Contents

Immediately in Effect (IIE) SOP Premarket Data Issues

Overview

Purpose

This Standard Operating Procedure (SOP) describes the process that the Center for Devices and Radiological Health (CDRH) must follow to clarify and more quickly inform stakeholders when CDRH changes its expectations about

- new scientific information that could affect data submitted as part of an Investigational Device Exemption (IDE), or
- premarket submission.

What does premarket submission include?

Premarket submission includes the following:

- Premarket notification (510(k))
- Premarket Approval (PMA), or
- Humanitarian Device Exemption (HDE), that includes combination products that
  - contain a device constituent part for which CDRH has jurisdiction, and
  - need to be disseminated in a timely manner.

Public health emergency

On February 4, 2020, the Secretary of Health and Human Services determined that a public health emergency exists nationwide as a result of confirmed cases of COVID-19. During this public health emergency, FDA may deviate from procedures outlined in this SOP, for Level 1 Immediately in Effect Guidance Documents addressing this public health emergency.

Reference: *For more information, contact CDRH-Guidance@fda.hhs.gov.*

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The table below lists the contents of this SOP.

1. Implementation Guidelines and Background

Overview

Contents

The table below lists the topics in this section.

1.1. Implementation Guidelines

General scenario

For implementation in a general scenario, consider the issues raised by new scientific information with the benefit of input from other stakeholders who have expertise and viewpoints.

Even though these outside-the agency viewpoints may differ, they may add appropriate balance.

Instance of immediate implementation

Immediate implementation is applicable in the following scenarios:

- Public health emergencies
- When new premarket regulatory expectations outweigh the need for pre-implementation feedback from affected stakeholders

Mode of immediate implementation

During instances of immediate implementation, CDRH does the following:

Step	Action
1	Communicate through Level 1, Immediately in Effect (IIE) Guidance Documents using Good Guidance Practices (GGPs).
2	Publish a Federal Register document announcing the guidance, post the IIE guidance documents on its website.
3	Contemporaneously issue other relevant communication to the affected industry stakeholders summarizing the information in the IIE guidance, if necessary.

Note: *FDA's guidance documents do not*

- *create or confer any right for or on any person, and*
- *operate to bind FDA or the public.*

1.2. Background

Change implementation - current trend

Currently, manufacturers learn of the changes soon after or at the time the CDRH implements and submits them.

The changes typically are regarding data or how to gather specific data in support of an IDE, 510(k), PMA, or HDE.

Change implementation - review

Reviewers may implement changes on a case-to-case basis with immediate supervisory concurrence when it is necessary to protect public health. The changes entail

- requesting new clinical data, or
- using a new test method.

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.

Publishing time

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.

Solution to the delay

CDRH believes that timely communication with industry about changes in premarket regulatory expectations is important.

- **FDA's GGP regulation:** FDA's GGP regulation provides a mechanism for communicating and implementing certain changes in regulatory expectations quickly, without requiring prior public comment.
- **FDA's Immediately in Effect (IIE) guidance:** Under 21 CFR 10.115(g)(2), FDA may issue an IIE guidance when prior public participation is not "feasible or appropriate."

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1.2. Background, Continued

Preamble: 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:

- Public health reasons for the immediate implementation of the guidance document
- Statutory requirement, executive order, or court order that requires immediate implementation
- The guidance document that presents a less burdensome policy that is consistent with public health

Guidelines towards IIE: CDRH

CDRH intends to follow the guidelines below toward IIE:

- Use the procedures described in 21 CFR 10.115(g)(2) to issue guidance documents addressing changes in premarket regulatory expectations.
- 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.
- Contemporaneously issue letters to affected industry stakeholders summarizing the information in the IIE guidance under specific circumstances.
- Post the IIE guidance documents on the FDA website.

To cater to this, CDRH has developed this SOP to facilitate issuance of such guidance documents.

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

2. Premarket IIE Document Processes

Overview

Contents

The table below lists the topics in this section.

2.1. Developing the Premarket IIE Guidance Document: Prerequisites and Process

Prerequisites to initiate development

To initiate the development of a premarket IIE guidance document, ensure the following prerequisites are met:

New scientific risks

New scientific information (e. g., product complaints/ recalls or unique risks that were 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.

Changed regulatory methods

As a result of the new scientific risks that have come to light, CDRH has changed 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.

Risk to public health outweighs pre-implementation feedback

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.

Initiating development – Process

The table below describes the stages in initiating development of a Premarket IIE Guidance:

***Note**: Ensure the prerequisites are met before initiating the development.*

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2.1. Developing the Premarket IIE Guidance Document: Prerequisites and Process, Continued

Initiating development – Process, continued

***Reference**: For more information about prerequisites about initiating the development, refer to Prerequisites to initiate development.*

Stage	Who	Does What
1	• Office of Device Evaluation (ODE), or • Office of In Vitro Diagnostics and Radiological Health (OIR) staff	• Conducts appropriate internal discussions with – subject matter experts and Branch, and/ or – Division management. • Presents the identified issue to the appropriate Office Level Management, including Office Director
2	Staff	Confirm that other CDRH Offices or FDA Centers are not implicated in any change resulting from the new scientific information.
3	• ODE, or • OIR Director	Concurs to follow the process outlined in Stages in Developing the Premarket IIE Guidance document instead of CDRH's standard guidance development process.

Developing the Premarket IIE Guidance document – Process

The table below describes the stages of development of the Premarket IIE Guidance Document:

Stage	Who	Does What
1	Appropriate staff and management	Present a briefing summary to the Center Science Council (CSC).
2	CSC	• Determines whether the new information warrants changes in CDRH's premarket regulatory expectations. • Recommends drafting the Premarket IIE Guidance document.
3	Senior CDRH leadership	Reviews CSC's recommendations to see if it meets regulatory and legal standards, such as the regulatory standard for issuance of IIE guidance.
4	Appropriate staff and management	Draft the Premarket IIE Guidance document.

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2.1. Developing the Premarket IIE Guidance Document: Prerequisites and Process, Continued

Developing the Premarket IIE Guidance document – Process, continued

Stage	Who	Does What
5	• Team of GGP Representative, or • ODE or • OIR Director or designee, and • CDRH Deputy Directors for Policy and Science, and • Office of Chief Counsel	Review the drafted Premarket IIE Guidance document.
6	Center Director	Provides final clearance of the Premarket IIE Guidance.
7	Appropriate staff	Issues Premarket IIE Guidance document.
8	Appropriate staff	Reviews comments and revises the document if necessary.

2.2. Presenting the Summary to the Center Science Council

Summary presentation

The appropriate staff and their management must present the Center Science Council (CSC) with a briefing summary of the following:

Reference: *See Appendix 1 for the Premarket IIE Guidance Document Center Science Council Briefing Summary.*

- The new scientific information available to CDRH
- How this new scientific information changes the risk/ benefit profile of the device or device type
- Any expected change in the Center's interpretation of or policy on a regulatory issue in light of this new scientific information
- Why such proposed changes are necessary
- The audience who should be aware of such proposed changes or communication
- What submissions should be affected (e.g., pending/future premarket submissions, pending/future IDE submissions)
- What existing guidance documents are impacted, if any
- Why a Premarket IIE Guidance Document is the only appropriate method for disseminating this information, and
- Whether and to whom any additional communication on this topic is necessary.

Determining the response

Based on the information and discussion points presented to CSC, the CSC determines the following for an appropriate response:

- Does the new information warrant changes in CDRH's premarket regulatory expectations?
- Must the CSC communicate new regulatory expectations using IIE procedures or the standard procedures for guidance development?
- Does the topic need additional expertise?

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2.2. Presenting the Summary to the Center Science Council, Continued

CSC's response on changes to premarket regulatory expectations

The table below describes CSC's response on receiving new information warranting change in premarket regulatory expectations.

If the new information ...	Then the CSC must...
warrants a change in premarket regulatory expectations	communicate using • an IIE Guidance Document, or • a draft guidance document using traditional procedures for prior public participation.
does not warrant a change in the regulatory expectations	determine whether it must issue a separate communication alerting stakeholders to new scientific information. ***Note:*** *Such communication is not addressed in this SOP.*

CSC's communication about change in regulatory expectations

If the Center is proposing a change in the regulatory expectation, then the CSC may provide a recommendation whether

- a traditional guidance document should be issued in draft and finalized, or
- the Center should issue a Premarket IIE Guidance Document under this SOP owing to any of the following reasons:
  - There are public health reasons for the immediate implementation of the guidance document.
  - There is a statutory requirement, executive order or court order that requires immediate implement.
  - The guidance document presents a less burdensome policy that is consistent with public health.

CSC's response to topics needing additional expertise

If the new information needs additional expertise for an appropriate response, the CSC follows appropriate mechanisms to obtain external expertise.

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2.2. Presenting the Summary to the Center Science Council, Continued

Reviewing CSC's recommendation

The Senior CDRH leadership reviews CSC's recommendation to ensure that CSC's recommendations meet regulatory and legal standards, such as the regulatory standard for issuance of IIE guidance.

2.3. Drafting the Premarket IIE Guidance Document

Stages in drafting the IIE Guidance Document

The table below describes the developmental stages of the IIE Guidance Document:

Stage	Description
1	Adherence to the Appendix 2 template.
2	Development of the Premarket IIE Guidance content.
3	Inclusion of references, if any.

IIE Guidance template

Use Appendix 2 as a template to develop the Premarket IIE Guidance document.

***Reference**: For more information about the template, refer to Appendix 2: IIE Guidance Documents on Premarket Issues.*

***Note**: The Premarket IIE Guidance document must ideally be 1-2 pages, and generally no more than 5 pages in length.*

Developing the Premarket IIE Guidance content

While developing the Premarket IIE Guidance document, do the following:

Step	Action
1	Identify the following: • Appropriate audience (e.g., all manufacturers of a specific device type) • New scientific information and source of information that supports CDRH's decision to issue a Premarket IIE Guidance
2	Discuss why this new scientific information warrants a change in regulatory expectations for the device type or is of importance to the specified audience.
3	Explain why public comment prior to issuance is not feasible or appropriate such that a Premarket IIE Guidance document is being issued.
4	Outline the changes in regulatory expectations. For example, such as changes in data expected to be submitted in light of this new scientific information.

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2.3. Drafting the Premarket IIE Guidance Document, Continued

Developing the Premarket IIE Guidance content, continued

Step	Action
5	• Explain why CDRH's regulatory expectations are changing. • Check if such changes apply only to – new IDEs or premarket submissions, or – IDEs, or premarket submissions already under review at CDRH?

If the changes apply to ...	Then ...
premarket submissions already under review at CDRH	identify how the new issues may be considered by the sponsor. For example: • 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;
• new IDEs, or • premarket submissions	(_____)

6	Identify and include the following: • Any recommended actions for the audience • The appropriate CDRH contact for additional information and questions • Any other pertinent information

Additional reference

Reference any other communication or publicly available information from CDRH related to the issue discussed in the Premarket IIE Guidance.

2.4. Reviewing and Clearing of the Premarket IIE Guidance Document

Stages in review and clearance The table below describes the stages of review and clearance of the Premarket IIE Guidance:

Stage	Who	Does What
1	GGP Representative	• Reviews the IIE Guidance for GGP conformance and document quality. • Develops an NoA to be published in tandem with the posting of the Premarket IIE Guidance Document on the CDRH website.
2	• ODE, or • OIR Director or designee	Reviews and clears the Premarket IIE Guidance with respect to content and Office-level policy.
3	CDRH Deputy Directors for Policy and Science	Review and clear the Premarket IIE Guidance with respect to content and Center-level policy.
4	Office of Chief Counsel (OCC)	Reviews the Premarket IIE Guidance for legal sufficiency and accuracy.
5	Center Director	Provides a final clearance of the Premarket IIE Guidance.

2.5. Issuing the Premarket IIE Guidance Document

Guidelines

Adhere to the following guidelines while issuing the Premarket IIE Guidance document:

- Post all Premarket IIE Guidance in one readily accessible location.
- Determine any other appropriate methods for distribution, such as email or postal mail.
- Identify the relevant stakeholders to distribute additional communication on this topic as appropriate.
- Determine the appropriate mechanism for distribution of additional communication.

Issuing the document

Issue premarket IIE Guidance as follows:

Step	Action
1	Publish an NoA in the Federal Register announcing availability of the Premarket IIE Guidance and requesting comments.
2	Post a copy of the Premarket IIE Guidance on the CDRH website.

2.6. Reviewing Comments and Revising the Premarket IIE Guidance

Reviewing by staff

The table below describes how to determine if the document needs to be revised based on the comments:

Step	Action
1	Collect comments from the docket within 60 days after the Premarket IIE Guidance was published.
2	• Review the comments. • Determine if and how comments should be incorporated into the guidance.
3	Maintain an administrative record of the comments and revisions.
4	Present the recommendations to the CSC for discussion. **If after the review, the CSC decides that revisions are ...** / **Then ...** not necessary: update the publicly available version of the guidance to indicate that • all comments are reviewed, and • no changes are made. necessary: • make the necessary revisions. • issue the revised guidance documents 90 days after the initial comment period closes, and • reference the previous version of the guidance document. ***Note**: Publicly report the number of Premarket IIE Guidance issued at periodic intervals.*

3. References

Overview

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The table below lists the topics in this chapter.

3.1. Abbreviations

List of terms and their full forms

The table below provides the full forms of the abbreviated terms used within this SOP.

Term	Full Form
CDRH	Center for Devices and Radiological Health
CFR	*To be added*
CSC	Center Science Council
GGP	Good Guidance Practice
HDE	Humanitarian Device Exemption
HFA	*To be added*
IDE	Investigational Device Exemption
IIE	Immediately in Effect
NoA	Notice of Availability
OCC	Office of Chief Counsel
ODE	Office of Device Evaluation
OIR	Office of In Vitro Diagnostics and Radiological Health
PMA	Premarket Approval
SOP	Standard Operating Procedure

3.2. Change History

Change Control Table

Following is the change control table listing effective dates pertaining to this SOP:

Version Number	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

4. Appendices

Overview

Contents

The table below lists the topic(s) in this chapter.

4.1. Appendix 1: Level 1, Immediately in Effect Guidance Documents on Premarket Issues

Appendix to use Use this appendix as a template to present the briefing summary to the Center Science Council.

APPENDIX 1: Level 1, Immediately in Effect Guidance Documents on PreMarket Issues CENTER SCIENCE COUNCIL BRIEFING SUMMARY		
Submitted by:	Office/Division:	Date:

Describe the device or device type and provide a brief regulatory history of the device or device type.	

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:	□ IIE Supported	□ IIE Not Supported	□ Other Action Supported (specify):

4.2. Appendix 2: IIE Guidance Documents on Premarket Issues

Appendix to use Use this appendix as a template to develop the Premarket IIE Guidance document.

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.