therapeutic effect or action." 21 C.F.R. § 3.2(k). A product may have a drug, biological product, or device mode of action. Because a combination product is comprised of more than one type of regulated article, and each constituent part contributes a mode of action, a combination product will typically have more than mode of action. PMOA is defined as "the single mode of action of a combination product that provides the most important therapeutic action of the combination product. The most important therapeutic action is the mode of action that is expected to make the greatest contribution to the overall intended therapeutic effects of the combination product." Id. § 3.2(m). When FDA cannot determine with reasonable certainty which mode of action is the PMOA, the first tier of the two-tiered assignment algorithm provides that FDA "will assign the combination product to the agency component that regulates other combination products that present similar questions of safety and effectiveness with regard to the combination product as a whole." Id. § 3.4(b). When no combination products present similar questions of safety and effectiveness regarding the combination product as a whole, "the agency will assign the combination product to the agency component with the most expertise related to the most significant safety and effectiveness questions presented by the combination product." Id.

When submitting to the agency a request for designation (RFD), the sponsor of the combination product must include in the RFD, among other things, a description of all known modes of action of the combination product, the sponsor's identification of the PMOA, and the sponsor's recommendation as to which agency component should have primary jurisdiction for the combination product. Id. § 3.7(c)(2)(ix), (3).

FDA emphasized in the preamble to the final rule that the rule applies only to the assignment of combination products to the appropriate agency component – it does not dictate the regulatory authorities to be applied to a combination product's review and regulation once it has been assigned to an agency component.

FDA stated that the rule will codify criteria FDA has generally used since 1990. In response to questions about the role of the Intercenter Agreements, which were developed in 1991, FDA confirmed that the Intercenter Agreements "continue to provide helpful guidance related to product jurisdiction, including the assignment of some types of combination products." However, FDA noted that the Intercenter Agreements do not address many types of combination products developed since 1991. Moreover, because the Intercenter Agreements may describe broad categories of products and because the PMOA for combination products within a broad category may vary based on specific characteristics and use, the Intercenter Agreements may not be appropriate for every combination product within a broad category.

The final rule will apply to RFD submissions received by FDA on or after the effective date of the rule, which is November 23, 2005.

link to pdf of Federal Register Notice:
http://www.fda.gov/OHRMS/DOCKETS/98fr/05-16527.pdf

GUIDANCE

In August and September 2005, the following documents were posted on the Office of Combination Products (OCP) website: a guidance document for industry and FDA staff regarding "How to Write a Request for Designation" and a jurisdictional update regarding the Intercenter Agreements. The RFD guidance document provides details for the submission of an RFD in a question and answer format.

The Intercenter Agreement jurisdictional update discusses the role of the Intercenter Agreements and the other resources available to provide transparency on the process for jurisdictional determinations. FDA stated that it does not intend to update the Intercenter Agreements because any revisions would be time-consuming and likely outdated nearly as fast as they could be published. Instead, FDA believes that transparency of the process would be better served by "clearly articulating the principles upon which jurisdictional determinations are based, and by providing specific examples of jurisdictional determinations that help illustrate these principles." To this end, FDA recently made available on the OCP website a list of approximately 140 "capsular descriptions of selected RFD decisions." http://www.fda.gov/oc/combination/determinations.html FDA has also made available on the OCP website jurisdictional updates for a variety of product classes. These updates are more detailed statements of the classification and assignment of product classes and reflect past FDA decisions. FDA selects product classes to be the subject of jurisdictional updates based on FDA's "perceptions of the current level of interest in the jurisdictional issue, the extent to which the class of products can be clearly described, the extent to which the existence and description of the class of products has been made public, and related factors."

http://www.fda.gov/oc/combination/updates.html FDA has also recently posted on the OCP website RFD decision letters for products that have been approved or cleared (redacted to remove trade secret and confidential information). http://www.fda.gov/oc/combination/rfd.html

REQUEST FOR COMMENTS

In September 2005, OCP issued requests for comments on two topics: (1) post-market adverse event reporting and (2) determining the number of marketing applications for combination products. For each topic, FDA published on its website a concept paper to stimulate public input. http://www.fda.gov/oc/combination/reqcomm905.html

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If you have any questions about any of these developments or product jurisdiction generally, please contact Michelle Butler or Jennifer Davis.