release tablets, 10 mg, may be approved by the agency.

Dated: March 17, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2005N–0098]

Food and Drug Administration/Drug Information Association Cross Labeling; Public Meeting; Combination Products and Mutually Conforming Labeling

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public meeting; request for comments.

SUMMARY: The Food and Drug Administration (FDA), in cooperation with the Drug Information Association (DIA), is announcing a public meeting to solicit views and provide an interactive forum for discussion of stakeholders' perspectives about, and experiences with, the legal and public health issues that arise when sponsors seek to develop or market a product of one type (device, drug, or biological product) that would be labeled for use with an already approved product of a different type, and the approved product's labeling would not be changed. The input received at the meeting and comments made to the docket after the meeting will be considered in developing draft guidance on this topic.

DATES: The public meeting will be held on May 10, 2005, from 8:30 a.m. to 5 p.m. Attendees must register to attend. Submit written or electronic requests to speak at the public meeting by April 26, 2005. Submit written or electronic comments by July 8, 2005.

ADDRESSES: The public meeting will be held at the Bethesda North Marriott Hotel & Conference Center, 5701 Marinelli Rd., North Bethesda, MD. A copy of the meeting's program and registration information is available on the Internet at*http://www.diahome.org/Content/Events/05028.pdf*, by contacting the Drug Information Association, P.O. Box 827192, Philadelphia, PA 19182–7192, or 215–442–6100.

Submit written comments to the Division of Dockets Management (HFA–305, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*.

FOR FURTHER INFORMATION CONTACT:

For information about the public meeting contact: Suzanne O'Shea, Office of Combination Products, Food and Drug Administration (HFG–3), suite 200, 15800 Crabbs Branch Way, Rockville, MD 20855, 301–427–1934, FAX: 301–427–1935, e-mail: *combination@fda.gov*.

To register to speak at the public meeting contact: Amanda Carmody, Drug Information Association, P.O. Box 827192, Philadelphia, PA 19182–7192, e-mail: *Amanda.carmody@diahome.org*, or 215–442–6176.

SUPPLEMENTARY INFORMATION:

I. Background

An increasing number of combined uses for drugs and devices, drugs and biological products, or devices and biological products are being developed where the two products are independently approved, manufactured, and distributed. In some cases, when one product is already approved for a particular indication, route of administration or dose, another sponsor may develop a separate product to be used with the approved product for an indication, route of administration or dose different from the one specified in the current labeling of the approved product. Frequently, the sponsors of the two products work together to develop safety and effectiveness data and to bring the two products to market with mutually conforming labeling, i.e., labeling for each product that provides directions for using that product with the other sponsor's product. In such cases, the two products are considered a combination product under § 3.2(e)(3) (21 CFR 3.2(e)(3)), which states that a combination product includes:

> A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant changed in dose* * *.

In order for the two products to have mutually conforming labeling of the type contemplated by § 3.2(e)(3), the sponsor of the approved product ordinarily must submit a supplement to its marketing application[1] to amend the currently approved labeling to include directions for using the two products together. When sponsors work together to develop mutually conforming labeling, they usually have an ongoing relationship that enables them to resolve scientific or legal issues that may arise as a result of the two products being the responsibility of two independent sponsors. For this reason, FDA encourages sponsors to work together as much as possible when bringing to market independently developed, manufactured, and distributed products that are intended to be used together.

On occasion, however, the two sponsors do not work together, and the sponsor of a new product unilaterally develops a product intended to be used with an already approved or cleared product. The sponsor of the new product is frequently willing to develop data demonstrating the safe and effective use of both products used together. When the new product is intended to be used with the approved product in a way that is significantly different from ways described in the current labeling of the approved product (e.g., for a different indication, route of administration or dose), refusal by the sponsor of the approved product to submit a supplement[2] may preclude mutually conforming labeling. In some cases, when the two sponsors do not work together, requiring that the two products have mutually conforming labeling could prevent the development of new products. FDA is concerned that valuable products may not be developed, manufactured, or distributed because of sponsor concerns about mutually conforming labeling.

Therefore, FDA is considering whether the agency should review and approve or clear drug-device, biologic-device, or drug-biologic products, where:

- One sponsor's new product is intended for use with another sponsor's approved or cleared product;
- The approved or cleared product would be used in a way that is significantly different from the use described in its current labeling, e.g., a different indication, route of administration, or dose;
- Data are available to demonstrate the safe and effective use of the two products together;
- There is no cooperation, ongoing relationship, or right of reference between the sponsors of the two products; and
- The sponsor of the new product asks FDA to review the new product for use with the approved product under

[1] In some cases, a new 510(k) might be required.

[2] Or in some cases, a new 510(k).

one drug, device, or biological product marketing application, depending on the regulatory identity of the new product.

In this situation, the sponsor of the approved product would not submit a supplement to its marketing application, or in some cases a new 510(k), to permit the inclusion of directions for using the approved product together with the new product. If the new product were to be approved or cleared, the labeling of the new product would provide directions for using the two products together, but the labeling of the approved product would not mention the new product or the use of the two products together. In other words, the two products would not be cross labeled and would not have mutually conforming labeling.

II. Hypothetical Situation

The following hypothetical is a concrete example of the type of situation that may be of most interest at the public meeting:

Company A[3] is currently marketing an approved drug product for intramuscular injection. Company B develops a device to deliver Company A's approved drug product for a different indication, to be delivered by a different method. No change in formulation to the drug product is needed.

Company B approached Company A to see if Company A would submit a supplemental new drug application to include the new indication and route of administration in the drug product labeling, but Company A refused. Company A also refused to provide a right of reference to data in its application.

Because Company B has been unable to obtain the cooperation of Company A, Company B approaches FDA and asks whether FDA would consider approving a device application stating that the device is intended to be used with drug product A delivered by the new route of administration for the new indication. Company B is willing to conduct all necessary studies to demonstrate that drug product A is safe and effective when delivered by the new route of administration by device B for the new indication.

The end user would obtain the device from Company B and the drug product from Company A. The drug product labeling would make no mention of device B, the new indication, or that the drug product can be delivered by the new route of administration.

III. Proposed Issues

The core issue is whether FDA should consider reviewing and possibly approving or clearing a new product (such as product B in the hypothetical) labeled for use in conjunction with an approved product (such as product A in the hypothetical) when there is no supplement for the combined use to the marketing application for the approved product,[4] and the labeling of the approved product would not mention the new product, or the use of the two products together. FDA has identified the following issues as being relevant to the core issue. Persons wishing to speak at the public meeting may address the following issues or other relevant issues.

A. Public Health Issues

1. What are the product development implications of mutually conforming labeling? Are products not developed because of a perception that mutually conforming labeling will be, or might be, required?

2. How important is it that drug and device labeling be consistent with respect to intended use, dose, dosage form, strength and route of administration for the safe and effective use of the drug and device together?

3. Should the decision whether mutually conforming labeling is needed for the safe and effective use of the products together be made on a case by case basis? If so, what factors should FDA consider in determining whether mutually conforming labeling is necessary?

4. To what degree should labeling conform? Does the labeling of the two products need to be identical? Consistent? Not contradictory? Is conformity more important for some parts of the labeling than others?

5. Under what circumstances can adequate instructions for use be conveyed in one product's label? For example, should FDA policy take into account the possibility that the labeling for a re-usable device might be lost over time?

6. How should FDA policy take into account the possibility that the product for which no supplemental marketing application was submitted (i.e., the approved product) might be reformulated or redesigned? Is it possible for Company B to sufficiently monitor product A to ensure that Company B is aware of formulation changes? Is it possible to identify in advance the characteristics of product A that should be monitored?

7. If mutually conforming labeling is not always required, what process should FDA follow in order to determine when it is required and when it is not required? When is the best time in the review process to make this determination?

8. Other public health issues; how can they be resolved?

B. Legal Issues

1. Why do manufacturers of the two products sometimes not cooperate in bringing the new product to market? Are there any steps FDA can take to increase the likelihood of cooperation between the two manufacturers?

2. How can FDA ensure that its approval of Company B's product does not improperly rely upon Company A's proprietary information?

3. How might approval of Company B's product affect the legal adequacy of the labeling for Company A's product?

4. What effect, if any, should the exclusivity of Company A's product have on whether FDA approves Company B's product without mutually conforming labeling? Should the existence of generic versions of Company A's product affect whether FDA approves Company B's product?

5. Would any other regulatory tools, such as conditions of approval on Product B, be useful in ensuring the appropriate degree of FDA oversight of the products used together?

6. Do the legal issues that arise in the absence of mutually conforming labeling exist independently of § 3.2(e)(3), or can some of these issues be addressed by revisions or clarifications to this part of the definition of a combination product?

7. Other legal issues; how can they be resolved?

IV. Goals of the Public Meeting

The purpose of this public meeting is to provide an interactive forum for discussion of FDA and industry perspectives about, and experiences with, the legal and public health issues that arise when sponsors seek to develop or market a product of one type (device, drug, or biological product) that would be labeled for use with an approved product of a different type and the approved product's labeling would not be changed.

The public meeting will be divided into two sections. Public health issues will be discussed in one session; legal issues will be discussed in the other session. Each session will begin with

[3] Companies A and B could be drug, device, or biological product companies. The two products that will be used together could be a drug and a device, a drug and a biological product, or a biological product and a device. For the sake of convenience only, this hypothetical refers to Company A as the manufacturer of an already approved drug, and Company B as the sponsor of a device to be used with drug product A.

[4] Or in some cases, a new 510(k).

formal presentations from members of industry and FDA. Following the formal presentations, time will be allotted to hear from members of the public who have pre-registered as speakers. After the pre-registered speakers, there will be a moderated discussion open to all members of the audience.

FDA is considering issuing draft guidance on this issue and believes it is important to receive input from all interested parties through a public meeting.

V. Speakers

Members of the public who would like to make a short statement (approximately 5 minutes) should register with DIA (see **ADDRESSES**) by April 26, 2005. Requests to speak should include the speaker's name and affiliation, and should identify the appropriate panel (public health or legal issues). DIA will notify persons who register by April 26, 2005, of the approximate time of their turn to speak. Speakers will be scheduled in the order DIA receives the requests.

If you need special accommodations due to a disability, please contact, at least 7 days in advance: Amanda Carmody, Drug Information Association, at *Amanda.carmody@diahome.org* or 215–442–6176.

VI. Request for Comments and Transcripts

Regardless of attendance at the meeting, interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the topics presented in this document. The agency welcomes comments before and after the meeting. Two paper copies of mailed comments are to be submitted, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday. Comments and a transcript of the public meeting will be made available on the Office of Combination Products Web site at *www.fda.gov/oc/combination*.

Dated: March 21, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2005D–0103]

Draft Guidance for Industry on Using a Centralized Institutional Review Boards Process in Multicenter Clinical Trials; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Using a Centralized IRB Process in Multicenter Clinical Trials.'' The draft guidance is intended to assist sponsors, institutions, institutional review boards (IRBs), and clinical investigators involved in multicenter clinical research in meeting the requirements of FDA's regulations by facilitating the use of a centralized IRB review process.

DATES: Submit written or electronic comments on the draft guidance by May 27, 2005. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; or the Office of Communication, Training and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448. Send one self-addressed adhesive label to assist that office in processing your requests.

Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT:

Nancy Stanisic, Center for Drug Evaluation and Research (HFD–1), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1660; or

Steve Ripley, Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–6210, 301–827–7975; or

Dave Lepay, Good Clinical Practice Program, Office of Science and Health Coordination (HF–34), Office of the Commissioner, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3340.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a draft guidance for industry entitled ''Using a Centralized IRB Review Process in Multicenter Clinical Trials.'' The draft guidance is intended to assist sponsors, institutions, IRBs, and clinical investigators involved in multicenter clinical research in meeting the requirements of 21 CFR part 56 by facilitating the use of a centralized IRB review process. The draft guidance: (1) Describes the roles of the participants in a centralized IRB review process; (2) offers guidance on how a centralized IRB review process might address local aspects of IRB review; (3) makes recommendations about documenting agreements between a central IRB and the IRBs at institutions involved in the centralized IRB review process concerning their respective responsibilities; and (4) makes recommendations concerning written procedures for implementing a centralized review process. Finally, the draft guidance discusses using a central IRB at clinical trial sites not already affiliated with an IRB.

This draft guidance applies to clinical investigations conducted under 21 CFR part 312 (investigational new drug application or IND regulations).

This level 1 draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance represents the agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the draft guidance. Two copies of any mailed comments are to be submitted, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.