

Guidance for Third Parties and FDA Staff

Third Party Review of Premarket Notifications

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This guidance supersedes “Third Party Review, An Instruction Manual for
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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Office of Device Evaluation

Office of In Vitro Diagnostic Device Evaluation and Safety

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Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet at: <http://www.fda.gov/cdrh/ode/guidance/2237.pdf>, or CDRH Facts-On-Demand. In order to receive this document via your fax machine, call the CDRH Facts-On-Demand system at 800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system. At the second voice prompt, press 1 to order a document. Enter the document number (**2237**) followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

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Guidance for Third Parties and FDA Staff

Third Party Review of Premarket Notifications

This guidance represents 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.

1. Introduction

FDA has developed this guidance document to help third party reviewers, i.e., accredited persons¹ and European Community (EC) conformity assessment bodies (CABs),² identify the key elements to consider when evaluating a premarket notification [510(k)] submission and documenting their review and recommendation. The review documentation summarizes the areas evaluated and the rationale for determining substantial equivalence. We believe attention to the content and format of the documentation, and particularly the review memorandum, will facilitate FDA's timely action on the submission.

This guidance document provides FDA recommendations about conducting and documenting third party reviews of Traditional, Abbreviated, and Special 510(k) submissions. It applies to devices regulated by the Office of Device Evaluation (ODE) and in vitro diagnostic (IVD) devices regulated by the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should

¹ Under Section 523 of the Federal Food, Drug, and Cosmetic Act.

² Parties designated under the Sectoral Annex on Medical Devices to the US/EC Mutual Recognition Agreement, as described in 21 CFR Part 26.

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be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

The Least Burdensome Approach

We believe we should consider the least burdensome approach in all areas of medical device regulation. This guidance reflects our careful review of the relevant scientific and legal requirements and what we believe is the least burdensome way for you to comply with those requirements. However, if you believe that an alternative approach would be less burdensome, please contact us so we can consider your point of view. You may send your written comments to the contact person listed in the preface to this guidance or to the Center for Devices and Radiological Health (CDRH) Ombudsman. Comprehensive information on CDRH's Ombudsman, including ways to contact him, can be found on the Internet at <http://www.fda.gov/cdrh/ombudsman/>.

2. Background Resources

CDRH provides information about the Third Party Review Program on its web site at <http://www.fda.gov/cdrh/thirdparty/>. This site contains links to several key resources, such as:

- **Implementation of Third Party Programs Under the FDA Modernization Act of 1997³**
- **List of Devices for Third Party Review under the FDA Modernization Act of 1997.⁴**

EC CABs should also refer to the CDRH web site on the US/EC Mutual Recognition Agreement at <http://www.fda.gov/cdrh/mra/index.html>. This site contains links to several key resources, such as:

- **Third Party Programs Under the Sectoral Annex on Medical Devices to the Agreement on Mutual Recognition Between the United States of America and the European Community (MRA)⁵**
- **List of Devices for MRA Review.⁶**

Substantial equivalence and related concepts are explained in:

³ <http://www.fda.gov/cdrh/thirdparty/apguide13.html>

⁴ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/current.cfm#4>

⁵ <http://www.fda.gov/cdrh/modact/eurma.pdf>

⁶ <http://www.fda.gov/cdrh/mra/devmrareview.html>

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- **Guidance on the CDRH Premarket Notification Review Program 6/30/86 (K86-3)**⁷
- **The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications**⁸
- **Guidance on the Use of Standards in Substantial Equivalence Determinations.**⁹

For information on 510(k) requirements see FDA's Device Advice web page.¹⁰

In addition, there are a number of guidances on specific devices and crosscutting scientific issues (e.g., biocompatibility, software). You may obtain these documents by using the Good Guidance Practices (GGP) database search engine.¹¹

3. Evaluating a 510(k) Submission

The steps in your evaluation should be:

1. Ensuring that the device is eligible for third party review.
2. Obtaining relevant FDA guidance and information.
3. Consulting, as needed, with the appropriate branch chief.
4. Screening the document for the required elements using the Screening Checklist.
5. Conducting the substantive review.
6. Identifying deficiencies.
7. Documenting your review.

Each step is discussed in detail below.

Step 1. Ensuring that the device is eligible for third party review

Section 523(a)(3) of the Federal Food, Drug, and Cosmetic (FD&C) Act (21 U.S.C. 360m(a)(3)) excludes all Class III devices, as well as any Class II device that is intended to be permanently implantable, life sustaining, or life supporting, or that requires clinical data in a 510(k) submission. You should refer to the eligible device lists and the guidance on **Implementation of Third Party Programs**, identified above, for additional information.

⁷ <http://www.fda.gov/cdrh/k863.html>

⁸ <http://www.fda.gov/cdrh/ode/parad510.html>

⁹ <http://www.fda.gov/cdrh/ode/guidance/1131.html>

¹⁰ <http://www.fda.gov/cdrh/devadvice/314.html>

¹¹ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfggp/search.cfm>

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The contact person (identified on the cover page) for this guidance document is available to assist you when you are uncertain about the eligibility of a device. If you discover that the device you intend to review is ineligible, you should inform the submitter and discontinue your review.

Step 2. Obtaining relevant FDA guidance and information

We recommend you request that the 510(k) submitter fully inform you of any substantive pre-submission communications with FDA about the device. You should also use CDRH's web site to obtain any relevant FDA guidance, or information about the legally marketed device the submitter is comparing to or other similar devices. This information may include the Indications for Use Statement, 510(k) Summary, and FDA's decision letter.¹²

Step 3. Consulting, as needed, with the appropriate branch chief

We recommend that you consult, as needed, with the appropriate ODE or OIVD branch chief, team leader, or designate. These consultations can contribute to timely and consistent 510(k) reviews by identifying relevant issues and review criteria. They are particularly important for first-time reviews of devices without device-specific guidance, as discussed in the guidance on **Implementation of Third Party Programs** referenced above. We intend to respond promptly to your inquiries.

Step 4. Screening the submission using the Screening Checklist

This step entails screening the submission to ensure that the submission is administratively complete. You should use the **Screening Checklist**, found on FDA's web page.¹³ If the submission is complete, it is ready for substantive review. If you identify any deficiencies, see **Step 6. Identifying Deficiencies**.

If the 510(k) submission refers to information in a Master File,¹⁴ you should contact the 510(k) Staff, ODE, at 301-594-1190.

Step 5. Conducting the substantive review

Substantive review focuses on substantial equivalence. Section 513(i) of the FD&C Act (21

¹²Indications for Use Statements, 510(k) Summaries, and FDA decision letters from cleared submissions may be found in FDA's 510(k) database using the search engine at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. The GGP database search engine allows users to search the inventory of guidances available by title words or origin, at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfggp/search.cfm>.

¹³ <http://www.fda.gov/cdrh/ode/checklist-f102.pdf>

¹⁴ "Master File" is defined in <http://www.fda.gov/cdrh/devadvice/pma/>.

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U.S.C. 360c(i)) discusses the meaning of substantial equivalence. **Guidance on the CDRH Premarket Notification Review Program 6/30/86 (K86-3)** explains the key points underlying substantial equivalence determinations. The guidance, **The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications**, describes alternative approaches to determining substantial equivalence using Abbreviated and Special 510(k) submissions. **Guidance on the Use of Standards in Substantial Equivalence Determinations** further explains how standards are used in 510(k) review. You should refer to these guidances in conducting your substantive review (see **Section 2**, above).

If you identify any deficiencies, you should contact the submitter. **Step 6. Identifying Deficiencies** of this guidance provides further instruction on how to identify deficiencies in a submission. When your substantive review is complete you should reach a conclusion on whether the submission has demonstrated substantial equivalence. Section 21 CFR 807.100(b) sets forth the criteria FDA uses to determine that a device is substantially equivalent.

Step 6. Identifying deficiencies

If you identify any deficiencies in the submission, you will need to contact the 510(k) submitter. You may use whatever form of communication, i.e., telephone, facsimile, electronic mail, or letter, you wish to resolve the matter as long as confidentiality can be maintained. You should, however, avoid the exchange of substantive data and information over the telephone to avoid errors that may arise in the absence of a written request and response. We recommend that you document your requests in writing and summarize in your review memorandum any modifications the submitter has made to the submission.

When requesting additional information from the 510(k) submitter, we recommend that you structure your requests in the following manner. Examples of well-constructed deficiencies and responses to FDA's requests are available in the guidance entitled, **Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA**, <http://www.fda.gov/cdrh/modact/guidance/1195.html>.

Your request should include:

- the aspect of the submission that is deficient or absent
- the reason you are requesting this information
- your recommendation about what should be submitted to adequately address the deficiency.

You should consider alternative approaches to address deficiencies.

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Step 7. Documenting your review

Once you have reached a conclusion on substantial equivalence, you should prepare your review documentation. Title 21 CFR 10.70 (“Documentation of significant decisions in administrative file”) provides a framework for documentation. The content of your documentation will vary based on the type of 510(k) submission and device. The review formats identified in the table below are the internal tools we typically use for each submission type shown. These tools may assist you in preparing your review documentation.

FDA Review Formats for Devices Other Than IVDs

Submission Type	Review Formats				
	Screening Checklist	510(k) Decision-Making Documentation	ODE Review Memorandum for Traditional and Abbreviated Submissions	Standards Data Sheet	Special 510(k) Device Modification Review Memo
Traditional	yes	yes	yes	no	no
Abbreviated	yes	yes	yes	yes	no
Special	yes	yes	no	no	yes

FDA Review Formats for IVD Devices

Submission Type	Review Formats				
	Screening Checklist	510(k) Decision-Making Documentation	OIVD Review Templates	Standards Data Sheet	Special 510(k) Device Modification Review Memo
Traditional	yes	yes	yes	no	no
Abbreviated	yes	yes	yes	yes	no
Special	yes	yes	no	no	yes

Each format is discussed below.

Screening Checklist

See Step 4 above.

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510(k) Decision-Making Documentation

FDA uses this format to document the key decision points leading to a determination on substantial equivalence, as discussed in **Guidance on the CDRH Premarket Notification Review Program 6/30/86 (K86-3)**.¹⁵ *See Appendix 1.*

ODE Review Memorandum for Traditional and Abbreviated 510(k) Submissions

See Appendix 2.

Standards Data Sheet

FDA uses the Standards Data Sheet to identify each standard relied upon in an Abbreviated 510(k) submission. *See Appendix 5.*

Special 510(k) Device Modification Review Memo

FDA uses the Special 510(k) Device Modification Review Memo to summarize the information in a Special 510(k) submission and FDA's recommendation on substantial equivalence. *See Appendix 4.*

OIVD Review Templates

Templates and instructions provided to FDA staff for the review of IVD devices are in **Appendix 3**. Numerous examples of completed templates are available on the OIVD web page.¹⁶

4. Organizing Your Third Party Submission

Upon completing your review, you should organize your Third Party Submission as follows. It should include the following items, individually tabbed, in the order shown:

- cover letter signed by your contact person (see contents recommended below)
- table of contents
- letter signed by the 510(k) submitter authorizing you to submit the 510(k) to FDA on its behalf and to discuss its contents with FDA
- certification that the reported information accurately reflects the data reviewed
- "510(k) Decision-Making Documentation"
- your review memorandum with supervisory sign off

¹⁵ <http://www.fda.gov/cdrh/k863.html>

¹⁶ <http://www.fda.gov/cdrh/oivd/index.html>.

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- for Abbreviated 510(k)s, a “Standards Data Sheet” for each standard
- “Screening Checklist”
- the 510(k) submitter’s initial 510(k) submission and any subsequent communications or submissions, arranged in reverse chronological order

The cover letter, identified above, should contain:

- purpose of the submission
- the name and address of your organization
- the telephone and fax number of your contact person
- the name and address of the 510(k) submitter
- the date you first received the 510(k) from the 510(k) submitter
- the trade name of the device
- the FDA classification name, regulation number, and product code
- your recommendation with respect to the substantial equivalence of the device

You should submit 2 copies, each copy in a separate jacket, to FDA at the address below:

**CDRH Document Mail Center
Mail Stop: HFZ-401
Attention: THIRD PARTY REVIEW
9200 Corporate Boulevard
Rockville, Maryland 20850 USA.**

You should clip a copy of the most recent version of the 510(k) Summary, if any, and the Indications for Use Statement to the inside front cover. The originals should remain in the 510(k) submission.

5. When FDA Requests Additional Information

After we receive your Third Party Submission, if we believe additional information is needed to make a substantial equivalence determination, we plan to promptly contact you. Generally, we will request any additional information by telephone, electronic mail, or facsimile. Our requests will describe our concerns and recommend the information that we believe we need to address our concerns. In addition, if we place the 510(k) submission “on hold” (i.e., officially suspend processing of the submission pending our receipt of additional information), we plan to send you a “hold” letter by mail.

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Once you receive our request for additional information, you should:

1. inform the 510(k) submitter of requests pertaining to the 510(k) submission
2. thoroughly review any additional information provided to you by the 510(k) submitter to ensure that it adequately responds to our concerns
3. revise your review documentation to resolve any deficiencies we identified in your previously submitted documentation
4. add or incorporate your review of the additional information, if any, provided by the 510(k) submitter
5. prepare a cover letter referencing the 510(k) number assigned by FDA and identifying the purpose of your submission
6. send (in duplicate) the cover letter, your additional or revised review documentation, and any additional information received from the 510(k) submitter to the address shown in **Section 4** above¹⁷

6. Dispute Resolution

We have developed a guidance document that provides an overview of dispute resolution processes for medical devices.¹⁸ The processes available for reviewing and reconsidering FDA decisions or actions on other 510(k) submissions are also available for Third Party Submissions.

We believe disputes are often the result of misunderstanding or miscommunication. We encourage you to seek clarification, as needed, from us or the 510(k) submitter during the course

¹⁷ The guidance, **Fax & E-mail Communication with Industry about Premarket Files Under Review**, describes FDA's practices and procedures for information submitted by facsimile or electronic mail. You should refer to this guidance at <http://www.fda.gov/cdrh/ode/a02-01.html>.

¹⁸ See **Medical Device Appeals and Complaints – Guidance on Dispute Resolution** at <http://www.fda.gov/cdrh/modact/dispresl.pdf>.

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of a review. We are available to participate in a telephone conference or meeting with you, or with both you and the 510(k) submitter, if this appears to be an expeditious way to resolve questions or concerns. If the 510(k) submitter disagrees with an FDA decision or action, you should maintain impartiality and exercise care to avoid the appearance of conflict of interest that may result from acting as an advocate on the 510(k) submitter's behalf.

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Appendix 1. 510(k) Decision-Making Documentation

The following two pages contain the 510(k) Decision-Making Documentation referred to in **Section 3. Evaluating a 510(k) Submission (Step 7)**.

[Go to Appendix 1](#)

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**Appendix 2. ODE Review Memorandum for Traditional
and Abbreviated 510(k) Submissions**

[Go to Appendix 2](#)

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Appendix 3. OIVD Review Memorandum Templates and Instructions

OIVD's review memorandum templates are referred to in **Section 3. Evaluating a 510(k) Submission**. Templates and Instructions are included as follows:

- Appendix 3A. [Review Memorandum Template and Instructions for Assay and Instrument Combination Submissions](#)
- Appendix 3B. [Review Memorandum Template and Instructions for Assay Only Submissions](#)
- Appendix 3C. [Review Memorandum Template and Instructions for Instrument Only Submissions](#)

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Appendix 4. Special 510(k) Device Modification Review Memo

The following page contains the Special 510(k) Device Modification Review Memo referred to in **Section 3. Evaluating a 510(k) Submission.**

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Appendix 5. Standards Data Sheet

The following page contains the Standards Data Sheet referred to in **Section 3. Evaluating a 510(k) Submission**.

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