Guidance for Industry

Draft Guidance: Likelihood of Facilities Inspections When Modifying Devices Subject to Premarket Approval

Draft Guidance – Not for Implementation

This guidance document is being distributed for comment purposes only.
Draft released for comment on August 5, 1999

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

Division of Program Operations
Office of Compliance

Preface

Public Comment:

For 90 days following the date of publication in the Federal Register of the notice announcing the availability of this guidance, comments and suggestions regarding this document should be submitted to the Docket No. assigned to that notice, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852.

Additional Copies:

World Wide Web/CDRH home page at http://www.fda.gov/cdrh/ochome.html or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 1269 when prompted for the document shelf number.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. XX-XXXX]

Guidance for Industry on The Likelihood of Facilities Inspections When Modifying Devices Subject to Premarket Approval: Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the **draft** guidance entitled **"Guidance for Industry on The Likelihood of Facilities Inspections When Modifying Devices Subject to Premarket Approval ."** This guidance is not final nor is it in effect at this time.

The industry has experienced difficulties in planning the implementation of manufacturing and/or other changes involving a device with an approved premarket approval application (PMA), product development protocol (PDP), or humanitarian device exemption (HDE), when a FDA inspection may or may not be necessary. This draft guidance document will help firms determine whether a FDA inspection is needed and more easily manage the time frames associated with implementing changes in manufacturing facilities, manufacturing methods or procedures, labeling, design or performance.

DATES: Written comments concerning this guidance must be received by (insert date 90 days after date of publication in the **Federal Register)]**.

ADDRESS: See the **SUPPLEMENTARY INFORMATION** section for information on electronic access to the guidance**.** Submit written requests for single copies on a 3.5" diskette of the guidance document entitled "**Guidance for Industry on The Likelihood of Facilities Inspections When Modifying Devices Subject to Premarket Approval "** to the Division of Small Manufacturers Assistance (HFZ-220), Center for Devices and Radiological, Food and Drug Administration, 1350 Piccard Dr., Rockville, MD 20850. Send two self-

addressed adhesive labels to assist that office in processing your request, or fax your request to 301-443-8818.

Written comments concerning this guidance must be submitted to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments should be identified with the docket number found in brackets in the heading of this document.

Submit written comments on "**Guidance for Industry on The Likelihood of Facilities Inspections When Modifying Devices Subject to Premarket Approval"** to the contact person listed below.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background

During recent FDA/medical device industry grassroots forums, industry representatives discussed difficulties they have experienced in planning for changes related to

devices with applications approved through the Premarket Approval (PMA), Product Development Protocol (PDP) or Humanitarian Device Exemption (HDE) processes. The industry representatives indicated that much of the difficulty was caused by uncertainty about FDA policies on what circumstances require submission of a PMA Supplement, when a PMA inspection may be required, or when documenting the change in the firm's files may be adequate.

FDA, with input from interested parties, developed this guidance document in an effort to help firms manage the time frames associated with implementing changes in manufacturing facilities, manufacturing methods or procedures, labeling or performance.

This guidance identifies factors that are involved in determining whether:

- a change in manufacturing methods or procedures can be implemented and the device can be distributed without prior notice to FDA, without any delay except that necessary to achieve compliance with the requirements of the Quality System/GMP regulation;
- a change in manufacturing methods or procedures can be implemented and the device can be distributed 30 days after prior written notice has been filed with FDA (30-Day Notice) in accordance with Section 515(d)(6)(A)(i) of the Food, Drug and Cosmetic Act, 21 U.S.C. § 321 et seq. (the Act) and 21 CFR 814.39, unless FDA notifies the holder of the PMA that the notice is inadequate; or
- a change in facilities can be accelerated when a firm meets the prerequisite conditions for an Express PMA Supplement for Facilities Change.

The guidance is intended to reduce the regulatory burdens and concomitant delays in the implementation of a manufacturing change while maintaining necessary safeguards. The factors that an applicant and/or FDA should take into consideration when determining the need for submission of a Supplement and the likelihood of an inspection are presented in a model decision procedure.

II. Significance of Guidance

This guidance document represents the agency's current thinking on changes to devices with approved PMAs, PDPs or HDEs. 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 applicable statute, regulations, or both.

The agency has adopted Good Guidance Practices (GGPs), which set forth the agency's policies and procedures for the development, issuance, and use of guidance documents (62 FR 8961, February 27, 1997). This guidance document is issued as a Level 1 draft guidance consistent with GGPs.

III. ELECTRONIC ACCESS

In order to receive draft guidance on "**Guidance for Industry on The Likelihood of Facilities Inspections When Modifying Devices Subject to Premarket Approval "** via your fax machine, call the CDRH Facts-On-Demand (FOD) system at **800.899.0381** or **301.827.0111** from a touch-tone telephone. At the first voice prompt press 1 to access DSMA Facts. At the second voice prompt press 2, and then enter the document number 1269 followed by the pound sign (#). Then follow the remaining voice prompts to complete your request.

Persons interested in obtaining a copy of the guidance may also do so using the World Wide Web (WWW). CDRH maintains an entry on the World Wide Web for easy access to information including text, graphics, and files that may be downloaded to a PC with access to the Web. Updated on a regular basis, the CDRH Home Page includes various Level 1 guidance documents for comment, device safety alerts, Federal Register reprints, information on pre-market submissions (including lists of approved applications and manufacturers' addresses), small manufacturers' assistance, information on video conferencing and electronic submissions, mammography matters, and other device-oriented information. The CDRH home page may be accessed at **http://www.fda.gov/cdrh**. "**Guidance for Industry on The Likelihood of Facilities Inspections When Modifying Devices Subject to Premarket Approval"** will be available at http://www.fda.gov/cdrh/**ochome**.

IV. Comments

Interested persons may comment on this Level 1 draft guidance (insert date 90 days from date of publication in the **Federal Register**), submit to**:** Dockets Management Branch (address above) written comments regarding this draft guidance. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance document and received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

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DATED:

THE LIKELIHOOD OF FACILITIES INSPECTIONS WHEN MODIFYING DEVICES SUBJECT TO PREMARKET APPROVAL

This guidance document represents the agency's current thinking on various types of PMA submissions (including PDP and HDE submissions) and the corresponding factors that influence the likelihood that an inspection will occur. 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.

BACKGROUND

During recent FDA/medical device industry grassroots forums, industry representatives discussed difficulties they have experienced in planning for changes related to devices with applications approved through the Premarket Approval (PMA), Product Development Protocol (PDP) or Humanitarian Device Exemption (HDE) processes. The industry representatives indicated that much of the difficulty was caused by uncertainty about FDA policies on what circumstances require submission of a supplemental application, when to expect an FDA inspection, or when documenting the change in the firm's files may be adequate.

In an effort to help such firms predict when they can implement changes in manufacturing facilities, manufacturing methods or procedures, labeling, design or performance, FDA, with input from interested parties, developed this guidance document.

This guidance document is primarily based on established policy and procedures. The one exception is a modification to the Pilot PMA Supplement Program, now referred to as Express PMA Supplements for Facilities Change, that will reduce the burden on firms that plan to move to a manufacturing facility that is not being used for manufacturing other devices, drugs or biologics. This change is based on a review of previous facility moves. Problems were rarely encountered when firms moved manufacturing to a new facility (i.e., not currently manufacturing other devices or drugs). In contrast, problems were encountered when firms moved manufacturing to facilities already manufacturing other devices or drugs, especially when they were dissimilar to the subject device. While the cause(s) of this phenomenon has not been fully established, it appears to be the affect of "force fitting" the manufacturing process of the subject device into an environment (including physical facilities, equipment, procedures and personnel) originally designed for other products. The Pilot PMA Supplement Program was originally described in a March 20, 1996 letter to device manufacturers from the Director, CDRH.

This guidance identifies factors that are involved in determining whether:

- a change in manufacturing methods or procedures can be implemented and the device distributed without prior notice to FDA and without any delay except that necessary to achieve compliance with the requirements of the Quality System/GMP regulation , 21CFR, Part 820;
- a change in manufacturing methods or procedures can be implemented and the device distributed 30 days after prior written notice has been filed with FDA (30-Day Notice) in accordance with Section 515(d)(6)(A)(i) of the Food, Drug, and Cosmetic Act, 21 USC §321 et seq. (the Act) , and 21 CFR 814.39, unless FDA notifies the holder of the PMA that the notice is inadequate; or
- a change in facilities can be accelerated when a firm meets the prerequisite conditions for an Express PMA Supplement for Facilities Change.

This guidance also identifies factors involved in deciding when a manufacturing change would ordinarily precipitate a preapproval inspection. A determination that a preapproval inspection would ordinarily be appropriate, however, does not preclude FDA from exercising discretion in deciding in a particular situation that a preapproval inspection is not necessary. Conversely, the guidance document in no way limits FDA from conducting a reasonable inspection within the meaning of Section 704 of the Act at any time it deems appropriate.

This guidance document is intended to reduce the regulatory burdens and concomitant delays in the implementation of a manufacturing change while maintaining necessary safeguards. Such safeguards include performing preapproval inspections where: (a) the PMA holder has a recent history of substantial deviations from Quality System/GMP requirements; (b) the device's manufacturing has not been inspected for compliance with Quality System/GMP requirements within the last two years; or (c) the nature of the change or the inadequacy of the documentation filed with FDA necessitates a preapproval inspection to verify the appropriateness of the change.

Finally, this guidance is intended to be complementary to a companion draft guidance document that resulted from a Center for Device and Radiological Health (CDRH) reengineering effort. The draft document, entitled Modification To Devices Subject To Premarket Approval-The PMA Supplement Decision Making Process, is available on the internet at http://www.fda.gov/cdrh, or FACTS-ON-DEMAND, 800-899-0381, Document Number 102.

THE MODEL

Attachment A contains the flow chart entitled Modification of Devices Subject to Premarket Approval and the Likelihood of Inspection. It also includes a step-by-step description of the decision process that is necessary to determine the likelihood of an inspection.

The model encompasses three types of changes. They are:

- changes in manufacturing method or procedures (the E pathway);
- changes in the location of a manufacturing facility (the F pathway); and
- changes to the device or its labeling (the G pathway).

CHANGES IN MANUFACTURING METHODS OR PROCEDURES (THE E PATHWAY)

Changes in manufacturing method or procedures for PMA devices were addressed in the Food and Drug Administration Modernization Act of 1997(FDAMA). FDAMA modified Section 515(d)(6) of the Food, Drug &Cosmetic Act to permit a manufacturer of a device with an approved PMA to submit a 30-Day Notice describing the change and controls used to assure that the change would not adversely affect the safety or effectiveness of the device. Manufacturers can proceed with the change 30 days after receipt of the notice by CDRH unless CDRH determines that the notice is inadequate. CDRH may also convert the 30-Day Notice to a 135-Day Supplement if the notice presents complex issues or too much data to be reviewed within 30 days. A guidance document explaining the requirements for a 30-Day Notice is available on the internet at http://www.fda.gov/cdrh/blbkmem.html.

FDA recognizes that some of the changes will be necessary to correct manufacturing problems that are identified by the firms' corrective and preventative action systems, or as the result of recalls. Because such changes must be implemented as quickly as possible, FDA will not normally conduct inspections as part of the review of 30-Day Notices or 135-Day Supplements. Furthermore, the recent inspectional history of the manufacturer will not generally be a consideration, unless major flaws in essential elements of the manufacturer's change control procedures and/or practices were noted during the last inspection and corrections have not been satisfactorily completed.

CHANGES IN THE LOCATIONS OF MANUFACTURING FACILITIES (THE F PATHWAY)

For a number of years, changes in the location of a manufacturing or sterilization facility have required inspection of the new facility to assure that it was capable of manufacturing the PMA device and was compliant with the requirements of the Good Manufacturing Practices regulation. The statutory requirement to obtain clearance for the move via a 180-day PMA Supplement has presented special problems for certain manufacturers. Depending on the circumstances, a move to a different manufacturing facility may be

inventory or time sensitive, with the result that the firm may experience economic hardship if it cannot obtain relatively rapid approval of its PMA Supplement. Many manufacturers of Class III devices now have a thorough understanding of the quality system/GMP requirements, and experience few problems when they move existing equipment and personnel to new facilities. Those firms that continue to have problems, usually attempt to move manufacturing to facilities where other devices, drugs or biologics are being manufactured. This is because the manufacturing equipment at those facilities cannot always be adequately qualified and the new personnel are unfamiliar with the product and its manufacturing and quality assurance requirements.

In 1996, FDA introduced a pilot program to facilitate the PMA Supplement review process when firms needed to change manufacturing facilities as quickly as possible. The Pilot Program for PMA Supplements, now referred to as Express PMA Supplements for Facilities Change (Attachment B), offers qualified firms an opportunity to consult with CDRH's Office of Compliance prior to initiating their move. The Office of Compliance, or the district office, as appropriate, will review the firm's protocols for validation/equipment qualification and, if necessary, offer suggestions. If the firm's protocols for validation/equipment qualification are satisfactory, or need only minor modifications, the firm will usually proceed with the move, conduct the necessary validation/qualification studies and submit the results of the studies in the PMA Supplement. If the data is satisfactory, the PMA Supplement will be approved without an on-site inspection of the new facility. Of the 35 PMA Supplements submitted under the Pilot Program since October, 1997, 60 per cent were approved within two weeks and the remainder approved within one month.

Originally, FDA required an inspection of all facilities that were not being used for device, drug or biologics manufacturing at the time of the facilities change, because it had no current information on the status of the facility. Experience has shown, however, that moves to such facilities usually present only minor problems, if any, because firms typically move the manufacturing equipment from the old facility or install new equipment with similar capabilities. In addition, the manufacturing personnel are often moved to the new facility whenever feasible. If the manufacturing personnel cannot be moved, the responsible management from the old facility usually transfers to the new facility and provides training to new personnel. The program for Express PMA Supplements for Facilities Change now allows for moves to such facilities without an on-site inspection of the new facility if: (1) the PMA Supplement is in order; and (2) the original manufacturing facility received an inspection within the last two years, and there are no recent substantial deviations from the quality system/GMP requirements.

CHANGES TO THE DEVICE OR ITS LABELING (THE G PATHWAY)

Changes related to the physical attributes of the device, the performance, intended use or the labeling will normally require submission of a PMA Supplement. Labeling changes that enhance the safety of the device or the use of the device may be submitted in a 30-Day "PMA Supplement-Changes Being Effected", and the change placed into effect prior to the receipt of an approval order [21 CFR 814.39(d)]. For guidance on other types of

labeling changes, refer to the draft companion guidance; Modification to Devices Subject to Premarket Approval-The PMA Supplement Decision Making Process.

Other changes to the device may be of such magnitude that they require a new PMA instead of a PMA Supplement. This may occur when the new device has a technological basis of operation or mode of operation different from the original device and the manufacturing process for the new device differs significantly from the manufacturing process used for the original device. Typically, a new PMA application will require submission of a complete Manufacturing Section and an on-site inspection.

Attachment A

THE LIKELIHOOD OF FACILITIES INSPECTIONS WHEN MODIFYING DEVICES SUBJECT TO PREMARKET APPROVAL

DESCRIPTION OF THE DECISION PROCESS

E1

The FDA Modernization Act of 1997 added a new Section 515(d)(6) to the FD&C act that permits a manufacturer of a device with an approved PMA to submit a 30-Day Notice for a change in manufacturing method or manufacturing procedure. Normally, manufacturers initiate such changes with the intention of reducing cost, or to compensate for a change in raw material or component. A change in manufacturing method or procedures that also results in a change to a device's performance specification, or a change in a device's design that requires a change in manufacturing method or procedure does not qualify for the 30-Day PMA Notice. Approval for such changes should be sought through a 180-Day PMA Supplement.

If the change will not impact on the device's performance specifications or design proceed to **E2.**

If the change is limited to the location of the manufacturing facility, proceed to **F1.**

E2

The following are some examples of changes to manufacturing method or manufacturing procedures that **could potentially** affect the safety or effectiveness of the device:

- purchasing controls,
- the sterilization type or process parameters with the same facility,
- a manual process to an automated process,
- a "joining" process where the toxicological and biocompatability properties of the new adhesive are 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,
- a cleaning method used to remove manufacturing material,
- manufacturing materials,
- clean room specifications,
- vendors of material, where specifications of the material are unchanged,
- a quality control test used to determine a specific attribute of an incoming component or raw material, the in process device or the finished device,
- the type of process used (e.g., changing from machining a part to injection molding the part), and
- the environmental conditions of the manufacturing, storage or distribution facility.

If your evaluation of the change indicates that the safety or effectiveness of the device will not be affected, proceed with the changes and retain records of the change in your files.

If you are uncertain whether the change will affect safety or effectiveness, or your evaluation indicates that the change may affect safety or effectiveness, submit a 30-Day Notice for the change. Guidance for submitting the 30-Day Notice can be found on the FDA World Wide Web; http://www.fda.gov/cdrh/ode/p98-4.html.

F1

Has the facility where the device is currently manufactured, and the facility to which manufacturing may be moved, received a Quality System/GMP inspection within the last two years?

If the facility to which the manufacturing is being moved is not being used at this time for manufacturing any device or drug, and the current facility received an inspection within the last two years, proceed to **F2**. If the facility to which the manufacturing is being moved has been used for manufacturing any device, drug or biologic and both facilities received an inspection within the last two years, proceed to **F2**.

If not eligible to proceed to F2, the sponsor should submit a 180-Day Supplement.

If the sponsor is unsure about the most recent inspection date and/or compliance status of the two facilities, contact the Field Programs Branch (HFZ-306) at 301-594-4695. Provide the full name and address of each facility as well as the registration number (if available). If the facility to which the manufacturing is being moved has never been used for manufacturing devices, but has been used for manufacturing drugs or biologics that are similar to the device (e.g. saline solution vs. contact lens cleaning solution), it may be necessary to consider its compliance status.

F2

If no substantial deviations from Quality System/GMP requirements have been identified in a recent inspection (as evidenced by a NAI or VAI inspection or close-out letter from FDA) proceed to **F3**. If Quality System/GMP problems were identified at either facility , but have not been resolved (as evidenced by a Warning Letter and no subsequent close-out letter from FDA, or a regulatory action such as seizure or injunction), the sponsor should submit a 180-Day Supplement for the move.

If the current facility was inspected within the last two years and no recent substantial deviations from Quality System/GMP requirements have been identified (as evidenced by a NAI or VAI inspection or close-out letter from FDA), and the manufacturing is being moved to a facility that is not being used at this time for manufacturing any device, drug or biologic proceed to **F3**.

F3

When the applicant intends to use existing equipment and personnel at the facility to which the manufacturing is being moved , it should determine whether that facility will use similar methods and procedures to those currently used. Also ascertain that the manufacturing process at the facility to which the manufacturing is being moved can be easily adapted to satisfy the manufacturing specifications of the device under consideration.

An example of similar manufacturing methods would be two manufacturing facilities using 100% EO sterilization (as opposed to one using radiation sterilization and the other EO). An example of similar manufacturing procedures would be two facilities using injection molding for components with similar injection pressures, temperature and speed.

If the answer is yes, proceed to **F4**. If the manufacturing process is not similar, the sponsor should submit a 180-Day Supplement.

If the manufacturing is being moved to a facility that is not being used to manufacture any device, drug or biologic at this time, and the manufacturing methods, procedures, and equipment (if not the same equipment, similar or equivalent equipment with the same capability) will not be changed, proceed to **F4**

F4

Does the applicant have adequate procedures, as required by 21 CFR Part 820, to assure that the manufacturing equipment and facilities are adequately requalified and/or revalidated as required?
When manufacturing equipment will be moved to a location where no device or drug manufacturing has occurred, or new manufacturing equipment is installed at a new location, the applicant should review its change control procedures to assure itself that all necessary equipment qualifications will be conducted prior to the resumption of manufacturing. If the move does not involve a transfer of manufacturing equipment it may still be necessary to qualify existing equipment at the facility to which the manufacturing is being moved to demonstrate that it has the capability to meet the manufacturing specifications of the device under consideration.

If the manufacturing process for the device under consideration has not been validated within the last year, it may also be necessary to revalidate the complete process after the move.

If adequate procedures and protocols are in place, you qualify for an “Express PMA Supplement For Facilities Change” (see Attachment C). If not, you should submit a 180-Day PMA Supplement.

When you submit a 180-Day PMA Supplement because the most recent inspection of either the current or anticipated manufacturing facility (that is currently manufacturing other drugs or devices) was conducted more than two years ago, FDA will probably conduct an inspection.

You may request assistance prior to submitting a PMA Supplement. For those requests regarding review of protocols for qualification/validation studies, the Office of Compliance will coordinate the requests, as necessary, with the District Office. As an alternative, the Office of Compliance will review the protocols and provide comment. If requested, a meeting with Center personnel to discuss technical issues will be scheduled within 15 days of the request. To request a pre-submission consultation, contact the Office of Compliance, Field Programs Branch (HFZ-306), 301-594-4695, FAX 301-594-4715.

Regardless of whether you requested a pre-submission consultation, you should contact the Office of Compliance (see above) to indicate your intention to submit the Supplement with completed qualification/validation data, and to request a date for inspection of the anticipated manufacturing facility. The Office of Compliance will coordinate a mutually satisfactory inspection date with the District and the firm. With the exception of firms with a recent substantial deviation from the QS/GMP requirements, the inspection will take place no later than 30 working days from the date the Office of Compliance receives a copy of the Supplement with complete information on the qualification/validation data.

Your request should include notification to CDRH that the procedures are complete and that the facility will be ready for inspection by the scheduled date.

If the qualification/validation data and other quality assurance requirements are satisfactory, the PMA Supplement will be approved by CDRH within 10 working days following completion of the inspection.

Firms that indicate a readiness for the inspection and are found not ready will be placed in the normal review and inspection queue.

G1

Are the anticipated changes limited to changes in labeling? If so refer to Chart B in the companion "PMA Modification Flowchart" for guidance. If other changes to the device are anticipated, proceed to **G2**.

G2

If you are anticipating a design change, will the changed device have a similar indication for use, mode of operation and technological basis of operation as the currently approved device? If any one of the three conditions is substantially affected by the design change, proceed to **G3**. If the design change will result in a device that is similar to the currently approved device, you should submit a 180-Day Supplement.

G3

There are certain changes that may trigger a request by the Office of Device Evaluation (ODE) to submit a new PMA rather than a PMA Supplement. If you anticipate a change in the indication(s) for use, for which significant new clinical data will be necessary to demonstrate the device's safety or effectiveness, you should consult with the appropriate division within ODE. You should also consult with the appropriate division if there will be a change in the patient population that will be treated with the device. Finally, if you anticipate that a design change will be so significant that a new generation of the device will develop, you should consult with the appropriate ODE division.

Attachment B

EXPRESS PMA SUPPLEMENTS FOR FACILITIES CHANGE

BACKGROUND

In the past, some firms whose PMA Supplements required inspection of the facility experienced delays in receiving approval. Some of the delay was caused by the limited number of field investigators to perform inspections, and headquarters staff to perform the reviews. Another source of delay was the inability of some firms to successfully transfer a manufacturing process to a different facility, even though the Supplement's information on process controls and qualification/validation protocols appeared to be adequate. As a result, facilities sometimes required repeated and time-consuming inspections before their PMA Supplements could be approved. FDA's offer to consult with firms should help alleviate both sources of delay, because needless inspections will be eliminated.

RECOMMENDED PROCEDURES FOR FIRMS

A firm may elect to follow the existing process or, if it qualifies, may choose to submit its PMA Supplement to the agency under the "express" system described below. If the express system is chosen, a firm can participate in the following way:

No Inspection Route

A firm that does not have a recent history of substantial deviations from the QS/GMP can contact the CDRH Office of Compliance, Field Programs Branch, HFZ-306, 301-594-4695 (fax 301-594-4715), indicating its intention to submit a PMA Supplement and requesting the compliance status of the anticipated manufacturing facility. The Office of Compliance should be advised if the anticipated manufacturing facility is not being used for manufacturing any device or drug, as such facilities will not normally be subject to a preapproval inspection.

You may request assistance prior to submitting a PMA Supplement. For those requests regarding review of protocols for qualification/validation studies, the Office of Compliance will coordinate the request, as necessary, with the District Office. As an alternative, the Office of Compliance will review the protocols and provide comment. If requested, a meeting with Center personnel to discuss technical issues will be scheduled within 15 days of the request. To request a pre-submission consultation, contact the above office.

If the Field Programs Branch determines that the anticipated facility qualifies for no inspection, the firm submits appropriate information on the process controls and completed qualification/validation studies as part of its PMA Supplement. This submission should contain a statement from the applicant attesting to its compliance

with the QS/GMP requirements. Two copies should be sent to CDRH's Office of Device Evaluation. At the same time, a duplicate copy should be sent directly to CDRH's Office of Compliance, Field Programs Branch, HFZ-306, 9200 Corporate Blvd., Rockville, MD 20850. The duplicate copy should be flagged: "Office of Compliance Copy."

If the Office of Compliance finds the process control and qualification/validation data are satisfactory, it will recommend approval of the new facility without conducting an inspection. This recommendation will be made within 30 working days from the date of receipt of the completed submission. Based on the Office of Compliance recommendation, the Office of Device Evaluation will approve the Supplement if it is otherwise in order.

Under certain circumstances, FDA may conduct an inspection of the facility following approval of the PMA Supplement. Such inspections will be conducted either because the facility has never been inspected, or to follow up on reports of problems associated with the product and/or the facility.

Attachment C

DEFINITIONS

Different Facility: A manufacturing facility or establishment located at a different mailing address which may, or may not, be under the same ownership and management control as the current facility where the applicant's finished device(s) are manufactured. Typically, the different facility will be assigned a different FDA registration number.

New Facility: A manufacturing facility or establishment that it is not currently being used for manufacturing devices or drugs. The facility may, or may not, be under the same ownership and management control as the current facility where the applicant's finished device(s) are manufactured. The facility may, or may not, be located in the immediate vicinity of the facility where the applicant's device(s) are manufactured and may, or may not, be assigned the same FDA registration number as those facilities.

Recent History of Substantial Deviations From QS/GMP Requirements: A QS/GMP inspection within the last two years identified objectionable conditions that resulted in a Warning Letter or other regulatory action, and which have not been corrected as indicated by a close-out letter from FDA. Facilities that remain under a temporary or permanent injunction would be considered to have a recent history of substantial deviations.

Close-Out Letter: A letter issued by either the FDA district office or CDRH Office of Compliance stating that the written response received from a firm, or recent inspectional findings, indicate that the corrections made by the firm appear to be adequate.

Similar Device: When compared the device under consideration, a similar device is one whose indications for use, mode of operation, technological basis of operation and materials are similar. The device under consideration may have different physical/chemical/electrical characteristics that require different manufacturing specifications. Examples include: various models of molded contact lenses, catheters that vary only in dimensions, or orthopedic implants with different shapes and dimensions.

Similar Process: When compared to the manufacturing process of the device under consideration, a similar process and its quality system could , taking into account modifications necessary to meet different specifications of the device under consideration, be used to manufacture that device.

Device Under Consideration: The device that is the subject of the PMA application or PMA Supplement.