Practical Implementation of Conformity Assessment of Medical Devices: US FDA

During this presentation, I will provide an overview of how FDA implements the Principles of Conformity Assessment for Medical Devices (GHTF/SG1/N78:2012).

- I will focus on each of the **5 conformity assessment elements** included in N78:
  - Quality management system (QMS)
  - System for post-marketing surveillance
  - Technical documentation
  - Declaration of conformity
  - Registration of manufacturers and their medical devices by the Regulatory Authority

Agenda

- Quality management system (QMS)
- System for post-marketing surveillance
- Technical documentation
- Declaration of conformity
- Registration of manufacturers and their medical devices by the Regulatory Authority

Agenda

- **Quality management system (QMS)**
- System for post-marketing surveillance
- Technical documentation
- Declaration of conformity
- Registration of manufacturers and their medical devices by the Regulatory Authority

Manufacturers are required to **establish** and **follow quality systems** to help ensure that their products consistently meet applicable requirements and specifications.

- Manufacturers need **only comply** with those **requirements applicable** to the operations in which they are engaged

FDA's quality system regulation includes requirements regarding the methods used in, and the facilities and controls used for

- design
- manufacture
- packaging
- labeling
- storage
- installation
- servicing

The quality system regulation applies to **finished devices** intended for **human use** that are **manufactured**, **imported**, or **offered for import** in any State or Territory of the **United States**, the District of Columbia, or the Commonwealth of Puerto Rico.

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H - MEDICAL DEVICES

PART 820 QUALITY SYSTEM REGULATION

Subpart A - General Provisions
§ 820.1 - Scope.
§ 820.3 - Definitions.
§ 820.5 - Quality system.

Subpart B - Quality System Requirements
§ 820.20 - Management responsibility.
§ 820.22 - Quality audit.
§ 820.25 - Personnel.

Subpart C - Design Controls
§ 820.30 - Design controls.

Subpart D - Document Controls
§ 820.40 - Document controls.

Subpart E - Purchasing Controls
§ 820.50 - Purchasing controls.

Subpart F - Identification and Traceability
§ 820.60 - Identification.
§ 820.65 - Traceability.

Subpart G - Production and Process Controls
§ 820.70 - Production and process controls.
§ 820.72 - Inspection, measuring, and test equipment.
§ 820.75 - Process validation.

Subpart H - Acceptance Activities
§ 820.80 - Receiving, in-process, and finished device acceptance.
§ 820.86 - Acceptance status.

Subpart I - Nonconforming Product
§ 820.90 - Nonconforming product.

Subpart J - Corrective and Preventive Action
§ 820.100 - Corrective and preventive action.

Subpart K - Labeling and Packaging Control
§ 820.120 - Device labeling.
§ 820.130 - Device packaging.

Subpart L - Handling, Storage, Distribution, and Installation
§ 820.140 - Handling.
§ 820.150 - Storage.
§ 820.160 - Distribution.
§ 820.170 - Installation.

Subpart M - Records
§ 820.180 - General requirements.
§ 820.181 - Device master record.
§ 820.184 - Device history record.
§ 820.186 - Quality system record.
§ 820.198 - Complaint files.

Subpart N - Servicing
§ 820.200 - Servicing.

Subpart O - Statistical Techniques
§ 820.250 - Statistical techniques.

Authority: 21 U.S.C. 351, 352, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360l, 371, 374, 381, 383; 42 U.S.C. 216, 262, 263a, 264.
Source: 61 FR 52654, Oct. 7, 1996, unless otherwise noted.

The **quality system regulation** for medical devices is included in **21 CFR Part 820**.

FOOD AND DRUG ADMINISTRATION

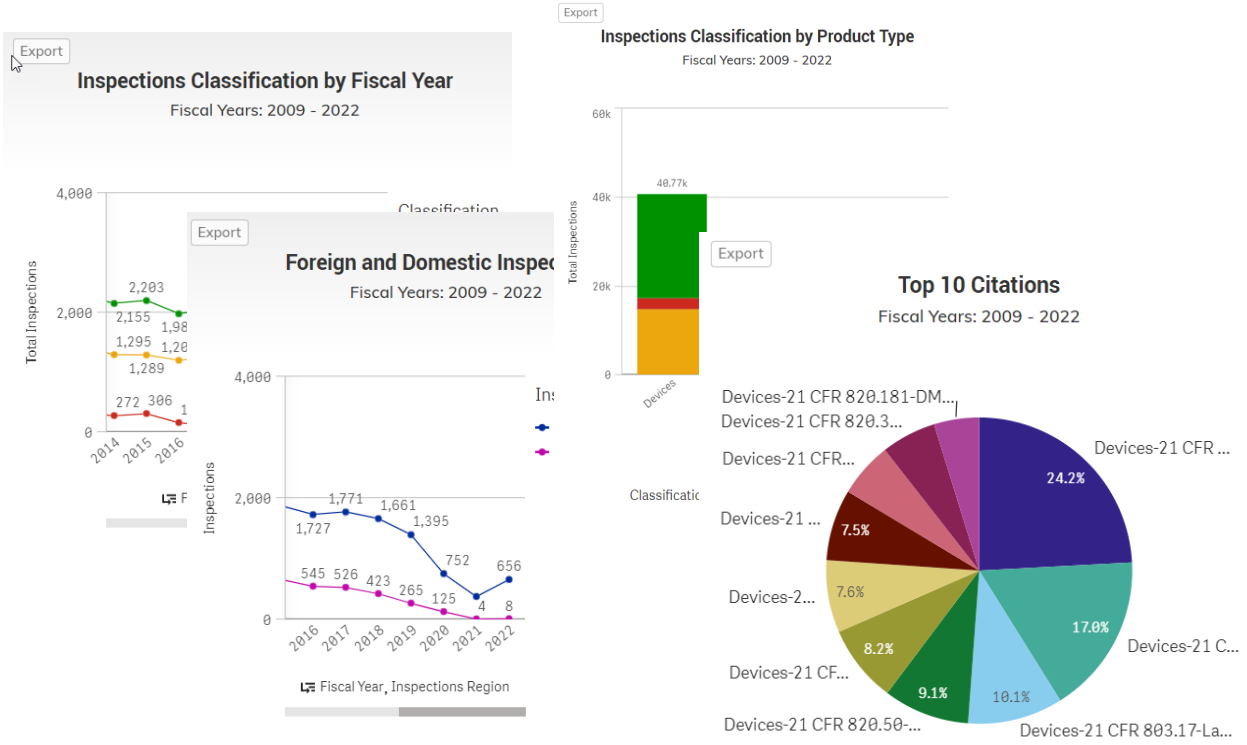
GUIDE TO INSPECTIONS OF QUALITY SYSTEMS

FDA **publishes** the **procedures** followed by staff during quality system **inspections.**

See Guide-to-Inspections-of-Quality-Systems.pdf (fda.gov).

FDA updates a "**Data Dashboard**" with information about some **completed inspections**.

See FDA Dashboards – Inspections



Inspections Details Help

Download Inspections Dataset

Record Count: 40,766

Select Inspection ID(s) to view corresponding Inspections Citations.

FEI Number	Legal Name	City	State	Zip	Country/Area	Fiscal Year	Inspection ID	Posted Citations	Inspection End Date
3002516162	Myriad Fiber Imaging Technologies, Inc.	Dudley	Massachu...	01571	United States	2022	1175802	Yes	07/29/
3002516162	Myriad Fiber Imaging Technologies, Inc.	Dudley	Massachu...	01571	United States	2022	1175802	Yes	07/29/
3010667677	Dvl-Op Medico	Valencia	California	91355	United States	2022	1176028	No	07/28/

Inspections Citations Details

CFR Reference | FDCA Reference

Download Citations Dataset

Record Count: 44,907

Citations data include Form FDA 483 citations and may not necessarily represent citations on final classification letters.

Inspection ID	FEI Number	Legal Name	Inspection End Date	Program Area	Act/CFR Number	Short Description	Long Desc
1175802	3002516162	Myriad Fiber Imaging Technologies, Inc.	07/29/2022	Devices	21 CFR 820.70(g)(1)	Maintenance schedule, Lack of or inadequate schedule	Schedules equipment
1175802	3002516162	Myriad Fiber Imaging Technologies, Inc.	07/29/2022	Devices	21 CFR 820.198(a)	Lack of or inadequate complaint procedures	Procedures formally de
1175079	3015733038	Advanced Facialdontics LLC	07/22/2022	Devices	21 CFR 803.17	Lack of Written MDR Procedures	Written MI
1175079	3015733038	Advanced Facialdontics LLC	07/22/2022	Devices	21 CFR 820.20(e)	Quality System Procedures	Quality sys

FDA accepts Medical Device Single Audit Program (MDSAP) audit reports as a substitute for routine Agency inspections.

- MDSAP allows an MDSAP recognized Auditing Organization to conduct a **single regulatory audit** of a medical device manufacturer that **satisfies** the relevant **requirements** of the **regulatory authorities** participating in the program.
- See [Medical Device Single Audit Program (MDSAP) | FDA].

- **MDSAP Members**
  - Therapeutic Goods Administration of Australia
  - Brazil's Agência Nacional de Vigilância Sanitária
  - Health Canada
  - Japan's Ministry of Health, Labour and Welfare, and the Japanese Pharmaceuticals and Medical Devices Agency
  - U.S. Food and Drug Administration
- **MDSAP Official Observers:**
  - European Union (EU)
  - United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA)
  - The World Health Organization (WHO) Prequalification of In Vitro Diagnostics (IVDs) Programme
- **MDSAP Affiliate Members:**
  - Argentina's National Administration of Drugs, Foods and Medical Devices (ANMAT)
  - Ministry of Health of Israel (NEW)
  - Republic of Korea's Ministry of Food and Drug Safety
  - Singapore's Health Sciences Authority (HSA)

Quality systems regulations have changed over time and are increasingly harmonized with international approaches.

- **1978**: quality system regulations are **first** effective
- **1990**: quality system regulations are amended to include **design controls** and, where possible, be consistent with
  - International Organization for Standards (ISO) **9001**:1994 "Quality Systems--Model for Quality Assurance in Design, Development, Production, Installation, and Servicing"
  - ISO committee draft (CD) revision of ISO/CD **13485** "Quality Systems--Medical Devices--Supplementary Requirements to ISO 9001."
  - **Global Harmonization Task Force** (GHTF)
- **2022**: quality system regulation edits **proposed** to harmonize with and incorporate ISO 13485: 2016

Agenda

- Quality management system (QMS)
- **System for post-marketing surveillance**
- Technical documentation
- Declaration of conformity
- Registration of manufacturers and their medical devices by the Regulatory Authority

Medical device **manufacturers** and other firms involved in the **distribution** of devices must follow certain requirements and regulations **once devices are on the market**.

- **Tracking** systems
- **Reporting** of device malfunctions, serious injuries or deaths
- Post market **surveillance** and post approval **studies**

Manufacturers are required to **track certain devices** from their manufacture through the distribution chain.

- Tracking information may be used to **facilitate notifications** and **recalls** ordered by FDA in the case of serious risks to health presented by the devices.
- **Types of devices** subject to a tracking order may include any **Class II or Class III device**:
  - the failure of which would be reasonably likely to have **serious adverse health consequences**;
  - which is intended to be **implanted** in the human body for more than one year; or
  - which is intended to be a **life sustaining or life supporting** device used outside a device user facility.
- See Medical Device Tracking Guidance for Industry and Food and Drug Administration Stafft (fda.gov)

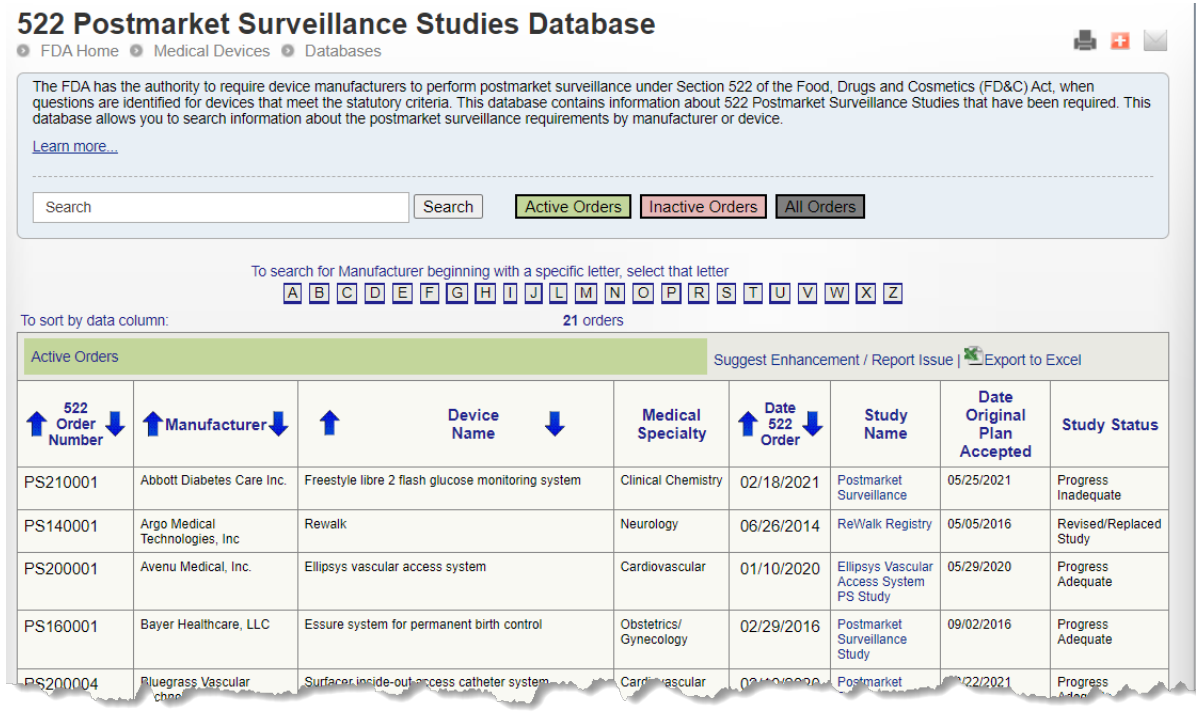
Complaint handling and procedures for **corrective and preventive actions** are required by FDA's quality system regulation.

- Each manufacturer shall **maintain complaint files**. Each manufacturer shall establish and maintain procedures for **receiving, reviewing, and evaluating** complaints by a formally designated unit.
  - See CFR - Code of Federal Regulations Title 21 (fda.gov)
- According to FDA's quality system regulation, each **manufacturer** shall establish and maintain procedures for implementing **corrective and preventive action**.
  - See eCFR :: 21 CFR 820.100 -- Corrective and preventive action.

Manufacturers, **importers**, and **device user facilities** are required to **submit** certain **information** about **suspected device-associated deaths, serious injuries, and malfunctions**.

- **Mandatory reporting** from manufacturers, importers, and device user facilities
- **Voluntary reporting** from health care professionals, patients, and consumers
- See MDR Database Search (fda.gov)
- See MAUDE - Manufacturer and User Facility Device Experience (fda.gov)
- See Medical-Device-Reporting-for-Manufacturers---Guidance-for-Industry-and-Food-and-Drug-Administration-Staff.pdf (fda.gov)

Manufacturers may be required to complete **post market surveillance** and **post approval studies**.



522 Postmarket Surveillance Studies Database

FDA Home ⊙ Medical Devices ⊙ Databases

The FDA has the authority to require device manufacturers to perform postmarket surveillance under Section 522 of the Food, Drugs and Cosmetics (FD&C) Act, when questions are identified for devices that meet the statutory criteria. This database contains information about 522 Postmarket Surveillance Studies that have been required. This database allows you to search information about the postmarket surveillance requirements by manufacturer or device.

Learn more...

Search | Search | Active Orders | Inactive Orders | All Orders

To search for Manufacturer beginning with a specific letter, select that letter

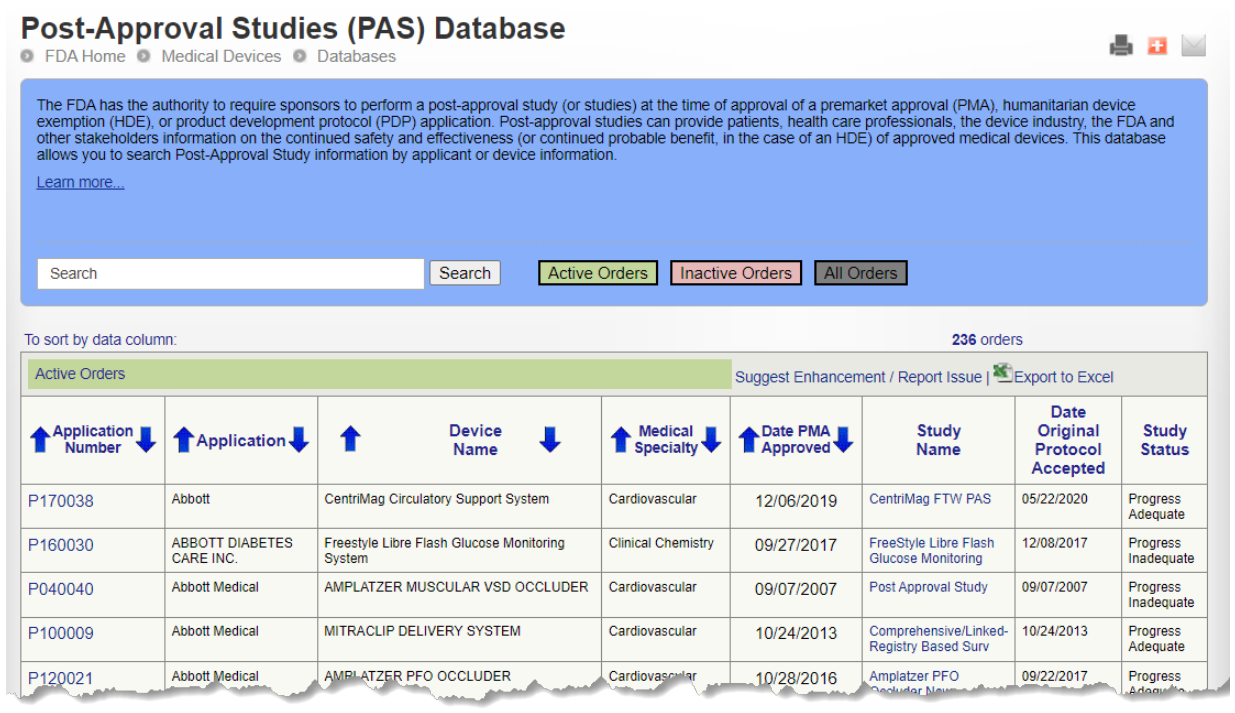
A B C D E F G H I J L M N O P R S T U V W X Z

To sort by data column: 21 orders

Active Orders | Suggest Enhancement / Report Issue | Export to Excel

522 Order Number	Manufacturer	Device Name	Medical Specialty	Date 522 Order	Study Name	Date Original Plan Accepted	Study Status
PS210001	Abbott Diabetes Care Inc.	Freestyle libre 2 flash glucose monitoring system	Clinical Chemistry	02/18/2021	Postmarket Surveillance	05/25/2021	Progress Inadequate
PS140001	Argo Medical Technologies, Inc	Rewalk	Neurology	06/26/2014	ReWalk Registry	05/05/2016	Revised/Replaced Study
PS200001	Avenu Medical, Inc.	Ellipsys vascular access system	Cardiovascular	01/10/2020	Ellipsys Vascular Access System PS Study	05/29/2020	Progress Adequate
PS160001	Bayer Healthcare, LLC	Essure system for permanent birth control	Obstetrics/ Gynecology	02/29/2016	Postmarket Surveillance Study	09/02/2016	Progress Adequate
PS200004	Bluegrass Vascular	Surfacer inside-out access catheter system	Cardiovascular		Postmarket	/22/2021	Progress

[522 Postmarket Surveillance Studies Database (fda.gov)]



Post-Approval Studies (PAS) Database

FDA Home ⊙ Medical Devices ⊙ Databases

The FDA has the authority to require sponsors to perform a post-approval study (or studies) at the time of approval of a premarket approval (PMA), humanitarian device exemption (HDE), or product development protocol (PDP) application. Post-approval studies can provide patients, health care professionals, the device industry, the FDA and other stakeholders information on the continued safety and effectiveness (or continued probable benefit, in the case of an HDE) of approved medical devices. This database allows you to search Post-Approval Study information by applicant or device information.

Learn more...

Search | Search | Active Orders | Inactive Orders | All Orders

To sort by data column: 236 orders

Active Orders | Suggest Enhancement / Report Issue | Export to Excel

Application Number	Application	Device Name	Medical Specialty	Date PMA Approved	Study Name	Date Original Protocol Accepted	Study Status
P170038	Abbott	CentriMag Circulatory Support System	Cardiovascular	12/06/2019	CentriMag FTW PAS	05/22/2020	Progress Adequate
P160030	ABBOTT DIABETES CARE INC.	Freestyle Libre Flash Glucose Monitoring System	Clinical Chemistry	09/27/2017	FreeStyle Libre Flash Glucose Monitoring	12/08/2017	Progress Inadequate
P040040	Abbott Medical	AMPLATZER MUSCULAR VSD OCCLUDER	Cardiovascular	09/07/2007	Post Approval Study	09/07/2007	Progress Inadequate
P100009	Abbott Medical	MITRACLIP DELIVERY SYSTEM	Cardiovascular	10/24/2013	Comprehensive/Linked-Registry Based Surv	10/24/2013	Progress Adequate
P120021	Abbott Medical	AMPLATZER PFO OCCLUDER	Cardiovascular	10/28/2016	Amplatzer PFO	09/22/2017	Progress

[Post-Approval Studies (PAS) Database (fda.gov)]

FDA confirms that required post market surveillance **processes are in place** during the **QMS inspection.**

- The Corrective and Preventative Actions (CAPA) section includes **inspectional objectives** for **CAPA, medical device reporting, corrections and removals, and medical device tracking**.
- See Corrective and Preventive Actions (CAPA) | FDA

Additional focus has been placed on **Real World Evidence** to monitor **post market safety** and adverse events and to make regulatory decisions.

- **Real world data** could include routinely collected data from a variety of sources:
  - Electronic health records (EHRs)
  - Claims and billing activities
  - Product and disease registries
  - Patient-generated data including in home-use settings
  - Data gathered from other sources that can inform on health status, such as mobile devices
- See Real-World Evidence | FDA
- See Strengthening-Our-National-System-for-Medical-Device-Postmarket-Surveillance.pdf (fda.gov)

Agenda

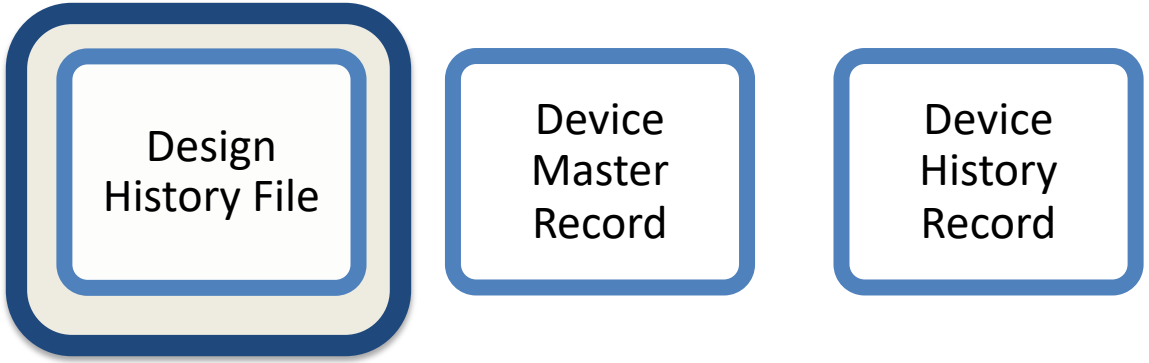
- Quality management system (QMS)
- System for post-marketing surveillance
- **Technical documentation**
- Declaration of conformity
- Registration of manufacturers and their medical devices by the Regulatory Authority

Manufactures must maintain three types of **technical documentation.**

Design History File

Device Master Record

Device History Record

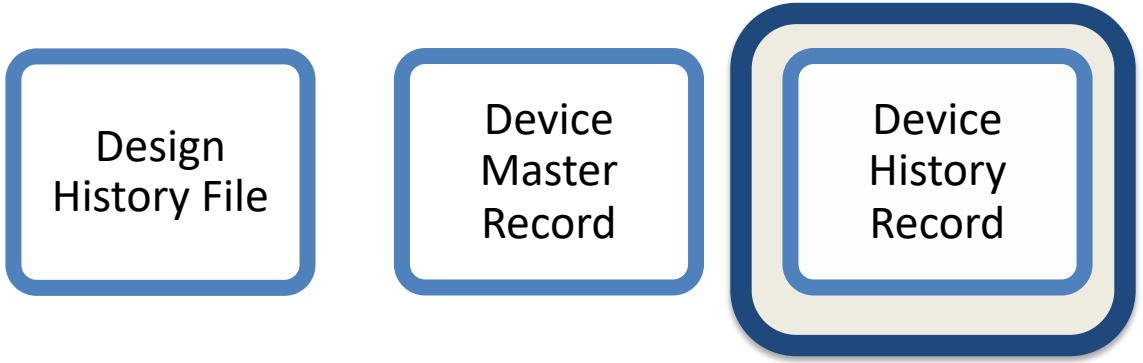


Manufactures must maintain **Design History Files** for each type of device.

- Compilation of records that describe the **design history of a finished device**
- Contains or references the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of [the quality system regulations].
- See CFR - Code of Federal Regulations Title 21 (fda.gov)
- See Design Control Guidance (fda.gov)

Manufactures must maintain **Device Master Records** for each type of device.

- Compilation of documentation that describes **how to build and test the device**
- Includes:
  - Device specifications including appropriate drawings, composition, formulation, component specifications, and software specifications
  - Production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications
  - Quality assurance procedures and specifications including acceptance criteria and the quality assurance equipment to be used
  - Packaging and labeling specifications, including methods and processes used
  - Installation, maintenance, and servicing procedures and methods.
- See CFR - Code of Federal Regulations Title 21 (fda.gov)



Manufactures must maintain **Device History Records** for each batch, lot, or unit.

- Compilation of records documenting **how the device was made**
- Includes:
  - The dates of manufacture;
  - The quantity manufactured;
  - The quantity released for distribution;
  - The acceptance records which demonstrate the device is manufactured in accordance with the DMR;
  - The primary identification label and labeling used for each production unit; and
  - Any unique device identifier (UDI) or universal product code (UPC), and any other device identification(s) and control number(s) used.
- See CFR - Code of Federal Regulations Title 21 (fda.gov)

In order to market a medical device, a manufacturer may need to submit a premarket submission.

In order to market a medical device, a manufacturer may need to submit a premarket submission.

510(k)

- Demonstrates that the new device is **"substantially equivalent"** to a predicate device in terms of intended use, technological characteristics, and performance testing
- See https://www.fda.gov/premarket-notification-510k
- For **low to moderate risk** devices (some Class I and most Class II devices)

PMA

- Demonstrates **reasonable assurances of safety and effectiveness** for the device's intended use
- See https://www.fda.gov/premarket-approval-pma
- For **higher risk** devices (Class III devices)

De Novo classification

- Pathway for certain **new types of devices** to obtain marketing authorization as **class I or class II devices**
- See De Novo Classification Request | FDA

FDA's **voluntary eSTAR program** is an interactive PDF form that **guides applicants** through the process of preparing a comprehensive medical device submission.

Current eSTAR Versions[1]:

eSTAR PDF Template (you *MUST* right-click and download)	This eSTAR template may be used to voluntarily submit to CDRH:	Content is approved for collection under OMB numbers[2]:
Non-In Vitro Diagnostic eSTAR Version 2	510(k) and De Novo medical device submissions for Non-In Vitro Diagnostic devices	0910-0120, 0910-0844
In Vitro Diagnostics eSTAR Version 1	510(k) and De Novo medical device submissions for In Vitro Diagnostic devices	0910-0120, 0910-0844

See Voluntary eSTAR Program | FDA

IMDRF/RPS WG/N9(Edition 3) FINAL:2019

IMDRF International Medical Device Regulators Forum

FINAL DOCUMENT

International Medical Device Regulators Forum

Title: Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVD MA ToC)

Authoring Group: Regulated Product Submissions Table of Contents Working Group

Date: 21 March 2019

Elena M. Astapenko, IMDRF Chair

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The **IMDRF Table of Contents** technical document includes information specific to FDA premarket submissions.

- The Table of Contents document provides an **internationally harmonized**, modular, format for use when filing medical device submissions to regulatory authorities for market authorization.
- See Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVD MA ToC) (imdrf.org)
- See In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC) | International Medical Device Regulators Forum (imdrf.org)

Agenda

- Quality management system (QMS)
- System for post-marketing surveillance
- Technical documentation
- **Declaration of conformity**
- Registration of manufacturers and their medical devices by the Regulatory Authority

Premarket Notification Truthful And Accurate Statement

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[As Required by 21 CFR 807.87(l)]

I certify that, in my capacity as (*the position held in company*) of

(company name), I believe to the best of my knowledge, that all data

and information submitted in the premarket notification are truthful and

accurate and that no material fact has been omitted.

_____

(Signature)

See Premarket Notification Truthful And Accurate Statement | FDA

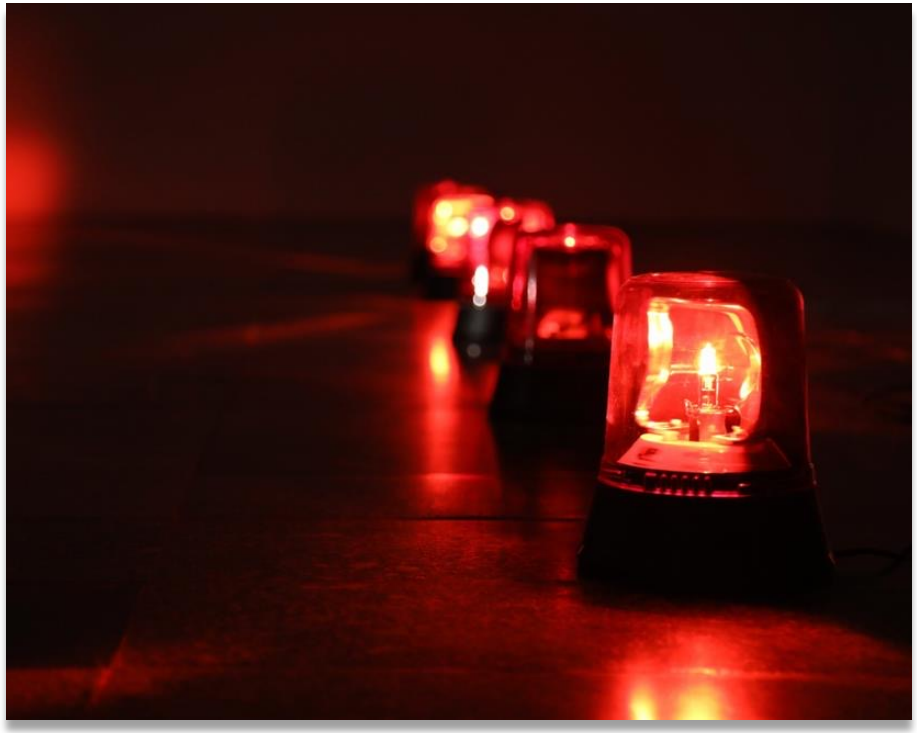
FDA requires a “truthful and accuracy statement” for premarket notifications.

Agenda

- Quality management system (QMS)
- System for post-marketing surveillance
- Technical documentation
- Declaration of conformity
- **Registration of manufacturers and their medical devices by the Regulatory Authority**

Registration and **listing** provide the FDA with the **location** of medical device establishments and the devices manufactured at those establishments.

- Knowing where devices are made increases the ability to **prepare for** and **respond to public health emergencies**.
- See Device Registration and Listing | FDA



Registration

- **Establishments** that are involved in the **production** and **distribution** of medical devices intended for **commercial distribution** in the **United States** (U.S.), including those that are imported for export only, are required to **register annually** with the FDA.
- Congress has authorized FDA to collect an annual establishment **registration fee** for device establishments.

The annual registration user fee for fiscal year 2022 follows:

Year	FY 2022
Fee	$5,672

Listing

- Generally, establishments that are required to register with the FDA are also required to **list** the **devices** that are **made there** and the **activities** that are **performed on those devices**.
- If a device requires a premarket submission before being marketed in the U.S., then the owner/operator should **also provide the FDA premarket submission number** (510(k), De Novo, PMA, PDP, HDE).

FDA publishes tables indicating **who must register, list**, and pay the annual fee.

Domestic establishments

Activity	Register	List	Pay Fee
Contract manufacturer (including contract packagers)	**YES** 807.20(a)(2)	**YES** 807.20(a)(2)	**YES**
Contract sterilizer	**YES** 807.20(a)(2)	**YES** 807.20(a)(2)	**YES**
Device being investigated under IDE	**NO**	**NO** 807.40(c)	**NO**
Domestic Distributor that does not import devices	**NO** 807.20(c)(3)	**NO**	**NO**
Any establishment located in a foreign trade zone involved with the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for commercial distribution in the United States	**YES**	**YES**	**YES**
Import agent, broker, and other parties who do not take first possession of a device imported into the United States	**NO**	**NO**	**NO**
Initial Importer	**YES** 807.40(a)	**NO** Identify manufacturers per 807.20(a)(5)	**YES**
Maintains complaint files as required under 21 CFR 820.198	**YES**	**YES**	**YES**

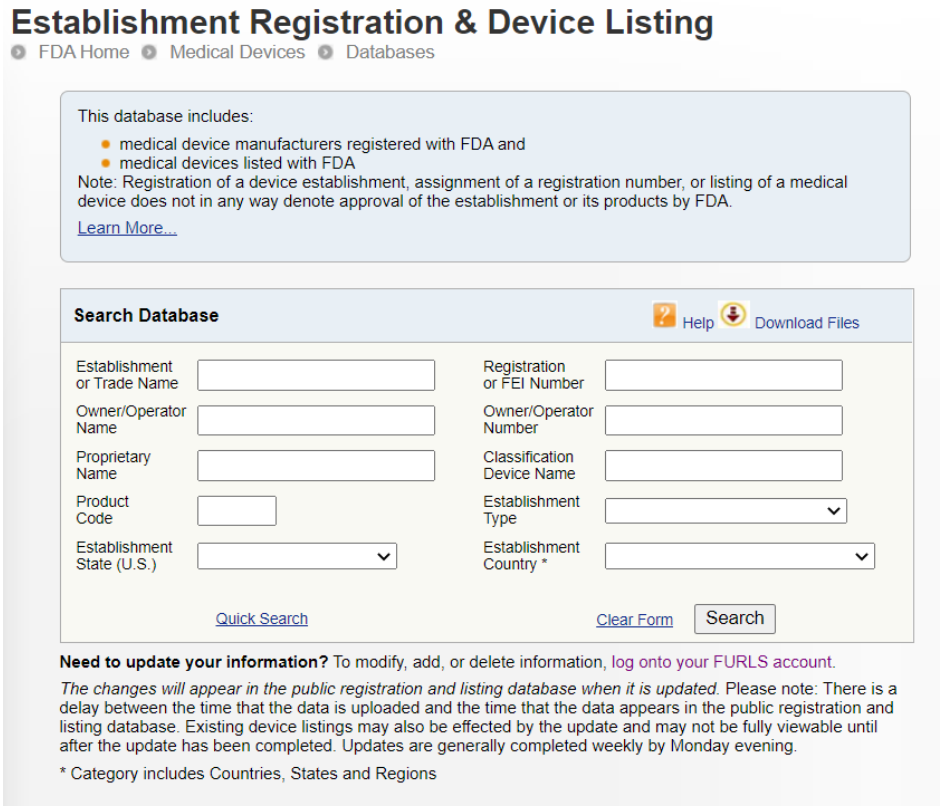
Foreign Establishments

Activity	Register	List	Pay Fee
Contract Manufacturer (including contract packagers)	**YES** 807.40(a)	**YES** 807.40(a)	**YES**
Contract Sterilizer	**YES** 807.40(a)	**YES** 807.40(a)	**YES**
Custom Device Manufacturers	**YES** 807.20(a)(2)	**YES** 807.20(a)(2)	**YES**
Device Being Investigated under IDE	**NO** 812.1 (a)	**NO** 812.1(a), 807.40(c)	**NO**
Foreign Exporter of devices located in a foreign country	**YES** 807.40 (a)	**YES** 807.40 (a)	**YES**
Foreign Manufacturers (including Kit Assemblers)	**YES** 807.40(a)	**YES** 807.40(a)	**YES**
Maintains complaint files as required under 21 CFR 820.198	**YES**	**YES**	**YES**
Manufacturer of accessories or components that are packaged or labeled for commercial distribution for health-related purposes to an end user	**YES** 807.20(a)	**YES** 807.20(a)	**YES**

See Who Must Register, List and Pay the Fee | FDA.

Some information regarding **Registration** and **Listing** is available to the **public**.

- Firm's registration or owner/operator number can be found in the **Public Registration and Listing database**
- Medical device listing number(s) are not available publicly
- See [How to download listing information from FURLS (fda.gov)]



Registration and **listing** do **NOT denote approval** of the establishment or its products by FDA.

- **FDA does not certify registration and listing** information for firms that have registered and listed.
- **FDA does not issue Registration Certificates** to medical device establishments.

- This concludes my talk. ***Thank you*** for your attention as we discussed how FDA implements the Principles of Conformity Assessment for Medical Devices (GHTF/SG1/N78:2012).

  5 conformity assessment elements included in N78:

  - Quality management system (QMS)
  - System for post-marketing surveillance
  - Technical documentation
  - Declaration of conformity
  - Registration of manufacturers and their medical devices by the Regulatory Authority