



July 23, 2010

VIA ELECTRONIC SUBMISSION

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

Re: Comments on Draft Guidance for Industry and Food and Drug Administration Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions; Availability; Docket No. FDA-2010-D-0194

Dear Sir or Madam:

The Combination Products Coalition (“CPC”) is pleased to offer its comments on the *Draft Guidance for Industry and Food and Drug Administration Staff; Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions*. Our comments focus on specific areas of the draft guidance that may intersect with policy development on combination products. We ask that the Agency consider these potential impacts as it finalizes the guidance.

By way of background, the CPC is a group of leading drug, biological product, and medical device manufacturers with substantial experience and interest in the combination products area. One of the principal goals of our organization is to work with the Agency on issues affecting combination products, in order to advance our common missions of providing the best possible health care for patients. Because of our diverse, cross-industry membership, we think the CPC brings a broad and unique perspective to issues affecting combination products.

As an initial matter, we want to commend the Agency on the stakeholder outreach and discussion it has conducted with respect to the infusion pump issues under consideration. We believe dialogue such as this is a critical factor in developing policy that is beneficial for patients, the Agency, and the industry. We strongly urge the Agency to continue this type of outreach and discourse as it finalizes the guidance and develops other regulations, policy, and guidance documents.

We have a general comment and several specific comments on the draft guidance.

General Comment

In terms of the guidance's substance, we agree with the general principles in the guidance concerning the information and data that should be submitted in a premarket notification submission for an infusion pump. At a high level, the approach the guidance articulates should enable applicants to pursue indications in an appropriately efficient manner, thereby facilitating patient access to these important technologies.

However, we believe the Agency should clarify that the guidance document relates to non-combination products only. As explained below, some of the concepts in the guidance could be misinterpreted as applying to drug-device or biological-device combination products, but this would not be an appropriate result, as the long-standing regulatory position of both the agency and industry is that infusion pumps and the drugs or biological products they dispense are not considered combination products under the definition in 21 CFR § 3.2(e).¹

This overall clarification is warranted in many specific instances, as explained in more detail below.

Specific Comments

Below follow the CPC's specific comments on the guidance. For ease of reference, our comments refer to the line-numbered version of the guidance.

- 1. Page 7, lines 7-9: "If the infusion pump is labeled for use with a specific device, drug, or biologic, you should provide information demonstrating that this use is consistent with the FDA approved labeling for that device, drug or biologic."**

We believe the guidance should clarify this statement to ensure it is not interpreted to mean that such drug/pump systems are combination products. This will avoid any inadvertent impact on regulatory policy for cross-labeled and other combination products. We specifically recommend the guidance include a clear explanation that it is not intended to encompass combination products, including cross-labeled combination products that are defined in 21 CFR § 3.2(e)(3).

The guidance also should clarify what information is required to demonstrate that the proposed use of the infusion pump is "consistent with" the FDA-approved labeling for the device, drug, or biologic with which it will be used. The concept of a new yet consistent use is

¹ See e.g., FDA, Intercenter Agreement Between the Center for Drug Evaluation and Research and the Center for Devices and Radiological Health (Oct. 31, 1991), available at: <http://www.fda.gov/CombinationProducts/JurisdictionalInformation/ucm121177.htm> (last accessed June 17, 2010) (This document provides several examples of separate (non-combination product) drug and device entities, including: drug delivery pump and/or catheter infusion pump for implantation) ; see also 56 Fed. Reg. 58754, *Assignment of Agency Component for Review of Premarket Applications* (Nov. 21, 1991) (The Preamble explains: "[T]he definition of a combination product is intended to exclude most concomitant use of drugs, devices, and biological products.")

not foreign to the Agency,² but to be truly useful, the guidance should elaborate on its meaning in this instance.

- 2. Page 7, lines 11-14: "For each route of administration identified in your statement of intended use, you should identify an FDA approved drug or biologic to demonstrate that at least one such product is approved for infusion through the proposed route of administration and at the proposed dosage." This recommendation also appears on page 22, lines 22-26.**

We are unclear on how this statement in the guidance is interpreted consistently with the language quoted in our first comment, specifically: "If the infusion pump is labeled for use with a specific device, drug, or biologic, you should provide information demonstrating that this use is consistent with the FDA approved labeling for that device, drug or biologic." (Emphasis added.) The statement at lines 11-14 seems to go farther and suggest that each route of administration in the infusion pump must conform exactly to the labeling of an approved drug or biological product. We believe that this goes too far. In practice, often the labeling for drugs or biological products administered through infusion are not labeled specifically for infusion, let alone at a specific dosage for infusion (e.g., X mL within Y hours). We believe a more practical approach – and one that will ensure the safety and efficacy of the products' intended purposes – is to recommend that the premarket submission provide information demonstrating that the dosage level is consistent with the level specified in the drug labeling.

Additionally, similar to our first comment, without a clarification that the guidance does not apply to combination products, this language in the guidance causes confusion about whether the guidance intends to encompass combination products within its scope. As noted earlier, we believe that it should not.

- 3. Page 30, lines 2-13: The guidance recommends that the labeling of pumps containing reservoirs include information regarding the stability and compatibility of certain fluids with the device. The guidance suggests that "[a]ll recommendations regarding the fluids should be consistent with the manner in which FDA has approved those products." In this regard, the guidance suggests that the infusion pump labeling would include the following statement: "Before using different [fluid(s)] with this pump, check the [fluid(s)] label to make sure it can be used with the pump."**

Our comments above pertaining to the necessary elaboration on the meaning of the words "consistent with" also apply here.

Additionally, the guidance document should substantially revise the recommended included statement "... check the [fluid(s)] label to make sure it can be used with the pump." Typically drug and biological product labeling does not reach this level of specificity on stability

² Draft Guidance for Industry: New Contrast Imaging Indication Considerations for Devices and Approved Drug and Biological Products (Dec. 2009).

and compatibility with respect to equipment that can be used with the drug or biological product. Further, some drugs have proprietary assays that would not allow the pump manufacturer access to such stability and compatibility information. In these cases, it would be impossible to include information on the stability and compatibility of the drug or biological product with the device, unless it is a USP method. With this in mind, we recommend this labeling disclaimer be revised as follows: “Before using different [fluid(s)] with this pump, check the [fluid(s)] label to ensure there are no contraindications for or warnings regarding use of the [fluid(s)] with the pump.”

Finally, we believe the guidance should clarify that this recommendation would not apply to a pump reservoir that is available off-the-shelf.

4. Page 30, lines 31-37. The guidance addresses home use labeling.

The draft guidance does not clearly and comprehensively address what the manufacturer should include in the home use instructions. We believe the guidance should incorporate additional guidance or, at minimum, should reference existing agency requirements and guidance on device labeling for patients and home use in order to clarify the Agency’s expectations with respect to these products.³

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We hope that our comments are helpful to the Agency as it finalizes the guidance. If the CPC can help in any way, please do not hesitate to contact us.

Respectfully submitted,



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³ FDA, CDRH, *Guidance on Medical Device Patient Labeling* (Apr. 19, 2001); FDA, CDRH, *Write it Right: Recommendations for Developing User Instruction Manuals for Medical Devices Used in Home Health Care* (Aug. 1993).