SUBJECT:	IMPLEMENTATION DATE
MEDICAL DEVICE PMA PREAPPROVAL AND PMA POSTMARKET INSPECTIONS	March 5, 2012
	COMPLETION DATE
	March 5, 2016

DATA REPORTING

PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
73-91	83001 Premarket Approval Inspections 83001A Postmarket Inspections

Index for Compliance Program 7383.001

Part VI **References and Program Contacts**

Attachments:

Attachment A Notification of PMA Postmarket Inspection Form
Attachment B CDRH Office of Compliance Organizational Chart
Attachment C CDRH Office of In Vitro Diagnostic Devices Organizational Chart

FIELD REPORTING REQUIREMENTS

A. PMA PREAPPROVAL INSPECTIONS – PAC Code 83001:

All Premarket Approval (PMA) preapproval inspection assignments should be completed by the due date specified in the assignment. All PMA Establishment Inspection Reports (EIRs) must be received by the Center for Devices and Radiological Health (CDRH) within 30 calendar days from the ending date of the inspection.

Forward all PMA approval or non-approval recommendations to CDRH's Field Operations Branch (FOB) via e-mail at the address listed below. For non-approval recommendations, state the reasons why approval should not be granted. Districts must not wait for final completion of violative and non-violative inspection reports before notifying CDRH of their recommendation.

Once the EIR is completed, the endorsement coversheet should be labeled as "PMA Preapproval Inspection," include the PMA number that was covered during the inspection, and the FDA Field Accomplishments and Compliance Tracking System (FACTS) assignment number. Send the EIR, any FDA 483, exhibits, attachments, and firm's responses by e-mail to the PMA preapproval coordinator at CDRHPMAPROGRAM@fda.hhs.gov. Ensure that the subject line of the e-mail utilizes one of the following nomenclatures:

1. **PMA Preapproval – EIR –** Name of Manufacturer/Sterilizer Site **–** FEI Number
2. **PMA Preapproval – Firm's Response** – Name of Manufacturer/Sterilizer Site **–** FEI Number

Note: When an inspection is conducted that includes both a PMA preapproval inspection and another type of inspection covering commercially-marketed products (postmarket, routine, compliance follow up, etc.) and the recommendation is Official Action Indicated (OAI), the District may have direct reference to take administrative actions on the inspection covering the commercially-marketed products. However, CDRH would also need to review the inspection for the preapproval PMA device covered during the inspection before any direct reference action is taken on the commercial product so that consistent information is supplied to the firm for all products. If the documents related to the PMA preapproval inspection are placed in the Case Management System (CMS), an e-mail notification that includes the CMS number should be sent to CDRH's PMA preapproval coordinator at the e-mail address listed above.

B. PMA POSTMARKET INSPECTIONS– PAC Code 83001A:

All PMA postmarket inspection assignments should be completed by the due date specified in the assignment. The results of the postmarket inspection must be received by CDRH within 30 calendar days from the ending date of the inspection. A Notification of PMA Postmarket Inspection Form (Attachment A) should be completed for each inspection and returned to the PMA postmarket coordinator via e-mail.

For domestic PMA postmarket inspections where the District has classified the inspection as No Action Indicated or Voluntary Action Indicated, forward the FACTS coversheet and EIR narrative to the PMA postmarket coordinator via e-mail to the address listed below.

For domestic PMA postmarket inspections where CDRH review is requested or the District has classified the inspection as OAI, and all foreign PMA postmarket inspections, the endorsement coversheet should be labeled as "PMA Postmarket Inspection," include the PMA number that was covered during the inspection, and the FACTS assignment number. Send the EIR, any FDA 483, exhibits, attachments, the firm's responses, and any correspondence issued to the firm to the PMA postmarket coordinator at CDRHPMAPROGRAM@fda.hhs.gov. If the documents related to the PMA postmarket inspection are placed in CMS, an e-mail notification that includes the CMS number should be sent to CDRH's PMA postmarket coordinator. Ensure that the subject line of the e-mail utilizes one of the following nomenclatures:

1. **PMA Postmarket – EIR –** Name of Manufacturer/Sterilizer Site **–** FEI Number
2. **PMA Postmarket – Firm's Response** – Name of Manufacturer/Sterilizer Site **–** FEI Number

PART I

BACKGROUND

A. PREMARKET APPROVAL AND THE QUALITY SYSTEM REGULATION

Premarket approval is the process used by FDA to review and evaluate the safety and effectiveness of Class III medical devices. Class III medical devices are those that are life-supporting or life-sustaining, are for a use that is of substantial importance in preventing impairment of human health, or that present a potential unreasonable risk of illness or injury.[1] All Class III devices (with the exception of certain preamendment Class III devices) must obtain premarket approval from FDA before they can be introduced into interstate commerce. Manufacturers are required to submit a PMA application with substantial evidence that demonstrates the device is safe and effective for the intended use.

Assuring that only safe and effective devices are distributed is a two-phase process.

1. The inherent safety and effectiveness of a device is established during the design phase. A quality system will include proper consideration of such factors as performance requirements, the needs of the user, operational environments, proper selection of components, etc. Assurance that the design will embody the proper degree of safety and effectiveness is obtained through application of an appropriate design and development process requiring design verification and design validation, which includes clinical evaluation and/or laboratory testing.

2. Once the design has been determined to be safe and effective, the adequacy of the manufacturing process will determine whether the design can be consistently reproduced without degrading this inherent quality. The adequacy of the manufacturing process is established through proper process design and proven through appropriate process validation where applicable. Where deviations from device specifications could occur as a result of the manufacturing process, process control procedures must be established to include procedures for the monitoring and control of the process parameters and component and device characteristics during production.

In a PMA application, manufacturers are required to include descriptions of the methods used in, and the facilities and controls used for, the design, manufacture, processing, packing, storage, and, where appropriate, installation of the device. These requirements for FDA-regulated products are known as current good manufacturing practice (CGMP) requirements, which are promulgated in the Quality System (QS) regulation. The final QS regulation (21 CFR 820) was published in the Federal Register in October 1996 and became effective June 1, 1997. This regulation requires each manufacturer to prepare and implement QS procedures to assure that a formally-established and documented quality system is accomplished. The requirements in this part govern the methods used in, and the facilities and controls used for, the design, manufacture,

[1] 21 CFR 860.3

processing, packing, storage, and, where appropriate, installation of all finished devices intended for human use. The requirements in this part are intended to ensure that finished devices will be safe and effective and otherwise in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act). Under the authority of section 515(d)(2)(C) of the FD&C Act, approval of a PMA application for a device can be denied if a manufacturer does not conform to the QS regulation requirements.

B. THE MEDICAL DEVICE REPORTING REGULATION

The first Medical Device Reporting (MDR) regulation became final on December 13, 1984. As a result of changes mandated by the Safe Medical Devices Act of 1990 and the Medical Device Amendments of 1992, the 1984 MDR regulations (21 CFR 803 & 807) were revised and published on December 11, 1995. The FDA Modernization Act of 1997 made additional changes and a revised MDR regulation was proposed in May 1998. The final revised MDR regulation was published in the Federal Register on January 26, 2000. The latest version of the MDR regulation includes reporting requirements for manufacturers, user facilities, and importers. MDR reporting for medical device distributors (except importers) was revoked by the FDA Modernization Act of 1997. Distributors are, however, still required to maintain complaint records, per 21 CFR 803.18(d)(1-3). 21 CFR Part 803 requires manufacturers of medical devices, including in vitro diagnostic devices, to report to FDA whenever the manufacturer or importer receives or otherwise becomes aware of information that reasonably suggests that one of its marketed devices:

1. may have caused or contributed to a death or serious injury or,

2. has malfunctioned and the device, or any other device marketed by the manufacturer or importer, would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Note: importers (initial distributors) of medical devices are subject to 21 CFR Part 803. In addition, foreign manufacturers whose devices are distributed in the US are also subject to the MDR regulation requirements, per 21 CFR 803.58.

C. THE MEDICAL DEVICE TRACKING REGULATION

Under the authority of section 519(e) of the FD&C Act, the agency may issue a written tracking order that tells a manufacturer to implement a tracking program that meets the requirements of 21 CFR Part 821. Devices subject to tracking may include those that are permanently implanted or life sustaining/life supporting devices that are used outside a device user facility. These devices are considered reasonably likely to cause serious adverse health consequences if they fail. The regulation is intended to ensure that, in the event of a recall or safety alert, a tracked device can be traced by the manufacturer from the device manufacturing facility to the end user or patient.

D. THE CORRECTIONS AND REMOVAL REGULATION

The Corrections and Removal regulation, 21 CFR 806, requires manufacturers and importers to report promptly to FDA any corrections or removals of devices being undertaken to reduce risk to health.

E. THE REGISTRATION AND LISTING REGULATION

The Registration and Listing regulation, 21 CFR 807, requires manufacturers and foreign exporters to register and list their devices; and importers to register.

Note: A complete list of the types of domestic and foreign establishments that must register and list can be found at:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/ucm053165.htm.

PART II

IMPLEMENTATION

A. OBJECTIVES

This compliance program provides guidance to FDA field and CDRH staff for Premarket Approval (PMA) preapproval and PMA postmarket inspections and administrative/enforcement activities associated with PMAs. For purposes of this compliance program the term "PMA" will be used for not only the processing of original PMA applications and PMA Supplements, but also other various preapproval applications including: Product Development Protocols (PDP) and Humanitarian Device Exemptions (HDE). In addition, for purposes of this compliance program the term "manufacturer" may also refer to the manufacturer's designated contract manufacturers, sterilizers, and/or relabelers of the PMA device.

This is a continuing program, implemented on the basis of directed assignments made to the Field by CDRH.

1. PMA Preapproval Inspection

A PMA preapproval inspection is performed to assess a manufacturer's ability to design and manufacture the PMA device in accordance with the conditions specified in the PMA application and the requirements of the Quality System (QS) regulation. Prior to the approval of a PMA application, CDRH will typically issue an inspection assignment for manufacturing sites that are deemed necessary to be inspected. This assignment is issued after the manufacturer has demonstrated in its PMA application that both the design controls and the manufacturing processes and controls have been adequately established.

2. PMA Postmarket Inspection

A PMA postmarket inspection is typically conducted eight to twelve months after the PMA has been approved. This PMA postmarket inspection provides FDA with the first opportunity to evaluate the newly-approved product since it entered the marketplace. A PMA postmarket inspection also provides FDA with the first opportunity to assess a manufacturer’s compliance with the Medical Device Reporting (MDR) regulation, Corrections & Removal regulation, Registration and Listing regulation, and the Medical Device Tracking regulation (if applicable) for the PMA device, as these areas are not typically covered during a PMA preapproval inspection. This device-specific inspection is intended to assure that the manufacturer is making the device in accordance with the conditions specified in the PMA and that it complies with the requirements of the QS regulation, MDR regulation, Corrections & Removal regulation, Registration and Listing regulation, and Medical Device Tracking regulation.

B. PROGRAM MANAGEMENT INSTRUCTIONS

The following guidelines are suggested for implementing this compliance program:

1. PMA Preapproval Inspection

The assignment will be issued after the manufacturer has demonstrated in its PMA application that both the design controls and the manufacturing processes have been established. The assignment will identify the device to be covered and will have a specific reporting due date that must be met in order for the Agency to meet statutory deadlines for a decision on the application.

All assignments will be placed in the FDA Field Accomplishments and Compliance Tracking System (FACTS). The District Office or Office of Regulatory Affairs (ORA)/Division of Foreign Field Investigations (DFFI) will be notified electronically of the FACTS assignment number and a copy of the assignment memo will be attached to that e-mail.

The following information will be sent to the appropriate District Office/Investigator once the assignment has been entered into the FACTS database:

a. the PMA manufacturing section,
b. inspectional guidance, if any,
c. PMA review memos

For foreign site assignments, all applicable PMA documents will be sent via e-mail to the appropriate investigator as soon as the Office of Compliance (OC)/Field Operations Branch (FOB) is notified that an investigator has been selected and the inspection has been scheduled. The investigator may contact the CDRH reviewer if there are any questions regarding the information provided.

To facilitate communications with the firm on matters pertaining to the status of the inspection, the firm's response to the 483, or the need for a follow-up inspection, the District Office should identify a contact person for each particular PMA inspection assignment. The investigator should give to the firm at the close out of the inspection the name and telephone number of the contact person.

Note: Some PMAs may be granted "Expedited Review" status if the device offers a potential for clinically meaningful benefit as compared to the existing alternatives (preventative, diagnostic, or therapeutic), or when the new medical device promises to provide a revolutionary advance over currently-available alternative modalities. The granting of "Expedited Review" means that the application would receive priority review before other pending PMAs. Therefore, expedited PMA inspection assignments take a top

priority when scheduling PMA preapproval inspections.

2. PMA Postmarket Inspection

An assignment for a PMA postmarket inspection of manufacturers including contract manufacturers, sterilizers, relabelers, remanufacturers, and/or specification developers will occur approximately eight to twelve months after a PMA or PMA Supplement for new or alternate manufacturing sites has been approved. The assignment will be issued by OC/FOB with an inspection due date range that is between eight to twelve months after PMA approval.

Note: PMA postmarket inspection assignments will not be issued to designated sterilizer firms that meet certain criteria. Refer to Section III.B.3. for further guidance.

All PMA postmarket inspection assignments will be placed in FACTS. The District Office or ORA/DFFI will be notified electronically of the FACTS assignment number and a copy of the assignment memo will be attached to that e-mail.

Once an investigator has been selected and the inspection has been scheduled, the District Office or ORA/DFFI should notify via e-mail the PMA postmarket coordinator at CDRHPMAPROGRAM@fda.hhs.gov, identifying the investigator that will be conducting the inspection and the start date of the inspection. Copies of any cover letters for any PMA supplements submitted by the firm since the PMA was approved will be sent to the investigator electronically for review prior to the inspection.

The postmarket inspection should assure that the manufacturer of an approved PMA device:

a. Is complying with the requirements of the QS regulation, MDR regulation, Corrections & Removal regulation, Registration and Listing regulation, and Medical Device Tracking regulation (if applicable) for the PMA device (Refer to C.P. 7382.845 for guidance).

b. Has an adequate change control system in place and has obtained FDA approval (via a supplement) for any significant change in device design, labeling, or manufacturing process that may affect the safety or effectiveness of the device.

   Note: Any issues associated with safety and effectiveness of the device should not be assessed during the inspection; the relevant evidence should be collected and referred to CDRH for further follow up. Refer to Part III.B.2 for further discussion regarding the coverage of design controls.

PART III

INSPECTIONAL

BACKGROUND

This program includes inspectional guidance for determining compliance with the Quality System (QS) regulation, Medical Device Reporting (MDR) regulation, Medical Device Tracking regulation, Corrections and Removals regulation, and the Registration and Listing regulation for PMA inspections.

A. OPERATIONS

1. Inspectional Strategy

The QS inspectional goal is to perform a comprehensive assessment of the firm's quality management system for compliance with the appropriate regulations. Preapproval and postmarket PMA QS inspections should generally be conducted using the Quality System Inspection Technique (QSIT). Guidance for performing an inspection is provided in the Guide to Inspections of Quality Systems, August 1999, also called the QSIT Guide www.fda.gov/ora/inspect_ref/igs/qsit/qsitguide.htm.

Note: FDA has the authority to inspect component manufacturers, when necessary, but rarely performs inspections of component manufacturers outside of the PMA program. When inspecting a component manufacturer (except foreign component manufacturers), the investigator should issue an FDA 482, however; the investigator should not issue an FDA 483 to the component manufacturer. If issues are identified during the inspection of the component manufacturer, they should be further investigated at the finished device manufacturer during the PMA inspection. These issues should be handled through the device manufacturer's purchasing control activities under the requirements of 21 CFR 820.50 and acceptance activities under the requirements of 21 CFR 820.80 and any issues identified should be cited on the FDA 483 for the device manufacturer during the PMA inspection. If it is decided to conduct an inspection of a component manufacturer as part of the preapproval of a PMA, ***it is not necessary to add the component manufacturer to the routine follow-up or postmarket PMA inspection workload planning***.

a. PMA Preapproval Inspection

The PMA preapproval inspection will assess the firm's systems, methods, and procedures for the specific PMA devices to ensure that the firm's quality management system is effectively established (defined, documented, and implemented). All PMA preapproval inspections should be conducted as Level 2 Comprehensive Inspections, covering all four major subsystems (Management Controls, Design Controls, Corrective and Preventive Action (CAPA), and Production and Process Controls (P&PC)), as explained in the QSIT Guide. Refer to Part III of CP 7382.845, "Inspection of Medical Device Manufacturers," for

further guidance on Level 2 inspections.

Before initiating the premarket approval inspection, the investigator should review the manufacturing section of the PMA application and any other documents provided by Office of Compliance (OC)/Field Operations Branch (FOB) in preparation for the inspection. It is important to ensure that a manufacturer has completed all process validation activities at the time of the inspection. Refer to Section B for further instructions regarding process validation activities.

Inspectional time for the PMA preapproval inspection should be reported under PAC 83001; however, if the inspection also includes coverage of other areas, divide the inspectional hours between the relevant PAC codes, as appropriate.

b. PMA Postmarket Inspection

The PMA postmarket inspection will assess the firm's systems, methods, and procedures for the specific devices to ensure that the firm's quality management system is effectively established (defined, documented, and implemented) and effectively maintained. The PMA postmarket inspection should also confirm that commitments made by the firm at the time the applications were approved have been completed or are underway in accordance with those commitments.

Inadequately-controlled changes to a newly-marketed device often lead to complaints and/or service repairs as indicators of performance problems, as well as additional changes in the design, manufacturing process, and/or quality assurance systems relative to the PMA device. Therefore, there should be a focus on these areas to ensure that there are no indications of potential performance problems. The PMA postmarket inspection includes the assessment of postmarket information on the specific PMA devices covered during the inspection and should include:

- Review of any relevant recalls,
- Review of any relevant MDRs,
- Review of any corrections and removals,
- Review of complaints,
- Review of any significant changes in device specifications or in the manufacturing specifications, focusing on the firm's process validation activities, and
- Follow-up on any previous FDA 483 observations, to include the corrections, corrective actions, and systemic corrective actions for the observations and the related systems

Available postmarket information for the PMA device should be reviewed as much as possible as a part of the preparation for the inspection, in order to facilitate efficient time spent at the facility. This review of postmarket information should be documented in the EIR. Any potential problems identified as a result of the review of postmarket information should be investigated and developed during the inspection.

The PMA postmarket inspection can be conducted as a Level 1 (Abbreviated), or Level 2 (Comprehensive) inspection. Regardless of the type of inspection that is conducted, all applicable satellite systems must be covered during the PMA postmarket inspection, as these areas are not covered during a PMA preapproval inspection. For Level 1 inspections, the selection to cover either the P&PC subsystem or the Design Controls subsystem should be determined based upon the review of postmarket information (conducted prior to the inspection), subsystems that were covered during any previous inspection, and any other indicators such as design or manufacturing changes. Refer to Part III of CP 7382.845, "Inspection of Medical Device Manufacturers," for further guidance on Level 1 and Level 2 inspections.

Inspectional time for the PMA postmarket inspection should be reported under PAC 83001A; however if the inspection also includes coverage of other areas, divide the inspectional hours between the relevant PAC codes, as appropriate.

2. Inspectional Instructions

a. Required Statements

The following statement should be included on each FDA 483:

> This document lists observations made by the FDA representatives during the inspection of your facility. They are inspectional observations and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective actions in response to an observation, you may discuss the objection or action with FDA representatives during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

For all medical device inspections, the FDA 483 should contain the following additional statement:

> The observations noted in this form FDA 483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self audits to identify and correct any and all violations of the quality system requirements.

b. Satellite Program Areas

Refer to Part III of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of coverage of satellite program areas including MDRs, Corrections & Removals, Tracking, and Sterilization.

c. Sampling Records

Refer to Part III of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of sampling records for reviews.

B. SPECIAL SITUATIONS

1. Special Instructions Concerning Process Validation

At the time of the PMA application, a manufacturer may not have completed all of the required process validations and, therefore, CDRH may not have conducted a review of this data. It is expected that at the time of the inspection, the manufacturer will have completed validations of all processes requiring validation. Therefore, implementation of the process validation activities should be focused on during the inspection, as a thorough review of completed process validations may not have been conducted by CDRH during the review of the PMA application.

If it is identified during the inspection that process validation activities have not been successfully completed by the manufacturer, the investigator should conclude the inspection. Refer to Part V, Section A for further guidance on regulatory/administrative follow up.

2. Special Instructions Concerning Design Controls

Investigators should ensure that the design and development activities for the PMA devices are sufficiently covered during an inspection. In some cases, one facility may not cover all activities related to the PMA devices. There are a number of multi-establishment firms that conduct all design activities at a single facility (sometimes referred to as a research and development (R&D) center or a corporate design facility). If the establishment scheduled for inspection is serviced by an R&D center or a corporate facility, review the establishment jacket, before beginning the inspection, consult the agency's on-line OEI databases and/or directly contact the district involved. For PMA preapproval inspections, the R&D center or the corporate design facility should be inspected regardless of the facility's inspectional history. For PMA postmarket inspections, determine if the home district of the R&D center or the corporate design facility has conducted a design control inspection of that facility within the previous two years. If such an inspection was conducted, it will not be necessary to conduct a design control assessment at the establishment scheduled for inspection. If an inspection was not conducted within the previous two years, issue an assignment to the home district of the R&D center or the corporate design facility requesting a design control inspection for the devices listed in the PMA postmarket inspection assignment.

Some manufacturers may have their PMA devices designed under contract. These manufacturers must comply with the requirements for using contractors or service suppliers under 21 CFR 820.50 as well as ensure compliance with 21 CFR 820.30. The manufacturer must maintain or have readily accessibility copies of a Design History File for any PMA devices that are in production.

Observations relating to design controls placed on the Form FDA 483 should be limited to the

adequacy of the procedures and/or controls established by the manufacturer. Any issues related to the adequacy, safety, or efficacy of a particular design should not be placed on the Form FDA 483. Investigators should discuss any such issues in the EIR, collect complete documentation, and submit the documentation to CDRH for further review.

If the firm has made significant design or manufacturing changes to the PMA device that require the submission of a PMA supplement, the investigator should attempt to get CDRH/OC and/or OIVD concurrence during the inspection before placing the observation on the Form FDA 483. When CDRH concurrence cannot be obtained before the completion of the inspection, the observation should not be placed on the Form FDA 483. Investigators should discuss the issue in the EIR, collect complete documentation, and submit the documentation to CDRH for further review.

3. Special Instructions for Sterilization Processes

Sterilization processes for PMA devices may be conducted at the device manufacturer or a contract sterilizer. Inspectional coverage of the sterilization process should follow the Sterilization Process Controls section found in the QSIT Guide. Sterilization processes are covered as a sub-part of the Production and Process Controls subsystem under QSIT. The instructions for inspecting sterilization processes are applicable at the following types of facilities:

- device manufacturers that sterilize their own product,
- device manufacturers that use contract sterilizers, and
- contract sterilizers

Note: The portion of the inspection spent covering sterilization processes should be reported under PAC 82845S.

Refer to Part III, A.6, of CP 7382.845 "Inspection of Medical Device Manufacturers," for guidance on collection of samples relating to sterilization issues.

Many contract sterilizers have a significant number of customers who manufacture PMA devices. Therefore, inspectional assignments for PMA postmarket contract sterilizers may not be issued for each PMA product if the facility meets the following criteria:

1. The facility was inspected during the previous two years,
2. The facility was found to be in compliance with the Quality System regulation; and,
3. The same sterilization method was covered as the one identified in the PMA.

For domestic contract sterilizers, an e-mail will be sent from OC/FOB to the district office requesting confirmation that the criteria outlined above has been met and an inspection is not necessary.

PMA postmarket inspection assignments for contract sterilizers will still occur in

situations where the above criteria were not met or in the following situations where:

1. Changes in the sterilization process cannot be clarified or checked by reviewing sterilization records at the finished device manufacturer;
2. Information obtained from the manufacturer discloses a possible problem at the contract sterilizer; and/or,
3. Information needs to be verified.

Note: The inspectional policy/strategy described above is only applicable to PMA postmarket inspections of contract sterilizers. CDRH/OC will continue to issue PMA preapproval inspection assignments for contract sterilizers.

C. REPORTING

1. General reporting requirements for PMA preapproval and PMA postmarket inspections are listed in the Field Reporting Requirements section of this document. Refer to the IOM, Subchapter 5.10 – Reporting, for general EIR formats. Always include the device, device class, PMA number, and subsystems covered in the EIR.

2. QS Observations – If there are observed violations of the QS regulation requirements, place them on the Form FDA 483, even if the medical device has not been placed into interstate commerce yet. The submission of a PMA expresses the applicant's intention to place such device into interstate commerce once approval is granted and, therefore, observations need to be placed on the Form FDA 483. The QSIT Guide provides guidance concerning major QS requirements and the identification of major deficiencies. The most serious system deficiencies should be noted on the Form FDA 483 first, then by subsystems if possible.

   Note: Refer to the IOM, Subchapter 5.2.3.4 – Annotation of the FDA 483, for information concerning annotation of the Form FDA 483.

3. FDA Field Accomplishments and Compliance Tracking System (FACTS)

   a. When selecting specific manufacturing processes for the PMA devices to represent profile classes, investigators should give preference to:

      - CAPA indicators of process problems,
      - processes used to manufacture high-risk components and, subassemblies, as called out in the definition of the term "product" in 21 CFR 820.3(r),
      - processes that have a high risk of causing medical device failure,
      - processes that require process validation,
      - processes that are new to the manufacturer,
      - processes that cover a variety of process technologies and profile classes,
      - common processes used in multiple products, and
      - processes not covered during previous inspections.

Note: If all profile classes are not directly covered during an inspection, but are covered indirectly under CAPA, then all profile classes that the firm is involved with can be listed on the appropriate FACTS screen.

b. Since the QSIT approach covers systems, the findings from the inspection can apply to all profile classes at the firm.

PART IV

ANALYTICAL

Refer to Part IV of CP 7382.845, "Inspection of Medical Device Manufacturers," for a listing of the designated testing facilities and methodology for sample collection and analysis.

PART V

REGULATORY/ADMINISTRATIVE FOLLOW-UP

Refer to Part V of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of the specific criteria for determining Situation I and Situation II compliance decisions for PMA preapproval and PMA postmarket inspections.

A. PMA PREAPPROVAL INSPECTIONS

FDA expects that the PMA device manufacturer's facility will be in compliance with the requirements of the device Quality System (QS) regulation. The manufacturer should have procedures in place to assure that specifications for the device, components, packaging, and labeling accurately reflect the design, and that the manufacturing process will consistently produce devices that meet the approved design. In cases where QS deficiencies are identified, any follow-up correspondence related to the deficiencies identified during the PMA preapproval inspection of the PMA devices will be issued by CDRH.

1. Compliance Decision

a. Situation I

In cases where it has been determined that the QS deficiencies meet the criteria of Situation I, as outlined in Part V of CP 7382.845, "Inspection of Medical Device Manufacturers,"," FDA has the authority to withhold approval of the PMA application for that particular device. Therefore, the District should recommend withholding approval when the inspection identifies QS deficiencies that meet the criteria for Situation I, even though the District is not prepared to seek regulatory action because the deficiencies do not extend to other devices manufactured in the facility. Some significant QS deviation examples from Part V include, but are not limited to:

- Total failure to define, document, or implement a quality system or one of the seven subsystems, such as failing to complete any required validations of full-scale production processes for the specific device covered by the pending original PMA application, or no procedures that address corrective and preventive actions.

- A deficiency in one or more elements of the subsystems. The QSIT Guide can be utilized to provide guidance in determining what are considered to be "major" problems if not adequately addressed.

- The existence of products that clearly do not comply with the manufacturer's specifications and/or the Quality System regulation, and which were not adequately addressed by the Corrective and Preventive Action Subsystem (CAPA) program.

- Non-correction of major deficiencies from previous inspections.

If the criteria of Situation I is met, CDRH will issue a PMA Official Action Indicated (OAI) Letter to the device manufacturer outlining the deficiencies identified during the inspection. The PMA will remain on hold and approval of the application will be pending resolution of QS deficiencies and often a re-inspection.

When the PMA preapproval inspection is conducted in conjunction with another type of inspection that involves commercially-marketed devices, and the deviations extend beyond the scope of the PMA device to other devices manufactured in the facility, then the PMA application may be withheld and regulatory and/or administrative actions may be taken against the commercially-marketed devices to assure that the deviations are corrected. If legal action is not immediately warranted, a Warning Letter may be issued for only the commercially-marketed devices. Issuance of all Warning Letters should follow Chapter 4 of the Regulatory Procedures Manual (RPM), http://www.fda.gov/ora/compliance_ref/rpm/. A separate PMA OAI letter may also be issued to the firm outlining the deviations related to the PMA devices. In such cases, a copy of the Warning Letter should be sent to the PMA preapproval coordinator in support of the District's recommendation to delay or withhold approval or the PMA application. It is important that before any Warning Letter is issued that CDRH also performs a QS Review of the EIR for the PMA aspect in order to ensure a uniform and consistent message between these two communications to the medical device manufacturer.

b. Situation II

In cases where it has been determined that the inspection meets the criteria of Situation II, as outlined in Part V of CP 7382.845, "Inspection of Medical Device Manufacturers,"," and deviations have been identified, CDRH will issue a PMA Voluntary Action Indicated (VAI) letter to the device manufacturer outlining the deficiencies noted during the inspection.

Note: Districts should not recommend withholding the PMA application for inspections that meet the criteria of Situation II.

B. PMA POSTMARKET INSPECTIONS

The determinations for Situation I or Situation II and any regulatory/administrative follow-up actions for PMA postmarket inspections should follow the guidelines discussed in Part V of CP 7382.845, "Inspection of Medical Device Manufacturers."

1. Quality System Regulatory/Administrative Follow-Up

Refer to Part V of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of regulatory and administrative follow-up actions for QS deficiencies.

2. MDR Regulatory/Administrative Follow-Up

Refer to Part V and Attachment C of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of MDR requirements and regulatory and administrative follow-up actions for MDR deficiencies.

3. Tracking Regulatory/Administrative Follow-Up

Refer to Part V and Attachment D of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of tracking requirements and regulatory and administrative follow-up actions for tracking deficiencies.

4. Corrections and Removals Regulatory/Administrative Follow-Up

Refer to Part V and Attachment E of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of corrections and removals requirements and regulatory and administrative follow-up actions for corrections and removals deficiencies.

5. Registration and Listing Regulatory/Administrative Follow-Up

Refer to Part V of CP 7382.845, "Inspection of Medical Device Manufacturers," for a discussion of regulatory and administrative follow-up actions for registration and listing deficiencies.

PART VI

REFERENCES, ATTACHMENTS, AND PROGRAM CONTACTS

A. APPLICABLE REFERENCES

1. Guide to Inspections of Quality Systems, August 1999 (http://www.fda.gov/downloads/ICECI/Inspections/UCM142981.pdf)

2. Code of Federal Regulations, Title 21, Part 803, Medical Device Reporting.
   Code of Federal Regulations, Title 21, Part 806, Reports of Corrections and Removals.
   Code of Federal Regulations, Title 21, Part 807, Establishment Registration and Device Listing.
   Code of Federal Regulations, Title 21, Part 820, Current Good Manufacturing Practices/Quality System Regulation.
   Code of Federal Regulations, Title 21, Part 821, Tracking Requirements.
   Code of Federal Regulations, Title 21, Part 860, Medical Devices Classification Procedures.

3. Investigations Operations Manual (IOM) - Chapter 5, Subchapter 5.6, Devices (http://www.fda.gov/ora/inspect_ref/iom/)

4. Regulatory Procedures Manual (http://www.fda.gov/ora/compliance_ref/rpm/)

5. Federal Food, Drug and Cosmetic Act, As Amended
   Section 513 [U.S.C.360c](a)(1)(C) Classification Class III, Premarket Approval
   (http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/FDCActChapterVDrugsandDevices/ucm110188.htm)

6. Compliance Program Guidance Manual: Inspection of Medical Devices; (C.P. 7382.845), 2/2/2011.
   (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072753.htm)

7. MDUFMA – Medical Device User Fee Modernization Act of 2002. The act amends the Federal Food, Drug, and Cosmetic Act to provide the FDA new responsibilities, resources, and challenges. One particularly significant provision of MDUFMA is that which permits FDA to collect user fees for certain premarket reviews, including those applications received on or after October 1, 2002. On February 20, 2003, enabling appropriations were enacted, thus allowing the agency to immediately begin to collect fees for medical device applications. More information on MDUFMA and User Fees is available at
   http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/default.htm

8. Quality System Information for Certain Premarket Application Reviews; Guidance for Industry and FDA Staff, Issued March 3, 2003. (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070897.htm)

9. Guidance for Industry and FDA Staff: Expedited Review of Premarket Submissions for Devices, Issued February 29, 2008. (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089643.htm)

10. The Review and Inspection of Premarket Approval Application Manufacturing Information and Operations. Issued January 8, 2008. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077758.htm

11. Quality Management System –Medical Devices – Guidance on Corrective Action and Preventive Action and Related QMS Processes, Issued November 4, 2010. (http://www.ghtf.org/documents/sg3/sg3_n18.pdf)

12. Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers, Issued December 11, 2008. (http://www.ghtf.org/documents/sg3/sg3final-N17.pdf)

13. Implementation of Risk Management Principles and Activities within a Quality Management System, Issued May 20, 2005. (http://www.ghtf.org/documents/sg3/sg3n15r82005.pdf)

14. Quality Management Systems – Process Validation Guidance, Issued January 2004. (http://www.ghtf.org/documents/sg3/sg3_fd_n99-10_edition2.pdf)

Copies of CDRH QS publications and FDA guidance documents are available from the Division of Small Manufacturers International and Consumer Assistance (DSMICA), Telephone: 800-638-2041 or FAX 301-847-8149 or Email at: dsmica@fda.hhs.gov. Many of these publications are also available in the CDRH Good Guidance Practices (GGP) Database (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm).

Sources to obtain copies free of charge:

Internet (World Wide Web): FDA, CDRH, and ORA maintain web sites for easy access to information. The FDA home page is http://www.fda.gov; the CDRH home page is http://www.fda.gov/cdrh/; and the ORA home page is http://www.fda.gov/ora/.

Good Guidance Practices (GGP) Database: This is a searchable database that contains

all current CDRH guidance documents and provides links to the documents. (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfggp/search.cfm)

B. PROGRAM CONTACTS

1. ORA Contacts

a. Questions regarding inspectional requirements and/or technical assistance:

Division of Domestic Field Investigations
Medical Device Group
Telephone: (301) 796-0358

Or

Division of Foreign Field Investigations
Medical Device Group
Telephone: (301) 796-0357

2. CDRH Contacts

a. Questions regarding the interpretation of the PMA regulations and specific PMA inspection assignments should be directed to:

PMA Preapproval Inspection Assignments:

PMA Preapproval Coordinator
Field Operations Branch
Division of Risk Management Operations
Office of Compliance
Telephone: (301) 796-5815

PMA Postmarket Inspection Assignments:

PMA Postmarket Coordinator
Field Operations Branch
Division of Risk Management Operations
Office of Compliance
Telephone: (301) 796-5818

b. Questions regarding the interpretation/applicability of the device Quality System regulation or information contained in the manufacturing section of the PMA should be directed to:

Deputy Director for Regulatory Affairs

Office of Compliance
Telephone: (301) 796-5500

Jan Welch
Quality System/IVD Expert
Telephone: (301) 796-5776
Email: jan.welch@fda.hhs.gov

b. Questions regarding the MDR Regulation Interpretation and Policy should be directed to:

MDR Policy Branch
Division of Postmarket Surveillance
Office of Surveillance and Biometrics
Email: rsmb@fda.hhs.gov
Telephone: (301) 796-6670
Fax: (301) 847-8135 (call or send email alert if sending a fax)

c. Questions regarding the data retrieval of MDR reports should be directed to:

Information and Analysis Branch
Division of Postmarket Surveillance
Office of Surveillance and Biometrics
Email: MDR.Requests@cdrh.fda.gov

d. Questions regarding medical device software, quality system software, or production/manufacturing equipment software should be directed to:

John F. Murray
Software Compliance Expert
Office of Compliance
Telephone: (301) 796-5543
Email: john.murray@fda.hhs.gov

e. Questions regarding sterilization should be directed to:

Patrick Weixel
Office of In Vitro Diagnostic Devices
Telephone: (301) 796-5537
Email: patrick.weixel@fda.hhs.gov

f. Questions concerning in vitro diagnostic devices should be directed to:

James Woods
Deputy Director, Patient Safety and Product Quality

Office of In Vitro Diagnostic Devices
Telephone: (301) 796-6225
Email: james.woods@fda.hhs.gov

g. Questions concerning this compliance program should be directed to:

Melissa Torres
Office of Compliance
Telephone: (301) 796-5576
Email: melissa.torres@fda.hhs.gov

h. Refer to the CDRH/OC and OIVD Organizational Charts in Attachments B and C respectively, to identify the unit within OC or OIVD that is responsible for the type of PMA device for which you have a question or need guidance. The organizational chart contains the contact numbers for the enforcement divisions and branches in OC and OIVD.

C. ATTACHMENTS

Attachment A	Notification of PMA Postmarket Inspection Form
Attachment B	CDRH Office of Compliance Organizational Chart
Attachment C	CDRH Office of In Vitro Diagnostic Devices Organizational Chart

ATTACHMENT A

NOTIFICATION OF PMA POSTMARKET INSPECTION FORM

To: CDRH/OC/DRMO/FOB
Fax: 301-847-8128
Phone: 301-796-5818

From: _____

Subject: PMA Numbers: _____

PROCODE: _____

STERLIZATION METHOD: _____

PREVIOUS INSPECTION PERFORMED: _____

PMA APPROVAL DATE: _____

Device Name:

Firm:

Firm Address:

FEI:

FACTS#

****

POSTMARKET INSPECTION IS SCHEDULED (Date) _____

****

POSTMARKET INSPECTION ALREADY PERFORMED _____

DATE INSPECTED _____

****

FINAL DISTRICT DECISION: ☐ NAI ☐ VAI ☐ OAI **TURBO#** _____

PAC Code 83001A _____Hours Used

FDA 483 ISSUED ☐ YES ☐ NO – If yes please attach DATE _____

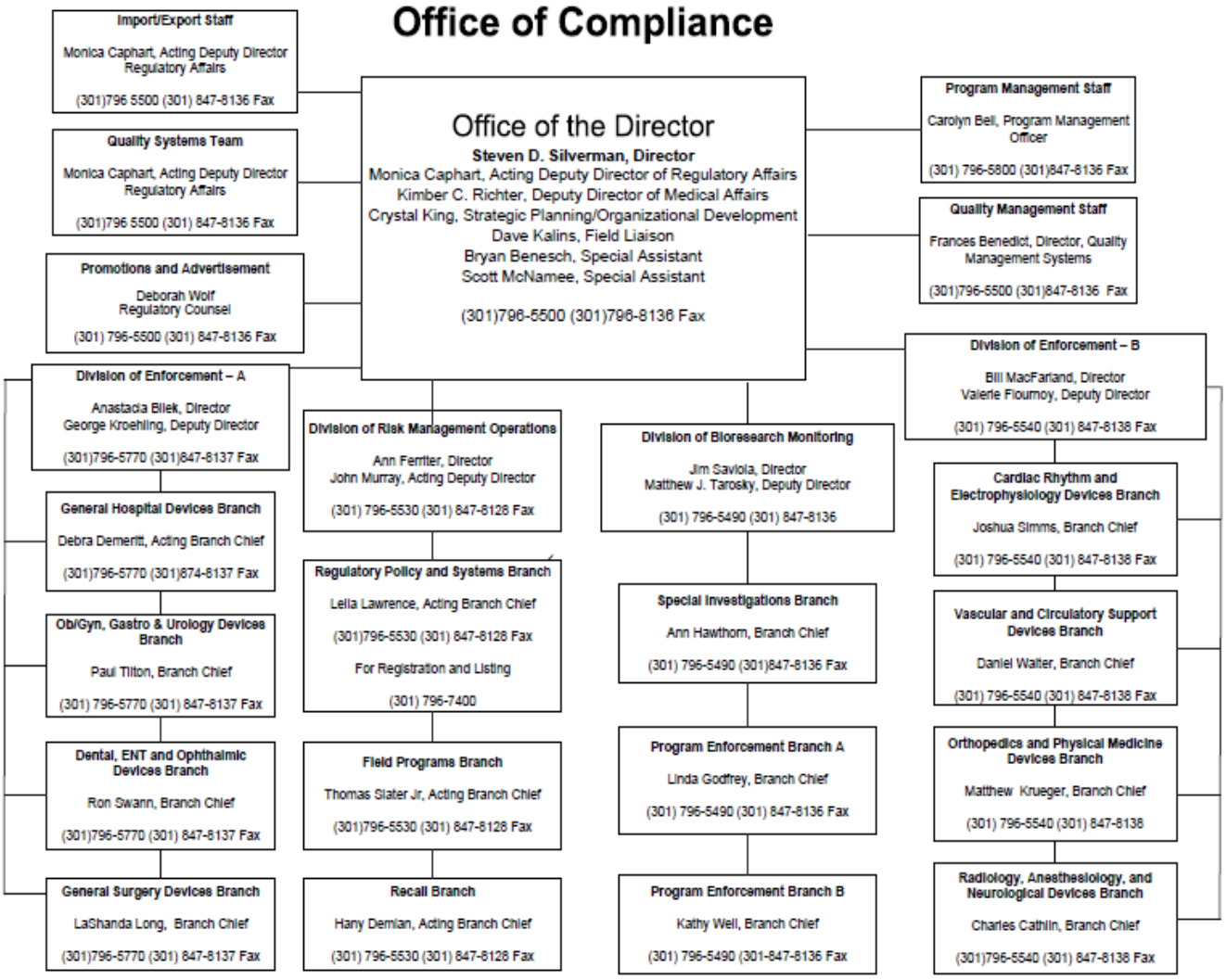
WL ISSUED ☐ YES ☐ NO – If yes please attach DATE _____
UNTITLED LETTER ☐ YES ☐ NO – If yes please attach DATE _____

OTHER LEGAL ACTION _____

Describe: _____
_____
_____
_____

ATTACHMENT B

CDRH OFFICE OF COMPLIANCE ORGANIZATIONAL CHART



ATTACHMENT C

CDRH OFFICE OF IN VITRO DIAGNOSTIC DEVICES ORGANIZATIONAL CHART