Enzyme

Introduction to FDA and Notified Bodies

Table of Contents

Introduction

A medical device is any healthcare product that does not achieve its principal intended purposes through a chemical action or by being metabolized.

Devices are therefore everything from tongue depressors to pacemakers, stents, MRI machines and digital therapeutics.

If you are developing drugs or medical devices (including diagnostics and any software used to help treat or help diagnose a patient), your company is operating in a regulated industry.

Before your company can commercialize your product, you must obtain authorization to commercialize from the FDA (in the US), and/or a Notified Body (in the EU). **Most products require some form of an approval process.**

To obtain marketing approval from the FDA or a Notified Body, your company is required to establish a **Quality Management System (QMS), also known as a QMS.**

Your QMS governs all daily business activities that can affect the quality of your product, from design and development to complaint handling. See our Introduction to QMS course to learn about quality management systems.

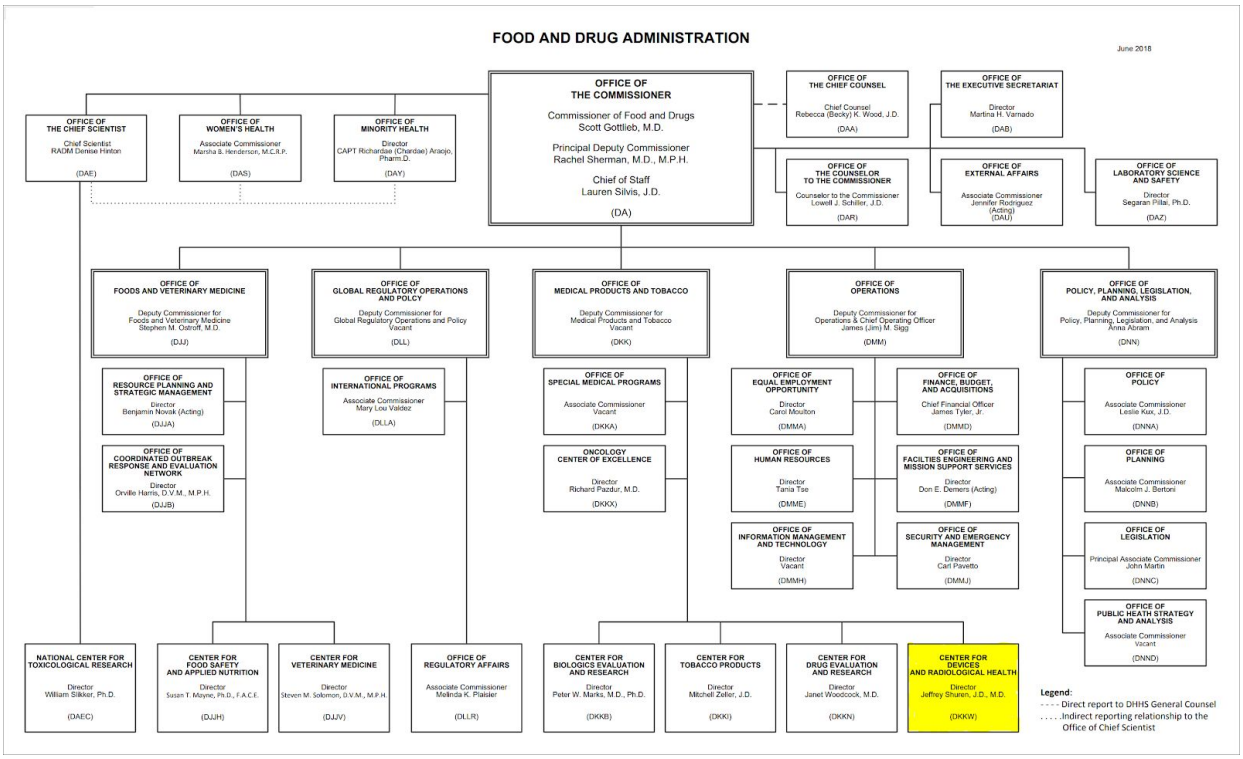
FDA and the EU regulate both product submission requirements *and* day-to-day business processes. Submission requirements represent a snapshot in time. Whereas, business process requirements are permanent and drive numerous activities your company is responsible for implementing, maintaining and demonstrating via providing evidence (records).

U.S. Regulations- FDA

In the United States, the FDA is responsible for protecting public health by regulating and supervising the safety of (but not limited to) drugs, dietary supplements, and medical devices.

FDA accomplishes this mission by establishing and enforcing high product standards and other regulatory requirements authorized or mandated by the Federal Food, Drug and Cosmetic Act (FD&C Act), its amendments, and other public health laws enacted into law.

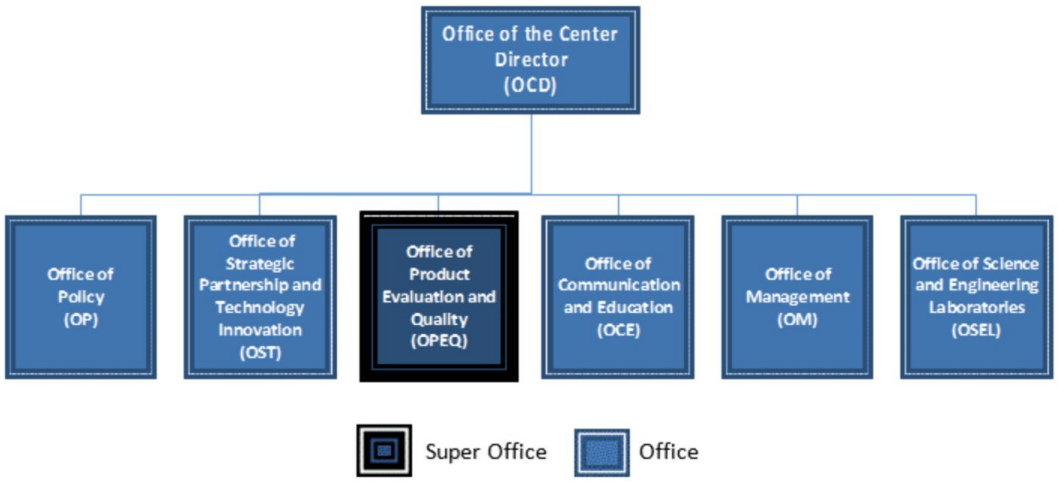
FDA employees serve as patient advocates when inspecting facilities, reviewing submissions, or when developing new guidance for the industry; many of them view their jobs as the last line of defense before patients are put into the path of harm - as nearly all products carry with them some form of risk.



Overall FDA Organization

The FDA is segmented by the variety of industries it regulates. Medical devices and in vitro diagnostics (IVDs), industries which are overseen by the **FDA Center for Devices and Radiological Health (CDRH).**

CDRH is further organized into various offices that are tasked with different aspects of regulating and supervising the medical device industry.



New CDRH Organization Chart

CDRH has started the process of combining several Offices to form a new Office of Product Evaluation and Quality (OPEQ) which will be sub-divided into offices based on product type and technology.

While the core concepts of regulations governing medical device product approvals and daily business activities are the same for all medical devices and geographical regions, there are additional specific requirements for a variety of product types.

CDRH publishes guidance documents spanning a wide variety of regulatory concepts, including special requirements for certain kinds of products; these Guidance documents, while not technically binding (see excerpt below contained in all Guidance documents), they are tacit FDA expectations for minimum good manufacturing practices.

EU Regulations

The European Union (EU) regulatory landscape is structured differently from the United States.

Before you can offer your medical products within EU nations, you must **first obtain a CE Marking.** This signifies that your product conforms to all applicable EU directives - indicating your product satisfies EU safety and performance requirements.

This conformity assessment is conducted by independent third party organizations, called Notified Bodies, who evaluate your company and product against the relevant EU legislation. Currently this legislation is called the Medical Device Directive and more recently a new EU Medical Device Regulation, or MDR, will go into effect in 2020 for medical devices.

Conforming to EU regulations typically also required the application of relevant international standards (e.g. ISO 14971 "Medical devices - Application of risk management to medical devices").

Standards

The **International Organization for Standardization (ISO)** publishes a wide variety of standards, similar to FDA's guidance documents, and several of these Guidance and Standard requirements may apply to your product.

FDA generally requires your company follow *current* **Good Manufacturing Practices (cGMP)** which implies applying appropriate Guidance and Standard documents.

FDA actively recognizes over 1,200 Standards it believes will aid a company in complying with US regulations. Many such standards will expedite FDA's review and enhance their trust of your processes and product, including, but not limited to:

- ISO 13485 *Medical devices - Quality management systems - Requirements for regulatory purposes* and
- IEC 62304 *Medical Device software - Software life-cycle processes*

Conversely, Notified Bodies focus almost exclusively on ISO Standards (plus the EU legislation) and do not require additional compliance to FDA Guidance documents. On occasion, if there is no applicable ISO standard for your product, and there *is* an FDA Guidance document, they may request your company adhere to it or demonstrate an equivalent or superior process or product design.

Therefore, after your company begins developing a product, and still well in advance of solidifying requirements and tests, the project team should identify all pertinent Guidance and Standard documents that apply to the product and processes.

This will expedite conversations with regulatory bodies and shorten the overall development timeline; it will better facilitate how the company fulfills its responsible for ensuring the safety and effectiveness of medical devices under *current* GMP, and it will greatly inform your Regulatory Strategy.

Regulatory Strategy

Well-timed regulatory strategies begin **early** in the development process. A product's path to market is impacted by it intended use, design and function as they directly impact the submission content and rigor required for pre-market testing.

Large companies have lived through many products cycles and learned the errors of both over- and under-committing to robust regulatory strategies.

Typically, under planning can lead to poor results and end up costing more than a complex product with a clear regulatory strategy. Therefore it is recommended for startups and small companies to involve their Regulatory Affairs employees and/or consultants early in the product development process.

Preparing For A Submission

Too many startups fail by making poor assumptions about timing, cost, and planning with respect to their eventual submission and the required regulatory and quality requirements.

It's a fallacy to believe that a submission document can be easily compiled and given to FDA right when your company is 'ready'.

Some tips to keep in mind are:

1. Know which approval/clearance process applies to your product

- Assuming a clinical trial is necessary, even preparing for one, can cost a company millions of dollars, It is important to complete all the pre-work for any particular submission type. Missing information can cause months, even quarters or years, of delays to getting a product to market
- FDA's Q-Submission process, one of which being Pre-Submissions, gives companies the opportunity to officially interact with FDA during product development and submission planning. It's a free service FDA provides upon request, and they highly recommend companies take full advantage of it.

2. Follow critical portions of the Quality System Regulation (21 CFR 820) that impact content and process leading up to submissions.

- Document Controls, Risk Management, Design Controls, and Training are all vital throughout the product life cycle.

3. Avoid remediation and fraud

- The cost of remediation multiplies as a company waits to correct egregious errors like fraud. Significant time is necessary to rectify false or inaccurate documentation, submissions etc. which includes gap analyses, summaries of missing data, re-testing, potentially re-designing the product, filing subsequent corrective submissions, etc.
- Examples of fraud include, but are not limited to:
    - Making false statements about performance, substantial equivalence, intended use, target patient population, etc.
    - Misrepresenting data collected during product development testing activities like design verification and design validation - through omission, inaccurate graphs/charts/tables, or fabricating evidence of testing, etc.
- Even if unintentional, fraud can significantly de-value your product and company; potential acquirers may detect these irregularities during the due diligence process and cause a buyer to back out. If the acquisition already took place when the acquirer learns the truth, your company leadership carries the risk of termination and civil action.

The single most cost-effective correction is to include appropriate and knowledgeable resources in the planning and execution of the entire product development life cycle. These professionals typically fall within the functions of "Regulatory Affairs" and "Design Assurance Engineering" (RA, DAE).

The Submission

Submission content and level of detail vary based on the Classification of your product.

Because medical devices can range from tongue depressors, to mobile apps, to implantable cardioverter defibrilators (ICDs), certain types of devices do not need submissions whereas some need clinical trials. Generally, that's driven by risk-to-patient.

Complete our Product Risk Classification course to learn more about how to classify your product.

Commercialization

Once your product is on the market, you will have to start tracking things like Nonconformances, Complaints and Corrective and Preventive Actions (CAPAs).

Enzyme's QMS can help you track these, and document recalls (hopefully never for your company).