Combination Products Coalition

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April 2, 2014

Margaret A. Hamburg, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: FDA Draft Guidance for Combination Product Good Manufacturing Practices

Dear Commissioner Hamburg:

The Combination Products Coalition[1] (the "CPC") requests that FDA publish guidance for Combination Product Good Manufacturing Practices as soon as possible. The need for such guidance is critical because FDA has already started to enforce new, and often unclear, regulatory requirements based on the final rule. We urge FDA to publish draft guidance within the next month or two so that our members, as well as other combination product manufacturers, (1) gain insight into FDA's current thinking and (2) have the opportunity to participate, through the Good Guidance Process, in developing standards that are reasonable and clear to ensure optimal compliance with the final rule.

Although the final rule addressed some of the issues the CPC raised following publication of the proposed GMP rule in 2009, many ambiguities remain. For instance, the final rule requires manufacturers to bring products already on the market into compliance with pre-manufacturing design controls, however, the final rule is silent on how manufacturers should accomplish this and exactly what documentation would be required by FDA. Instead, FDA noted that this issue would be addressed in the still pending guidance. Additionally, in the final rule, FDA noted that there is a difference between a co-packaged combination product and a "convenience kit." The final rule went on to say that no additional GMPs would apply to "off-the-shelf" devices that are included in convenience kits, if such devices are packaged and labeled in accordance with their existing marketing authorizations. However, the final rule does not explain how a manufacturer would determine when a convenience kit becomes a co-packaged combination product, thus triggering additional GMP requirements.[2]

[1] Founded in 2003, the Combination Products Coalition ("CPC") is an association of leading drug, biotech, medical device and diagnostic companies dedicated to improving regulation of combination products.

[2] For example, if a manufacturer co-packages a drug with a Class I device that is exempt from GMPs and design controls, and is not labeled for individual sale (e.g., Liquid Medication (KYX), ENT Syringe (KCP)

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It has been over a year since FDA published the final rule and more than six months since the rule became effective, and Combination product manufacturers are still without the guidance they need to ensure compliance. However, FDA has already taken enforcement action citing combination product GMP issues. Such enforcement action is unfair to the combination product industry because FDA has not yet provided adequate clarification on critical GMP compliance issues, and manufacturers cannot be expected to fully comply without understanding the standards to which FDA will hold them. We urge FDA to publish the guidance as soon as possible to ensure that manufacturers may fully comply with the final rule.

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We appreciate your consideration of our request and look forward to the publication of the combination product GMP Guidance.

Yours truly,

Bradley Merrill Thompson
On behalf of the Combination Products Coalition

cc: Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research
Jeffrey E. Shuren, M.D., J.D., Director, Center for Devices and Radiological Health
Karen Midthun, M.D., Director, Center for Biologics Evaluation and Research
Sally Howard, J.D., Deputy Commissioner for Policy, Planning, and Legislation
Jill Warner, J.D., Acting Associate Director, Office of Special Medical Programs
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or ENT dropper (KCM)), would additional GMP requirements apply (e.g., design controls to ensure that the device is appropriate for the specific use to which it is put in the combination product) or are there sufficient elements within the GMPs that would ensure that the manufacturer develops information to demonstrate that the finished product is safe and effective for its intended use?