Devices Proposed for a New Use with an Approved, Marketed Drug; FDA Public Hearing

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Purpose and Scope of the Public Hearing

The purpose of the public hearing was to obtain comment from stakeholders on the potential approach described below, for premarket review of devices referencing drugs (DRDs).

The approach described below might be appropriate, for example, for **drug delivery systems seeking to be labeled for use with an approved drug, for an indication for which that drug has not been approved** (e.g., to administer the drug to treat a different disease or condition or a new patient population).

The comments that FDA receives from this public hearing may help inform the further development of this approach.

Background

Medical products are often intended and labeled for use in conjunction with other medical products marketed by different sponsors. In some cases, the medical products are of different types (such as drug and device, biological product and device, or drug and biological product). Typically, the different sponsors collaborate when the two products are to be used together for a new intended use.

Sometimes, however, sponsors seek marketing authorization from FDA for a medical product for a new use with the approved, marketed medical product of another sponsor (*i.e.,* not included in the labeling for the approved, marketed product), and the sponsor of the approved, marketed product **does not** wish to pursue the new use or work with the other product sponsor.

In FDA's experience, the device referencing drugs (DRD)s may be proposed:

(1) To **enhance the safety or effectiveness** of the marketed drug for its already approved indication;

(2) for use with the approved drug **for an indication for which the drug is not approved**; or

(3) to provide some other benefit, such as increasing user comfort or convenience. Such new uses have generally also involved a change in **how the drug is used or administered**, such as a change in dose, route, or rate of administration.

DRDs have the potential to advance the public health by offering new uses with approved, marketed drugs that might not otherwise be developed, because the drug sponsor does not wish to pursue the new use. At the same time, DRDs raise unique public health, scientific, regulatory, and legal issues.

FDA has gained greater experience with these issues and believes that many of these issues for DRDs could be addressed under the approach described below.

A Potential Approach for Premarket Review of DRDs

When sponsors work together, they usually have an ongoing relationship that enables them to resolve many of the public health, scientific, regulatory, and legal issues that may arise as a result of two products being the responsibility of two independent sponsors. However, where collaboration between sponsors is not feasible, for example, because one sponsor does not wish to collaborate, FDA believes that the following factors could help address many of the public health, scientific, regulatory, and legal issues associated with DRDs.

In doing so, these factors could allow for a DRD to be reviewed and approved via **a device premarket authorization pathway** without approval of conforming labeling changes for the approved, marketed drug through a new drug application (NDA) or supplement to an NDA.

Factors:

DRD sponsors should be able to address the following issues as discussed below:

1. Safety and Effectiveness of the New Use of the Drug. The DRD sponsor is able to demonstrate the safety and effectiveness of the new use of the drug that is included in the DRD labeling, by providing substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use described in the proposed DRD labeling and showing that the drug is safe for use under the conditions prescribed.
2. User Confusion and Medication Error/Use Error. Given the potential for user confusion or medication error/use error, for example, due to certain differences in the labeling for the DRD and the approved drug that it is referencing, the DRD sponsor is able to demonstrate that the potential for user confusion or error has been adequately addressed. The DRD labeling must provide adequate directions for the new use with the approved, marketed drug.
3. Postmarket Change Management. The DRD sponsor is able to demonstrate that it is able to address safety or effectiveness issues associated with changes to the approved, marketed drug, for example, by demonstrating: That the likelihood of changes to the approved, marketed drug is low; changes to the drug are unlikely to raise safety or effectiveness issues with respect to the conditions of use with the drug as described in the DRD labeling; and periodic testing will be conducted and be adequate to assure ongoing safety and effectiveness of the combined use.
4. Postmarket Safety. The DRD sponsor is able to demonstrate that it has a postmarket safety plan to adequately address adverse events, including medication errors, related to the drug when used with the DRD.
5. Data Reliance. The DRD sponsor is able to provide all information needed to evaluate the safety and effectiveness of the new use with the approved drug referenced in the DRD labeling, without relying on any proprietary information for the approved drug (e.g., by instead relying on non-product-specific published literature, generalizable knowledge).

Submission Considerations

At the investigational stage, depending on the details of the investigational plan, a DRD sponsor may seek to submit an investigational new drug application (IND) or an investigational device exemption application (IDE). FDA believes that a PMA would generally be the appropriate device marketing application because, e.g., DRDs are expected to represent a new intended use or raise different questions of safety or effectiveness as compared to a legally marketed predicate device.

Questions for Commenters to Address

FDA welcomed all feedback on the potential approach and on any public health, scientific, regulatory, and legal issues raised by it. Below are some of the proposed questions in an effort to prompt substantive input from stakeholders:

- Are there public health, scientific, regulatory, or legal issues that should be considered with respect to this potential approach for DRDs? If so, are there ways to address those issues?
- Is each of the factors and submission considerations described above appropriate? If not, why not? What modifications would you propose and why? Are there additional factors or submission considerations that the Agency should take into account?
- Should the approach described in this notice be limited to certain situations, such as where the combined use would potentially address an unmet medical need for a serious or life-threatening condition?
- With respect to the user confusion and medication error/use error factor, are there other issues that DRD sponsors should address or that FDA should consider, to ensure that the DRD labeling provides adequate directions for the new use with the approved, marketed drug, without approval of conforming labeling changes for the approved, marketed drug? What issues should be considered with respect to promotional activities by the DRD sponsor and/or by any sponsors for the drug being referenced?
- With regard to the postmarket change management factor, what would be examples of circumstances in which the DRD sponsor would be able to adequately address this factor? What types of postmarket changes to the drug should the DRD sponsor be prepared to identify and address? What postmarket mechanisms, including specific testing or monitoring, would be appropriate to ensure ongoing safety and effectiveness of the combined use?
- When multiple versions of the drug, including generics, are marketed, what challenges exist in identifying which versions of the drug can be used with the DRD? How can DRD sponsors make this information clear to health care providers, pharmacists, and patients?
- Are there other possible approaches that may be used to seek marketing authorization for combined uses of drugs and devices where product sponsors are unable or unwilling to collaborate?