CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

Standard Operating Procedure for

"Notice to Industry" Letters

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) that needs to be disseminated in a timely manner. Where appropriate, CDRH will communicate new expectations as Notice to Industry Guidance Letters, which will comply with Good Guidance Practices, or CDRH will communicate other new scientific information as Notice to Industry Advisory Letters. The Center will post both types of Notice to Industry Letters on its website, and will also use additional methods for distributing the Letters to identified stakeholders.

BACKGROUND

The Task Force on the Utilization of Science in Regulatory Decision Making published a Preliminary Report and Recommendations in August 2010. In the report, the Task Force noted that when new scientific information changes CDRH's regulatory thinking, it has been challenging for the Center to communicate the change and its basis to all affected parties in a meaningful and timely manner. The Task Force recommended that the Center make use of more rapid tools for broad communication on regulatory matters, including establishing a standard practice for sending "Notice to Industry" Letters to all manufacturers of a particular group of devices for which the Center has changed its expectations for data submitted as part of an IDE or premarket application on the basis of new scientific information.

Currently, manufacturers typically learn of changes CDRH implements at the time of or soon after a decision is made through individual engagement with the Center, often not until after they have prepared a premarket 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 be published until a year or more after a Branch- or 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 regulatory expectations or about new scientific information is important. The Task Force recommended that CDRH use Notice to Industry Letters in these circumstances, although not required, and adopt a uniform template and terminology for such letters, including clear and consistent language to indicate when the Center has changed its regulatory expectations, the general nature of the change, and the rationale for the change. The Task Force contemplated that CDRH could potentially issue "Notice to Industry" Letters, if such letters constituted guidance, as "Level 1 – Immediately in Effect" guidance documents under 21 CFR 10.115(g)(2), and would open a public docket upon their issuance through a notice of availability in the Federal Register. Where appropriate, such letters would be followed as quickly as possible by new or revised guidance explaining the Center's new regulatory expectations (if any) in greater detail and revising the guidance where necessary in response to comments received, so that external constituencies have a fuller understanding of the Center's current regulatory thinking.

This Standard Operating Procedure (SOP) was developed to address this recommendation from the Task Force on the Utilization of Science in Regulatory Decision Making as outlined in the August 2010 Preliminary Report and Recommendations.

"NOTICE TO INDUSTRY" PROCEDURES

STEP 1: Initiate Development of a Notice to Industry Letter

Initiating development of a Notice to Industry Letter should be considered when the following criteria are met:

1. New scientific information has been identified that raises a new, important safety risk or calls into question the adequacy of currently used test methods or clinical trial designs to demonstrate or bear on safety, effectiveness, and/or substantial equivalency of a device type;
2. As a result, CDRH may need to change its regulatory expectations, such as a change in expected data submitted as part of an IDE or premarket application is necessary to support IDE approval or premarket approval or clearance; and
3. There is not an appropriate alternative mechanism to protect the public health in a timely manner, such as issuing a draft guidance for public comment prior to finalizing the document.

If the above criteria are met, then Office of Device Evaluation (ODE) or Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD) staff should present the identified issue to the appropriate Office-Level 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/OIVD Director, the process outlined below should be followed, instead of CDRH's standard guidance development process.

A. The appropriate staff and their management should meet with the Center Science Council. A one page summary providing the following information should be presented and discussed:
    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 or other communication are necessary;
    5. The audience who should be aware of such proposed changes or communication; and
    6. What submissions should be affected (i.e., pending/future premarket submissions, pending/future IDE submissions).

B. If the Center is proposing a change in regulatory expectations, the Center Science Council should determine whether a traditional guidance document should be issued and finalized, or whether the Center should issue a Notice to Industry Guidance Letter as Level 1 – Immediately in Effect Guidance.

> Level 1 – Immediately in Effect Guidance Document: A Level 1 – Immediately in Effect Guidance Document should be issued if the Notice to Industry Letter contains recommendations for complying with regulatory requirements and would meet the definition of a guidance document (21 CFR 10.115(b)), but public comment prior to issuance is not feasible or appropriate due, for instance, to the potential public health impact of the actions described in the Notice to Industry Guidance Letter (21 CFR 10.115(g)(2)).

Alternatively, if the Center is not proposing new regulatory expectations, the Center Science Council should determine whether to issue a Notice to Industry Advisory Letter alerting stakeholders to new scientific information.

> Advisory: An Advisory should be issued if the Notice to Industry Letter would not constitute guidance; that is, if it describes new scientific information but does not contain recommendations for complying with regulatory requirements or describe the Agency's interpretation of or policy on a regulatory issue. For example, an Advisory may describe concerns about the accuracy of a certain test method and recommend that a manufacturer meet with CDRH early in the device development process to discuss possible alternative test methods.

STEP 2: Draft Notice to Industry Letter

Once a decision has been made by the Center Science Council to issue a Notice to Industry Letter, the appropriate template should be used to draft the letter (see Attachment 1 for the Notice to Industry Advisory Letter template and Attachment 2 for the Notice to Industry Guidance Letter template). The Notice to Industry Letter should generally be 1-2 pages, and no more than 3 pages in length. The Notice to Industry Letter should:

A. Identify the appropriate audience (e.g., all manufacturers of a specific device type);
B. Identify the new scientific information that supports CDRH's decision to issue a Notice to Industry Letter;
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. For a Notice to Industry Guidance Letter, explain why public comment prior to issuance is not feasible or appropriate such that it is being issued as Level 1 – Immediately in Effect Guidance;
E. Outline the changes in regulatory expectations, such as changes in data expected to be submitted in light of this new scientific information, if any;
F. If applicable, 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 much additional time the sponsor will have to address the new issues 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.

Note: The Notice to Industry Letter should reference any communication or other publicly available information from CDRH related to the issue discussed in the Notice to Industry Letter.

STEP 3: Review and Clearance of Notice to Industry Letter

The Draft Notice to Industry Letter should be reviewed and cleared as follows:

A. The Good Guidance Practices (GGP) Representative should review the Draft Notice to Industry Letter for GGP conformance and document quality. The GGP Representative will draft a Notice of Availability (NoA) to be published when the Notice to Industry Letter is available on the CDRH website. Note: This step is not required for a Notice to Industry Advisory Letter.
B. The ODE/OIVD Director or their designee should review and clear the Draft Notice to Industry Letter with respect to content and office-level policy.
C. The CDRH Deputy Directors for Policy and Science should review and clear the Draft Notice to Industry Letter with respect to content and center-level policy.
D. The Office of Chief Counsel (OCC) should review Draft Notice to Industry Guidance Letters for legal sufficiency and accuracy. Note: This step is not required for a Notice to Industry Advisory Letter.
E. The Center Director should provide final clearance of the Notice to Industry Letter.

STEP 4: Issue Notice to Industry Letter

Notice to Industry Letters should be issued as follows:

A. Post a copy of the Notice to Industry Letter on the CDRH website, either in the Guidance database for Notice to Industry Guidance Letters or under Letters to Industry for Notice to Industry Advisory Letters, as appropriate.
B. Publish a NoA in the Federal Register for Notice to Industry Guidance Letters.
C. Determine any other appropriate methods for distribution.
D. If it would be appropriate to distribute via mail, identify relevant stakeholders and determine the appropriate contact information for such stakeholders.
    a. Prepare Letters based on contact information collected.
    b. Add a copy of each Letter to the administrative record, if appropriate.
    c. Send an electronic and/or hard copy of the Letter to each identified contact.

STEP 5: Review of Comments and Revision of Notice to Industry Guidance Letters: Level 1 – Immediately in Effect Guidance

Comments submitted following issuance of a Notice to Industry Guidance Letter: Level 1 – Immediately in Effect Guidance should be reviewed by the appropriate staff to determine if revisions should be made to the document based on the comments.

A. Collect comments from the docket for 60 days after the Notice to Industry Guidance Letter was published;
B. Review comments and determine if and how comments should be incorporated into the guidance;
C. Recommendations should be presented to the Center Science Council for discussion.

Attachment 1

TEMPLATE FOR NOTICE TO INDUSTRY ADVISORY LETTER

Letter to Manufacturers of [insert specific device type]

[CERTIFIED MAIL] (if applicable)
[RETURN RECEIPT REQUESTED] (if applicable)

[insert date]

Dear **[insert specific device type]** Manufacturer:

FDA's records have identified you as the "Official Correspondent" for the Medical Device Manufacturer stated above. Please ensure that the following message is relayed to the Most Responsible Individual at the Medical Device Manufacturer.

The Food and Drug Administration (FDA) is notifying you of our concerns relating to **[identify new scientific information that is available to CDRH]** associated with the use of **[insert specific device type]**. As a result, although FDA is not issuing new guidance or regulations at this time, FDA may, in the future, take steps to improve the current premarket and postmarket regulatory processes associated with **[insert specific device type]**. **[Summarize the general actions FDA might take, or the areas in which FDA might take actions, if known (e.g., changes in testing recommendations, clinical study recommendations)]**. *[Note: specific recommendations will constitute guidance and should not be included in this Advisory]*. FDA believes that this effort will help mitigate current risks and reduce future risks associated with **[insert specific device type]**.

[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.]

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. For further information, please contact **[insert appropriate CDRH contact, title]** at **[insert phone number]** or **[insert email address]**.

Include if Office of Compliance related issues are applicable (e.g., issues identified related to design controls, recall strategy, etc): **[We also recommend early discussions with FDA's Office of Compliance regarding [describe Office of Compliance related issues]**. FDA also may conduct pre- or post-clearance inspections in certain circumstances, in accordance with its statutory authority. For further information, please contact **[insert appropriate Office of Compliance contact, title]** at **[insert phone number]** or **[insert email address]**.

[If applicable, discuss additional pertinent information regarding identified issue (e.g., workshop, additional communication/guidance forthcoming).]

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

Sincerely,

Director, Center for Devices and Radiological Health
Food and Drug Administration

Attachment 2

TEMPLATE FOR NOTICE TO INDUSTRY GUIDANCE LETTER: LEVEL 1 – IMMEDIATELY IN EFFECT GUIDANCE

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 should 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*.

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

Letter to Manufacturers of [insert specific device type]

[CERTIFIED MAIL] (if applicable)
[RETURN RECEIPT REQUESTED] (if applicable)

[insert date]

Dear **[insert specific device type]** Manufacturer:

FDA's records have identified you as the "Official Correspondent" for the Medical Device Manufacturer stated above. Please ensure that the following message is relayed to the Most Responsible Individual at the Medical Device Manufacturer.

The Food and Drug Administration (FDA) is notifying you of our intent to improve the current premarket and postmarket 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]**. The FDA believes that this effort will help mitigate current risks and reduce future risks associated with **[insert specific device type]**.

[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 the logistics of the changes (e.g., how review clock, deletion policy, etc will be affected.]**

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 deals with a short-term or highly time-sensitive issue, 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.

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. For further information,

please contact **[insert appropriate CDRH contact, title]** at **[insert phone number]** or **[insert email address]**.

Include if Office of Compliance related issues are applicable (e.g., issues identified related to design controls, recall strategy, etc): **[We also recommend early discussions with FDA's Office of Compliance regarding [describe Office of Compliance related issues]**. FDA also may conduct pre- or post-clearance inspections in certain circumstances, in accordance with its statutory authority. For further information, please contact **[insert appropriate Office of Compliance contact, title]** at **[insert phone number]** or **[insert email address]**.

[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 today will result in safer and more effective **[insert specific device type]**. We look forward to working with you on this important public health issue.

Sincerely,

Director, Center for Devices and Radiological Health
Food and Drug Administration