Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance for Industry

Combination Products
Timeliness of Premarket Reviews

Dispute Resolution Guidance

Additional copies of this guidance are available at:

http://www.fda.gov/oc.combination/default.htm

or from:
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Comments and suggestions regarding this draft document should be submitted within 60 days of publication of the *Federal Register* notice announcing the availability of the draft guidance. Submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1601, Rockville, MD 20857. Alternatively, electronic comments may be submitted to http://www.fda.gov/dockets/ecomments. All comments should be identified with the docket number listed in the notice of availability that published in the *Federal Register.*

For questions regarding this document, contact Suzanne O'Shea at 301-827-9229 or by email at suzanne.oshea@fda.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Combination Products

TABLE OF CONTENTS

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COMBINATION PRODUCTS TIMELINESS OF PREMARKET REVIEWS DISPUTE RESOLUTION GUIDANCE

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. Introduction

On October 24, 2002, Congress passed the Medical Device User Fee and Modernization Act of 2002 (MDUFMA). Among other things, this act created the Office of Combination Products within the Office of the Commissioner of Food and Drugs (OCP). One of OCP's functions is to assure the timely premarket review of combination products. OCP does not have the authority to direct a reviewing division to take any particular action, but it has been made responsible for resolving disputes about the timeliness of premarket reviews of combination products:

> Any dispute regarding the timeliness of the premarket review of a combination product may be presented to the Office for resolution, unless the timeliness of the dispute is clearly premature. 21 U.S.C. § 353(g)(4)(F)(i).

This guidance document provides information to an applicant wishing to submit a request that OCP resolve a dispute about the timeliness of a review of an application(s) covering a combination product.[1]

II. What is a premarket review timeliness dispute?

For the purpose of this guidance document, a timeliness dispute arises when FDA does not review and act on an applicant's submission within the applicable time frame, and the applicant presents the issue to OCP for resolution.

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[1] A center assigned primary jurisdiction for the premarket review of a combination product frequently accomplishes the review using consultation or collaboration with another center. These internal consultations and collaborations have time frames associated with them, but issues arising from their timeliness are not covered by this guidance document. This guidance document covers only disputes arising from the timeliness of the overall premarket review process for the marketing application.

III. What are the applicable time frames?

The Prescription Drug User Fee Act (PDUFA) and MDUFMA set performance goals for many types of drug, device, and biologic premarket applications. (Goals pertaining to biologic license applications are contained in both PDUFA and MDUFMA.) These goals reflect current expectations about the portion of premarket applications that will be reviewed within a specified time frame. Performance goals apply to only a portion of all applications of a certain type;[2] they do not require that every application be reviewed in accordance with the applicable time frame. Nevertheless, because PDUFA and MDUFMA goals reflect current expected review time frames, OCP believes it is appropriate to use them as guidelines to evaluate whether timeliness dispute resolution requests are premature.

Current PDUFA performance goals can be found at www.fda.gov/oc/pdufa/PDUFAIIIGoals.html. Current MDUFMA performance goals can be found at www.fda.gov/cdrh/mdufma/presentations/mdufma.html (Part III).

OCP expects to consider PDUFA and MDUFMA performance goals in timeliness disputes related to combination product reviews in the following ways:

1. OCP believes that premarket applications covering combination products will be subject to the same user fee performance goals as marketing applications covering non-combination products.

2. When a combination product is to be reviewed under one premarket application, OCP believes that the performance goals associated with that type of premarket application would apply. For example, if a combination product consisting of drug and device constituent parts is to be reviewed only under a new drug application, then the performance goals associated with new drug applications would apply.

3. When a combination product is reviewed under two premarket applications, FDA believes that the performance goals associated with both types of premarket applications would apply. For example, if a combination product consisting of drug and device constituent parts is to be reviewed under both a device application and a new drug application, then the performance goals associated with device applications would apply to that portion of the review covered by the device application. Similarly, the performance goals associated with new drug applications would apply to that portion of the review covered by the new drug application.

[2] For example, under current PDUFA performance goals, FDA is to review and act on 90 percent of priority original NDA and BLA submissions within 6 months. Similarly, under MDUFMA performance goals, in 2005, FDA is to issue 75 percent of its "major deficiency" letters on PMA's within 150 days.

4. OCP believes that performance goals will apply to combination products whether or not the application is subject to a user fee.

5. With the exception of actions on amendments containing a complete response to an "approvable" letter, MDUFMA goals do not go into effect until 2005. Until then, OCP intends to use the 2005 goals as a reference point while considering complaints about the timeliness of review.

IV. When should a timeliness dispute resolution request be presented to OCP?

The Office of Combination Products is available as a resource to sponsors and applicants for combination product issues throughout the development of a combination product. We recommend that sponsors and applicants try to resolve issues and disputes with the lead division, office and center before contacting OCP. If an issue remains unresolved after working with the lead center, we suggest that sponsors and applicants contact OCP for assistance in facilitating resolution to the issue.

Center ombudsmen are available to assist you. For issues arising within the Center for Biologics Evaluation and Research, contact:

Sheryl Lard-Whiteford, Ph.D.
Ombudsman
Center for Biologics Evaluation and Research
1401 Rockville Pike (HFM – 4)
Rockville, MD 20857
301-827-5413

For issues arising within the Center for Devices and Radiological Health, contact:

Les Weinstein, Esq.
Ombudsman
Center for Devices and Radiological Health
9200 Corporate Blvd. (HFZ-5)
Rockville, MD 20850
301-827-7991

For issues arising within the Center for Drug Evaluation and Research, contact:

Warren Rumble
Ombudsman
5515 Security Lane (HFD-006)
Suite 500
Rockville, MD 20852
301-594-5480

OCP expects that timeliness dispute resolution requests ordinarily would be presented to OCP after the time stated in the relevant PDUFA or MDUFMA performance goal has passed.

The purpose of a timeliness dispute resolution request is to obtain the relevant review as quickly as possible, rather than to impose any sanction on the reviewing Center. In keeping with this perspective, OCP recommends that dispute resolution requests be presented to OCP before the reviewing Center has issued the premarket review. For example, if a relevant performance goal states that a particular action is to be taken within 60 days, and the Center issues the review on day 63, a timeliness dispute resolution request presented to OCP on day 65 would do nothing to further the goal of obtaining review as quickly as possible.

On occasion, a reviewing division may inform an applicant in advance that an applicable time frame will not be met. In that case, a request for a timeliness dispute resolution made to OCP before the time stated in the relevant performance goal has passed would further the goal of obtaining review as quickly as possible. OCP recommends that you base such a timeliness dispute resolution request on a letter, facsimile, FDA meeting minutes, or some other statement from FDA that the performance goal will not be met.

Dispute resolution requests under this guidance are not intended for prospective concerns about the reviewing division's ability to meet performance goals in the future, or for planning discussions. OCP recommends that resolution of such issues be facilitated through informal procedures outside the scope of this guidance.

V. What is the process for presenting a timeliness dispute resolution request to OCP?

If an applicant believes that a date for action on an application has passed without action, or if the reviewing division in the lead center informs the applicant that an applicable time frame will not be met, OCP recommends that the applicant discuss the status of the review with the reviewing division and/or the Office to which the reviewing division reports within the lead center. If the reviewing division or appropriate Office

within the lead center does not provide the applicant with a satisfactory response, it would be appropriate to direct the timeliness dispute to OCP.

OCP encourages timeliness disputes to be presented by letter, fax or e-mail.

OCP's mailing address is:

Office of Combination Products
15800 Crabbs Branch Way
HFG – 3
Suite 200
Rockville, MD 20855

OCP's fax number is:

301-827-9230

OCP's e-mail address is:

combination@fda.gov

VI. What information should be included in a timeliness dispute resolution request?

A timeliness dispute resolution request should include the following information:

1. Contact information for the applicant,
2. The name of the product, and information about why the product is a combination product,
3. The Request for Designation number if the product went through the Request for Designation process,
4. The FDA Center and reviewing division that is responsible for issuing the premarket review,
5. The application number assigned by the reviewing Center or division,
6. The type of application,
7. Any relevant user fee performance goal,
8. The date the applicant believes the action was due,
9. The name and telephone number of the FDA contact person for the application,

10. A summary of the information provided by the reviewing division in the lead center regarding the timeliness of the review, and
11. A summary of the applicant's perspective on issues or barriers to progress affecting the timeliness of the premarket review process.

VII. How will OCP respond to a request for resolution of a timeliness dispute?

Upon receipt of a timeliness dispute resolution request, OCP expects to place a telephone call to the Director of the reviewing division in the lead center, and to the appropriate Center Ombudsman. When appropriate, OCP will convene a meeting with the reviewing division, the Center Ombudsman, and/or with the applicant. The purpose of the telephone call and/or meeting will be to determine:

1. whether the Division Director and the Center Ombudsman agree that the relevant user fee performance goal has not been met,
2. the current status of the review,
3. issues that need to be resolved before the review can be completed,
4. what OCP can do to facilitate the completion of the review as quickly as possible, and if necessary and feasible, a plan for the completion of the review, including a target date for completion of the review.

OCP will then place a telephone call to the applicant to discuss the current status of the review, and when appropriate and feasible, the review division's plan for completing the review. OCP intends to provide this information to the applicant within ten days after the timeliness dispute is presented to OCP.

If the reviewing division fails to meet the new target date for completion of the review, the applicant should advise OCP if further follow-up is requested. OCP will then follow up with the reviewing division on behalf of the applicant.