30-Day Notices and 135-Day PMA Supplements for Manufacturing Method or Process Changes, Guidance for Industry and CDRH

This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Office of Device Evaluation

Document issued on: February 19, 1998

Until May 26, 1998, comments and suggestions regarding this document should be submitted to Docket No. 98D-0080, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 12420 Parklawn Drive (HFA-305), Room 1-23, Rockville, MD 20857. Such comments will be considered when determining whether to amend the current guidance.

After May 26, 1998, comments and suggestions may be submitted at any time for Agency consideration to, Kathy M. Poneleit, 9200 Corporate Blvd, HFZ-402, Rockville, MD 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Kathy M. Poneleit at 301-594-2186 or Walter W. Morgenstern at 301-594-4699.

Additional Copies: World Wide Web/CDRH home page at http://www.fda.gov/cdrh or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 795 when prompted for the document shelf number.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health
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30-Day Notices and 135-Day PMA Supplement
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30-Day Notices and 135-Day PMA Supplements

New section 515(d) (6) of the act added by the FDA Modernization Act of 1998 (Pub. L. 105-115), provides that PMA supplements are required for all changes that affect safety or effectiveness unless such change involves modifications to manufacturing procedures or method of manufacture. Those types of manufacturing changes will require a 30-day Notice or, where FDA finds such notice inadequate, a 135-day PMA supplement. The purpose of this guidance[1] is to describe what changes generally will qualify for the 30-day Notice and what changes generally will not. For those changes in manufacturing that generally will not qualify for 30-day Notices, FDA requests PMA holders to submit supplemental PMAs or consult the agency on a case by case basis.

What Changes Qualify for Submission of a 30-Day Notice?

Changes that qualify for submission as a 30-day Notice are:

- changes to the manufacturing process, or
- changes in method of manufacture.

If these changes result in changes in the designed performance specifications, or the PMA designated physical or chemical specifications of the finished device, FDA recommends that they be submitted in the form of a 180-day PMA supplement (as per 21 CFR § 814.39). For example, if a manufacturing change in the curing process causes a device to become opaque but the performance specifications are for a clear product, a 30-day Notice is not applicable.

Changes that potentially qualify for a 30-day Notice are often intended to:

- reduce manufacturing and/or labor cost,
- reduce manufacturing time,
- reduce waste,
- compensate for a change in suppliers of raw material or components.

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Examples of manufacturing process or methods changes that would be likely to qualify for a 30-day Notice include changes in or from:

- purchasing controls,
- the sterilization type or process parameters within the same facility,
- a manual process to an automated process,
- a "joining" process where the toxicological and biocompatibility properties of the new adhesive is well known, and not considered to be a potential problem,
- a "joining" process where a different solvent or energy source is used to join the parts,
- cleaning methods used to remove manufacturing materials,
- manufacturing materials,
- clean room specifications,
- vendors of a material, where specifications of the material are unchanged (would probably only be submitted when the material was critical to performance of the device),
- a quality control test used to determine a specific attribute of an incoming components or raw material, the in process device or the finished device,
- the type of process used, (e.g., machining a part to injection molding the part), and
- the environmental conditions of the manufacturing, storage or distribution facilities.

Changes that qualify for a “Special PMA Supplement - Changes Being Effected” under 21 CFR 814.39(d)(2) for changes in quality controls or manufacturing process that add a new specification or test method, or otherwise provide additional assurance of purity, identity, strength, or reliability of the device can be submitted either as a “Special PMA Supplement - Changes Being Effected” or a 30-day Notice at the discretion of the PMA holder.

What Changes Do Not Qualify for Submission of a 30-Day Notice?

Examples of changes that the FDA does not believe qualify for submission of a 30-day Notice include any change in manufacturing needed to accommodate a change in:

- manufacturing/sterilization site,
- design or performance specifications,
- material specifications, when the toxicological and/or biocompatibility properties of the material, when used in similar applications, are not well known, and
- device operating software.

FDA recommends that submissions for these nonqualifying changes be in the form of a 180-day PMA supplement or alternate submission, e.g., Real-Time PMA supplement, Pilot PMA supplement for a manufacturing site change, etc.

Neither a 30-day Notice nor a PMA supplement is required if the change was a modification to the manufacturing procedures or method not affecting the safety and effectiveness of the product.

Contents of 30-Day Notices and 135-Day PMA Supplements

The 30-day Notice should contain the following:

1. a description of the change,
2. reason for the change,
3. rationale for implementation via the 30-day Notice,
4. a summary of the data or information supporting the change (a few concise pages with tables summarizing the key results) including the information specified below as applicable,

    - A summary of the procedures established for the identification, documentation, validation, review and approval of the manufacturing changes covered by the notice.
    - If the changed procedures are to be routinely verified by sampling and independent measurement, summarize the statistical rational for the sampling method.
    - If the changed procedures are validated, the process parameters should be monitored and controlled. The 30-day Notice should summarize how this will be done.
    - A summary of the completed validation study that demonstrates that the manufacturing change can be made without significantly changing the final device operation.
    - If the manufacturing change involves changes in components or raw material, a summary of the procedures established for evaluation of new suppliers, if any. Describe the type and extent of control to be exercised over the component or raw material, including specifications for the incoming material.
    - If the change involves use of a new contractor for manufacturing or quality control testing, a summary of the procedures and criteria established for evaluation of that contractor.
    - Summarize the change controls necessary for modifying the manufacturing or quality control instructions or specifications for the device.

5. statement of conformity to the requirements of the Quality System/GMP regulation, regarding change control, validation and document control found in 21 CFR Part 820, and
6. appendices of supporting data, where appropriate.

The information to be included in a 30-day Notice is only that necessary to evaluate the importance of the change, the declaration of conformity to 520(f), and the information specified above as applicable. More detailed data supporting the change may be provided in the form of appendices to facilitate the review process. A 30-day Notice may include all the information needed in a PMA supplement.

Should it be necessary to evaluate the change as a 135-day PMA supplement, the information to be submitted is as specified in 21 CFR 814.39(c).

Submissions for manufacturing procedures or method of manufacturing which qualify for review as a 30-Day Notice may not include requests for approval of other types of changes. *Submissions which contain device design, labeling changes, etc., in the same submission as the manufacturing changes will be automatically placed in the 180-day review queue.*

Action on a 30-Day Notice or 135-Day PMA Supplement

If the change qualifies as a 30-day Notice as described above, the change may be made 30 days after FDA receives the 30-day notice *unless* FDA informs the PMA holder within that 30 day period that the 30-day Notice is not adequate and describes the additional information or action required.

FDA will find a 30-day Notice not adequate if a detailed review of the data supporting the change must be performed.

If the 30-day Notice was not adequate, but contained data meeting appropriate content requirements for a PMA supplement, then the 30-day Notice will become a 135-day PMA supplement with the time spent reviewing the 30-day Notice subtracted from the 135 day review clock. The applicant must be informed in writing of the need to review the submission as a 135-day PMA Supplement and any additional data required to complete the review. This correspondence will issue within 30 days of receipt of the 30-day Notice.

If the 30-day Notice was not adequate and did not contain data meeting appropriate content requirements for a PMA supplement, the applicant will be informed that the 30-day Notice is not approved. The letter will either direct them to submit a 135-day PMA supplement or if the submission is too incomplete to make that determination, the applicant will be directed to submit either a 135-day PMA supplement or a new 30-day Notice (applicant's choice). This correspondence must issue within 30 days of receipt of the 30-day Notice.

If no action occurs within 30 days of FDA receipt of the 30-day Notice as required by section 515(d)(6)(A)(i) of the Federal Food, Drug, and Cosmetic Act (the act), the applicant may proceed with the change without receiving approval from FDA.

A flow chart is attached which shows the decision making process for action on a 30-day Notice.

Joint Review by OC and ODE

Review of 30-day Notices and 135-day PMA supplements will be performed jointly between the Office of Compliance (OC) and the Office of Device Evaluation (ODE). *OC will have the lead in the review of the submission, maintenance of the administrative record and construction of any written correspondence*. Each review division within OC and ODE will have a designated point-of-contact who is responsible for the coordination/evaluation of the 30-day Notice process. The PMA Staff will maintain the list of points-of-contact. Given the short review time frames and the joint office review, adequate communication (e-mail, fax, phone, etc.) between the Offices must take place regarding these submissions. The designated OC point-of-contact will be responsible for assuring identification of issues related to the Quality System regulation. The ODE designated point-of-contact will be responsible for assuring identification of issues related to safety and effectiveness due to the proposed manufacturing change. Within 5 days following receipt of the 30-day Notice, the ODE and OC designated points-of-contact will confer to

determine if the manufacturing change qualifies for a 30-day Notice. Within 10 days of receipt, the points-of-contact should consider whether the supplement can be completed as a 30-day Notice or the Notice is not adequate and a 135-day PMA supplement is needed to implement the change. A meeting of the points-of-contact should be considered to review the submission if it will facilitate the process. The ODE designated point-of-contact will communicate the review(s) and any deficiencies electronically (via disk, "L drive" or E-Mail) to the OC point-of-contact who is coordinating the review process for the 30-day Notice. Questions raised by the ODE point-of-contact regarding the submission will follow the format of a deficiency letter for incorporation into written correspondence to the PMA holder. The deficiency letter will contain the integrated deficiencies of both offices. If any changes are necessary to an ODE proposed deficiency (including not incorporating the proposed deficiency into the letter), the ODE designated lead will be notified. The OC draft of the proposed correspondence will be shared with the ODE point-of-contact for final comment. The letter will be forwarded to ODE, PMA Staff for signature by day 25. The letter will be faxed by the PMA Staff to the PMA holder.

Should there be scientific disagreement between OC and ODE, appropriate dispute resolution procedures should be followed. For example see ODE Guidance Memorandum #G93-1 "Documentation and Resolution of Differences of Opinion on Product Evaluations."

Submission of a 30-Day Notice

To facilitate the review of a 30-day Notice, applicants are requested to clearly identify in their cover letter that the submission is a **30-DAY NOTICE.** *Failure to properly identify the submission will cause it to be regarded by the agency as a supplemental PMA and will not allow the submitter to take advantage of the 30-day Notice provision. Rather, the submission will be placed automatically in the 180-day review queue for PMA supplements.*

Applicants are requested to submit three identical copies simultaneously. To facilitate joint review by OC and ODE, **one copy** should be sent to:

Food and Drug Administration
Office of Compliance
Field Programs Branch (HFZ-306) / ATTN: 30-day Notice
2098 Gaither Road
Rockville, Maryland 20850

The remaining **two copies** (the official copies) should be sent to:

Food and Drug Administration
Office of Device Evaluation
Document Mail Center (HFZ-401) / ATTN: 30-day Notice
9200 Corporate Blvd.
Rockville, Maryland 20850

PMA Letters and Database Tracking Considerations

Several new boilerplates have been created to facilitate the 30-day Notice/135-day supplement process.

- Rejection Letter For “30-Day Notices”
- 30-Day Notice Not Adequate but Is Complete - Now 135-Day Supplement
- 30-Day Notice Not Adequate and Not Complete - Now 135-Day Supplement
- 30-Day Notice Not Adequate and Not Complete - Cannot Determine if 135-Day Supplement or New 30-Day Notice Is Needed

The PMA database will be modified to enable tracking and reporting for the 30-day Notices and 135-day PMA supplements.

Effective Date

This guidance is effective February 19, 1998.

30-Day Notices and 135-Day PMA Supplements for Manufacturing Changes