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Center for Devices and Radiological Health Standard Operating Procedure (SOP)

Level 1, Immediately in Effect Guidance Documents on Premarket Data Issues

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A. PURPOSE

This document describes the Center for Devices and Radiological Health's (CDRH's, or Center's) process to clarify and more quickly inform stakeholders when CDRH has changed its expectations relating to, or otherwise has new scientific information that could affect data submitted as part of an Investigational Device Exemption (IDE) or premarket submission, including a Premarket Notification (510(k)), a Premarket Approval (PMA), or a Humanitarian Device Exemption (HDE), including combination products containing a device constituent part for which CDRH has jurisdiction, that needs to be disseminated in a timely manner. Generally, the issues raised by new scientific information should be thoroughly considered with the benefit of input from other stakeholders who have expertise and viewpoints that may add appropriate balance, even when these outside-the agency viewpoints may differ. However, in some instances there are public health reasons for the immediate implementation of new premarket regulatory expectations that outweigh the need for pre-implementation feedback from affected stakeholders. In these instances, CDRH will communicate through Level 1, Immediately in Effect (IIE) Guidance Documents using Good Guidance Practices (GGPs). As it does currently, the Center will publish a *Federal Register* document announcing the guidance, post the IIE guidance documents on its website, and may also contemporaneously issue other communications to affected industry stakeholders summarizing the information in the IIE guidance.

FDA's guidance documents do not create or confer any rights for or on any person and does not operate to bind FDA or the public.

B. BACKGROUND

Currently, manufacturers typically learn of changes CDRH implements regarding what data or how to gather specific data in support of an IDE, 510(k), PMA, or HDE at the time of or soon

after a decision is made through individual engagement with the Center, often not until after they have prepared that submission. Reviewers may implement these changes, such as requesting new clinical data or using a new test method, on a case-by-case basis, with immediate supervisory concurrence when it is necessary to protect the public health. For example, a reviewer may request that sponsors test their implantable device for durability because new data demonstrates that this type of device is prone to failure due to premature wear and tear of the technology. Although CDRH may issue a detailed guidance document, the document may not publish until a year or more after a Branch- or a Division-level decision has been made to request the information because of the resource constraints in developing guidance documents.

Therefore, CDRH believes that timely communication with industry about changes in premarket regulatory expectations is important. FDA's GGP's regulation provides a mechanism for communicating and implementing certain changes in regulatory expectations quickly, without requiring prior public comment. Under 21 CFR 10.115(g)(2), FDA may issue a IIE guidance when prior public participation is not "feasible or appropriate." In the preamble to the final GGP's rule, FDA identified the following three examples in which IIE guidance could be appropriate because prior public comment may not be feasible or appropriate: 1) there are public health reasons for the immediate implementation of the guidance document; 2) there is a statutory requirement, executive order or court order that requires immediate implementation; or 3) the guidance document presents a less burdensome policy that is consistent with public health.

Under these circumstances, CDRH intends to use the procedures described in 21 CFR 10.115(g)(2) to issue guidance documents addressing changes in premarket regulatory expectations. CDRH would open a public docket upon issuance of the guidance through a Notice of Availability (NoA) in the Federal Register, and, subsequently, make changes to the guidance, if appropriate based on public comment. In certain circumstances, CDRH plans to contemporaneously issue letters to affected industry stakeholders summarizing the information in the IIE guidance. The IIE guidance documents will be posted on the FDA Web site. CDRH has developed this Standard Operating Procedure (SOP) to facilitate issuance of such guidance documents.

This SOP is being implemented after considering the comments on this topic.

C. PREMARKET IIE GUIDANCE DOCUMENT PROCEDURES

STEP 1: Initiating development of a Premarket IIE Guidance

- 1.1 Initiating development of a Premarket IIE Guidance should be considered when the following criteria are met:
 - a. New scientific information (e. g., product complaints/recalls or unique risks that are not previously identified such as a new failure mode identified during clinical use of the product) has been identified that raises a new, important safety risk or demonstrates that currently used test methods or clinical trial designs are inadequate to demonstrate safety, effectiveness, and/or substantial equivalence of a device type;

- b. As a result, CDRH needs to change its regulatory expectations, such as a change in the data that would be expected to be provided as part of an IDE, PMA, 510(k), or HDE because it is necessary to support an IDE approval or premarket approval or clearance; and
 - c. Consistent with 21 CFR 10.115(g)(2), prior public participation is not appropriate or feasible because the immediate risk to public health outweighs the need for pre-implementation feedback from affected stakeholders.
- 1.2 If the above criteria are met, then Office of Device Evaluation (ODE) or Office of In Vitro Diagnostics and Radiological Health (OIR) staff should present the identified issue to the appropriate Office-Level Management, including Office Director, following appropriate internal discussions with subject matter experts and Branch and/or Division management. Staff should also confirm that other CDRH Offices or FDA Centers are not implicated in any changes resulting from the new scientific information. Upon concurrence from the ODE or OIR Director, the process outlined below should be followed, instead of CDRH's standard guidance development process.

STEP 2: Presentation to the Center Science Council

- 2.1 The appropriate staff and their management should consult with the Center Science Council (CSC). A briefing summary providing the following information should be presented and discussed (see Appendix 1 for the [Premarket IIE Guidance Document Center Science Council Briefing Summary](#)):
1. The new scientific information that is available to CDRH;
 2. How this new scientific information changes the risk/benefit profile of the device or device type;
 3. Any expected changes in the Center's interpretation of or policy on a regulatory issue in light of this new scientific information;
 4. Why such proposed changes are necessary;
 5. The audience who should be aware of such proposed changes or communication;
 6. What submissions should be affected (e.g., pending/future premarket submissions, pending/future IDE submissions)¹;
 7. What existing guidance documents are impacted, if any;
 8. Why a Premarket IIE Guidance Document is the only appropriate method for disseminating this information; and
 9. Whether and to whom any additional communication on this topic is necessary.
- 2.2 Based on the information and discussion points outlined above, the CSC should determine the following:
- *Whether the new information warrants changes in CDRH's premarket regulatory expectations;*

The CSC should determine the appropriate response to the new information. If the new information warrants a change in premarket regulatory expectations, the

¹ Generally, previously cleared or approved submissions should be unaffected.

new information must be communicated using either IIE Guidance Document or a draft guidance document using the traditional procedures for prior public participation. If the new information does not warrant a change in regulatory expectations, the CSC should determine whether a separate communication should be issued alerting stakeholders to new scientific information. Such communications are not addressed by this SOP.

- *Whether new regulatory expectations should be communicated using IIE procedures or the standard procedures for guidance development.*

If the Center is proposing a change in regulatory expectations, the CSC may provide a recommendation whether a traditional guidance document should be issued in draft and finalized, or whether the Center should issue a Premarket IIE Guidance Document under this SOP because, for example: a) there are public health reasons for the immediate implementation of the guidance document; b) there is a statutory requirement, executive order or court order that requires immediate implement; or c) the guidance document presents a less burdensome policy that is consistent with public health. The CSC's recommendation will be reviewed by Senior CDRH leadership to ensure the CSC recommendations meet regulatory and legal standards, such as the regulatory standard for issuance of IIE guidance.

- *Whether additional expertise on the topic is required before determining the appropriate response to the new information.*

If so, the appropriate mechanisms should be followed to obtain external expertise.

STEP 3: Develop Premarket IIE Guidance Document

- 3.1 Once a decision has been made by the Center to issue a Premarket IIE Guidance, the guidance should be developed using Appendix 2 as a template.
- 3.2 The Premarket IIE Guidance should ideally be 1-2 pages, and generally no more than 5 pages in length. The Premarket IIE Guidance should:
 - a. Identify the appropriate audience (e.g., all manufacturers of a specific device type);
 - b. Identify the new scientific information and source of information that supports CDRH's decision to issue a Premarket IIE Guidance;
 - c. Discuss why this new scientific information warrants a change in regulatory expectations for the device type or is of importance to the specified audience;
 - d. Explain why public comment prior to issuance is not feasible or appropriate such that a Premarket IIE Guidance Document is being issued;
 - e. Outline the changes in regulatory expectations, such as changes in data expected to be submitted in light of this new scientific information;
 - f. Explain why CDRH's regulatory expectations are changing;
 - g. Identify whether such changes apply only to new IDEs or premarket submissions or also to IDEs or premarket submissions already under review at CDRH;
 - h. If such changes apply to premarket submissions already under review at CDRH, identify how the new issues may be considered by the sponsor, (e.g., phasing in changes, acceptance of alternative measures, or proposed dates for

implementation) so that they are not unfairly disadvantaged by the change in regulatory expectations, if applicable;

- i. Identify any recommended actions for the audience;
 - j. Identify the appropriate CDRH contact for additional information and questions; and
 - k. Identify any other pertinent information.
- 3.3 In addition, the Premarket IIE Guidance should reference any other communication or publicly available information from CDRH related to the issue discussed in the Premarket IIE Guidance.

STEP 4: Review and Clearance of the Premarket IIE Guidance Document

The Premarket IIE Guidance should be reviewed and cleared as follows:

- 4.1 The GGP Representative should review the IIE Guidance for GGP conformance and document quality. The GGP Representative will develop a NoA to be published in tandem with the posting of the Premarket IIE Guidance Document on the CDRH Web site.
- 4.2 The ODE or OIR Director or their designee should review and clear the Premarket IIE Guidance with respect to content and Office-level policy.
- 4.3 The CDRH Deputy Directors for Policy and Science should review and clear the Premarket IIE Guidance with respect to content and Center-level policy.
- 4.4 The Office of Chief Counsel (OCC) should review the Premarket IIE Guidance for legal sufficiency and accuracy.
- 4.5 The Center Director should provide final clearance of the Premarket IIE Guidance.

STEP 5: Issue Premarket IIE Guidance Document

Premarket IIE Guidances should be issued as follows:

- 5.1 Publish a NoA in the Federal Register announcing availability of the Premarket IIE Guidance and requesting comments.
- 5.2 Post a copy of the Premarket IIE Guidance on the CDRH Web site. All Premarket IIE Guidance will be posted in one readily accessible location.
- 5.3 Determine any other appropriate methods for distribution, such as email or postal mail.
- 5.4 If it would be appropriate to distribute additional communications on this topic, identify relevant stakeholders and determine the appropriate mechanism for distribution.

STEP 6: Review of Comments and Revision of Premarket IIE Guidance

Comments submitted following issuance of a Premarket IIE Guidance should be reviewed by the appropriate staff to determine if revisions should be made to the document based on the comments.

- 6.1 Collect comments from the docket for 60 days after the Premarket IIE Guidance was published

- 6.2 Review comments and determine if and how comments should be incorporated into the guidance. Administrative record of the comments and revisions will be maintained.
- 6.3 Recommendations should be presented to the CSC for discussion.
- 6.4 Revised guidance documents should be issued 90 days after the initial comment period closes, and will reference the previous version of the guidance.
- 6.5 If after reviewing the comments the Center decides no revisions are necessary, the publicly available version of the guidance should be updated to indicate all comments have been reviewed and no changes are being made. This update should occur 90 days after the initial comment period closes.
- 6.6** Publicly report number of Premarket IIE Guidance issued at periodic intervals.

D. EFFECTIVE DATE

This SOP is effective March 26, 2014.

CHANGE CONTROL TABLE

VERSION #	REASON FOR CHANGE	EFFECTIVE DATE	APPROVING OFFICIAL (NAME/TITLE)
1.0	Original	Draft issued September 5, 2013.	Jeffrey Shuren, MD, JD Director, Center for Devices and Radiological Health
2.0	Finalizing Draft based on comments received	March 26, 2014	Jeffrey Shuren, MD, JD Director, Center for Devices and Radiological Health

E. APPENDICES

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**APPENDIX 1: Level 1, Immediately in Effect Guidance Documents on PreMarket Issues
CENTER SCIENCE COUNCIL BRIEFING SUMMARY**

Submitted by:	Office/Division:	Date:
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Describe the device or device type and provide a brief regulatory history of the device or device type.	
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1. What new scientific information is available to CDRH regarding the device or device type?	
2. How does this new scientific information change the risk/benefit profile of the device or device type?	
3. What changes are expected in CDRH's interpretation of or policy on a regulatory issue in light of this new scientific information?	
4. Why are these changes or other communication necessary?	
5. Who needs to be aware of the proposed changes or communication?	
6. What submissions would be affected? Please identify type of submissions (e.g., IDE, or PMA) and the status of the submissions (e.g., pending, or future).	
7. What currently available guidance documents are impacted?	
8. Why is Premarket IIE Guidance the most appropriate method for disseminating this information?	
9. Whether and to whom any additional communication on this topic is necessary.	

Recommendation:	<input type="checkbox"/> IIE Supported	<input type="checkbox"/> IIE Not Supported	<input type="checkbox"/> Other Action Supported (specify):
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APPENDIX 2

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Immediately in Effect Guidance Documents on Premarket Issues [insert specific device type]

Guidance for Industry and Food and Drug Administration Staff (add others as appropriate, e.g., Third Parties)

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.

You may submit comments and suggestions regarding this document within 60 days of publication in the Federal Register of the notice announcing the availability of the guidance. 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.regulations.gov>. Identify all comments with the docket number listed in the notice of availability that publishes in the Federal Register.

Level 1, Immediately in Effect Guidance Documents on Premarket Issues
[insert specific device type]

The Food and Drug Administration (FDA) is notifying affected industry of our intent to improve the current premarket regulatory processes associated with [insert specific device type].

[Summarize actions FDA intends to take]. These actions are being taken in light of [identify new scientific information that is available to CDRH]. FDA believes that this effort will help ensure that [insert specific device type] are safe and effective.

[Provide a more detailed discussion of the new scientific information identified above and discuss how this new scientific information changes the risk/benefit profile of the device type.]

As a result, CDRH intends to [describe the specific regulatory expectations or interpretation that is intended to change]. CDRH believes these changes are necessary because [explain rationale for change in regulatory expectations or interpretation]. These changes are expected to take effect [outline timeframe for implementation and effect on pending/future submissions (e.g., immediately and will affect pending submissions or immediately but will not affect pending submissions).] [If the changes are expected to affect pending submissions, additional details should be provided regarding how the new issues may be considered by the sponsor (e.g., phasing in changes, or acceptance of alternative measures).]

This guidance is being implemented without prior public comment because the agency has determined that prior public participation is not feasible or appropriate (21 CFR 10.115(g)(2)). CDRH made this determination because [insert reason, e.g., the guidance presents a less burdensome policy consistent with the public health, the guidance is required by statute, executive order or court order that requires immediate implementation, or the guidance requires immediate implementation for public health reasons]. CDRH will collect comments on this guidance until [enter date 60 days from publication], and will amend this guidance or otherwise re-issue guidance as appropriate based on the comments received.

[OPTION: *Include if meeting with affected manufacturers is appropriate:* We strongly recommend [insert specific device type] manufacturers meet with the Agency early in the device development process to discuss submissions regarding new [insert specific device type] or changes to existing devices. We intend to expeditiously schedule such meetings if a meeting is requested. For further information, please contact [insert appropriate CDRH contact, title] at [insert phone number] or [insert email address]. [end of option]

[OPTION: *Include if Office of Compliance related issues are applicable (e.g., issues identified related to design controls, PMA review, etc):* [We also recommend early discussions with FDA's Office of Compliance regarding [describe Office of Compliance related issues]. [end of option]

[OPTION: *Include if CDRH has determined that pre-clearance inspections are necessary for a 510(k) device:* FDA has determined that it is necessary to conduct pre-clearance or inspections of [insert specific device type] manufacturers in accordance with its statutory authority because there is a substantial likelihood that failure to comply with current good manufacturing practices will potentially present a serious risk to human health. [If appropriate, provide additional information regarding need for pre-clearance inspection.] For further information, please contact [insert appropriate contact, title] at [insert phone number] or [insert email address]. [end of option]

[If applicable, discuss additional pertinent information regarding identified issue (e.g., workshop,

additional communication/guidance forthcoming).]

FDA believes these actions, early communication between the FDA and [insert specific device type] manufacturers, and additional actions being announced by the Agency will result in [insert specific impact]. We look forward to working with you on this important public health issue.