# Overview of FDA and Regulatory Processes

Introduction to Biological Products, Including Vaccines, Cell and Gene Therapies, and Other Advance Therapies

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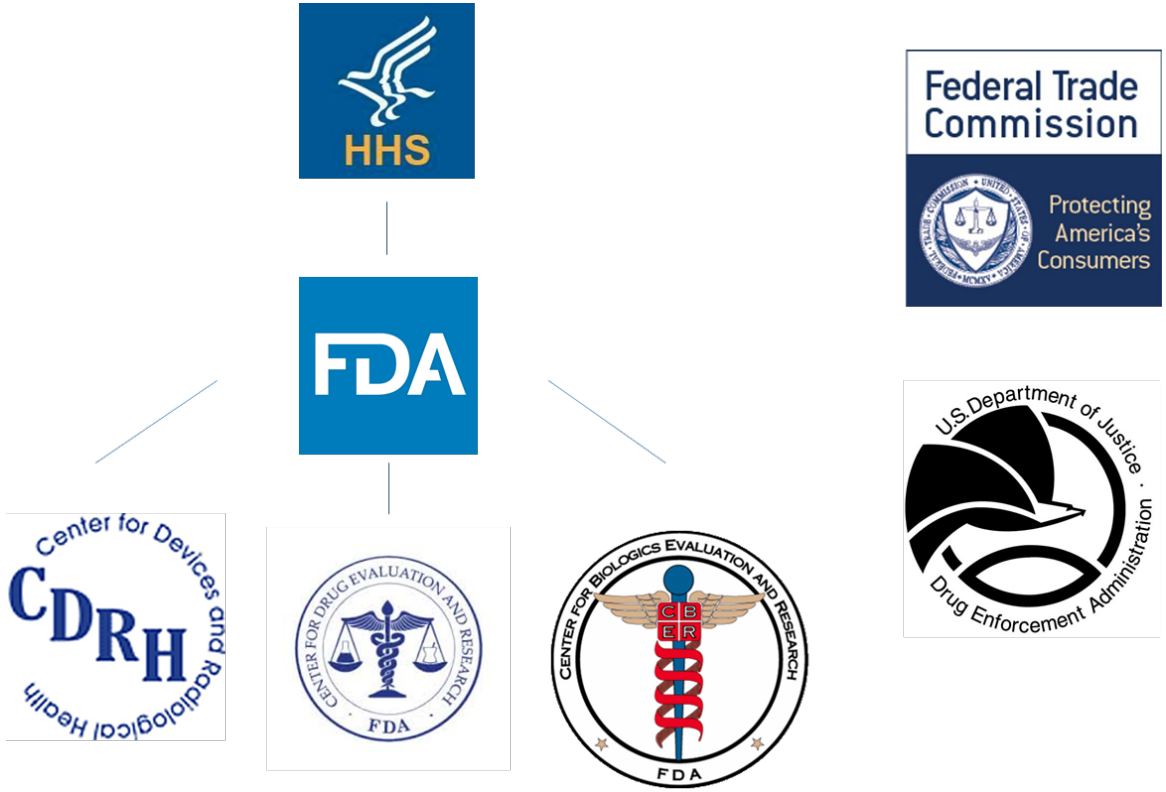
FDLI

# Overview of the U.S. Food and Drug Administration

# FDA's Role in the Federal Government



# Agencies Under HHS




# Regulatory Oversight: From NIH to FDA

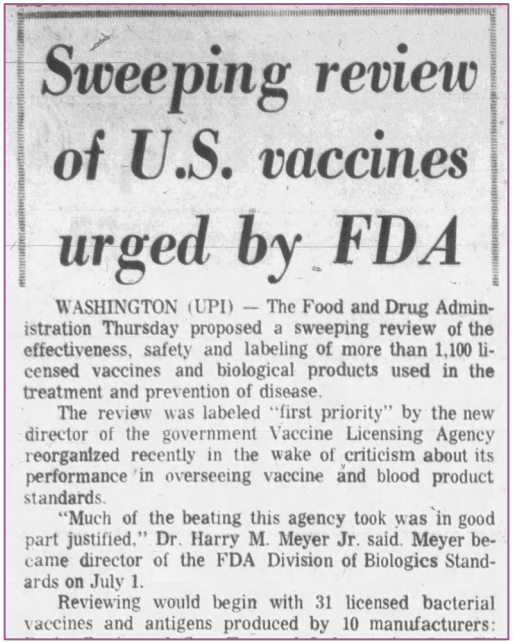
## 32 Ineffective Drugs Allowed To Remain On the Market

By CARL C. CRAFT

WASHINGTON (AP) — Congressional investigators say 32 ineffective vaccines were allowed to remain on the market for at least 10 years while drug regulators quietly exchanged memos.

Furthermore, for three years the Division of Biologics Standards released flu vaccines even when its tests showed potency to be as low as less than one per cent of standards, says the General Accounting Office.

In releasing the GAO report Thursday, Sen. Abraham Ribicoff, D-Conn., said: "The DBS control official for influenza vaccine has stated that, in his opinion, if manufacturers



## *Sweeping review of U.S. vaccines urged by FDA*

WASHINGTON (UPI) — The Food and Drug Administration Thursday proposed a sweeping review of the effectiveness, safety and labeling of more than 1,100 licensed vaccines and biological products used in the treatment and prevention of disease.

The review was labeled "first priority" by the new director of the government Vaccine Licensing Agency reorganized recently in the wake of criticism about its performance in overseeing vaccine and blood product standards.

"Much of the beating this agency took was in good part justified," Dr. Harry M. Meyer Jr. said. Meyer became director of the FDA Division of Biologics Standards on July 1.

Reviewing would begin with 31 licensed bacterial vaccines and antigens produced by 10 manufacturers:

# FDA's Mission

The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

FDA is responsible for advancing the public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health.

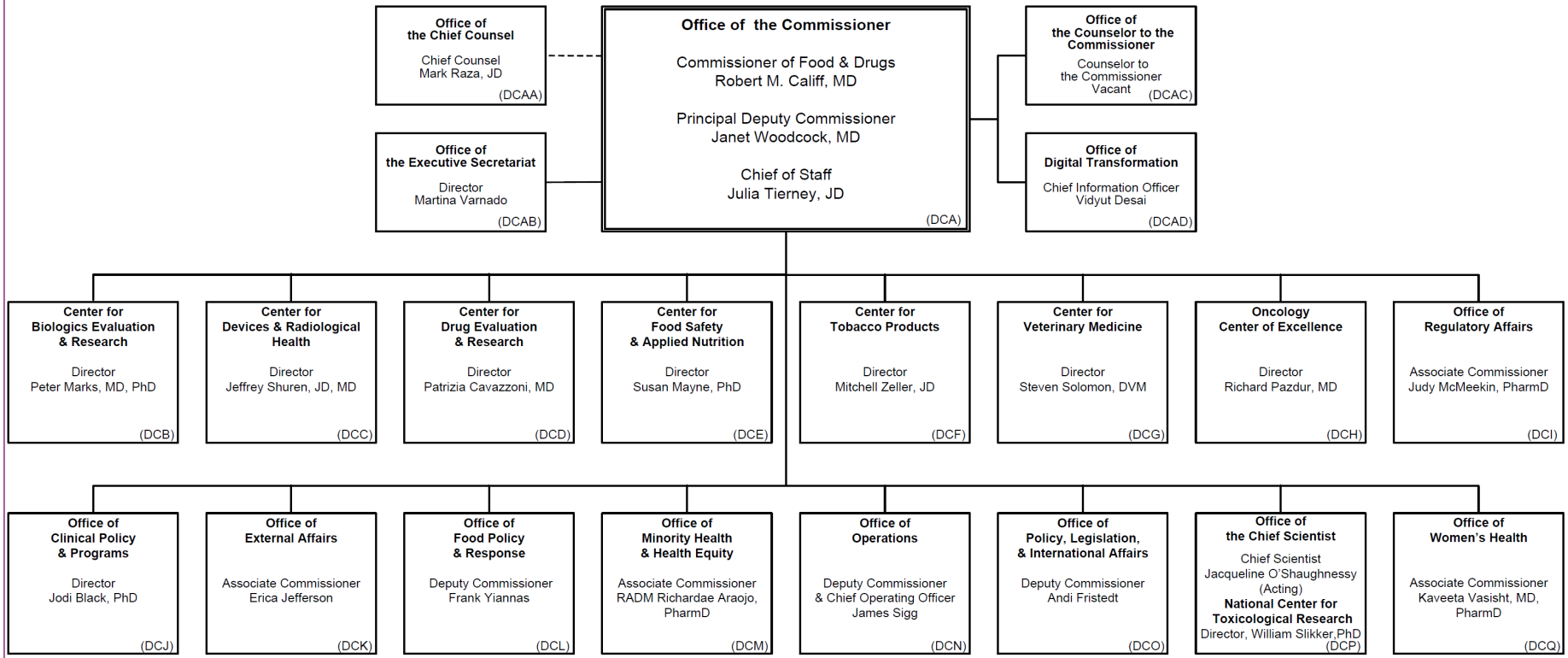
FDA also has responsibility for regulating the manufacturing, marketing, and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.

FDA also plays a significant role in the Nation's counterterrorism capability. FDA fulfills this responsibility by ensuring the security of the food supply and by fostering development of medical products to respond to deliberate and naturally emerging public health threats.

# FDA Structure

# Department of Health and Human Services
# Food and Drug Administration

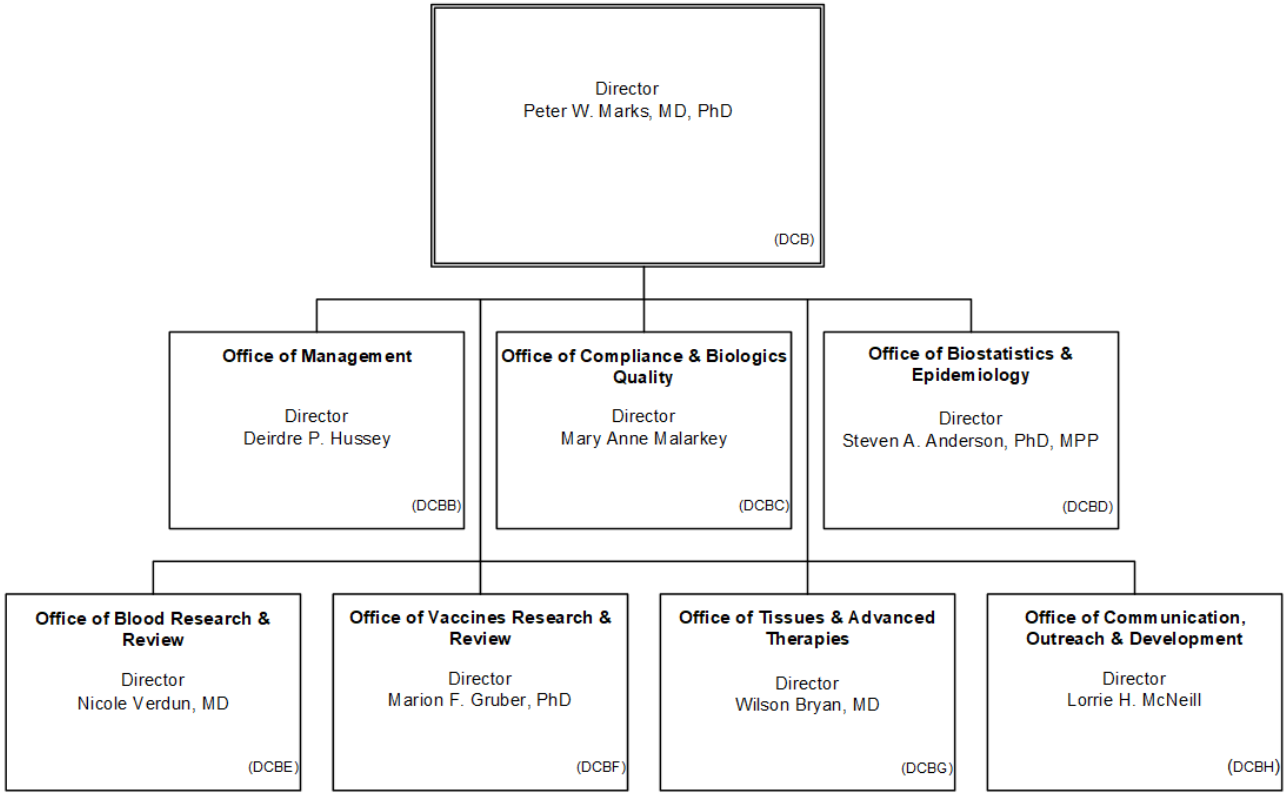
February 17, 2022



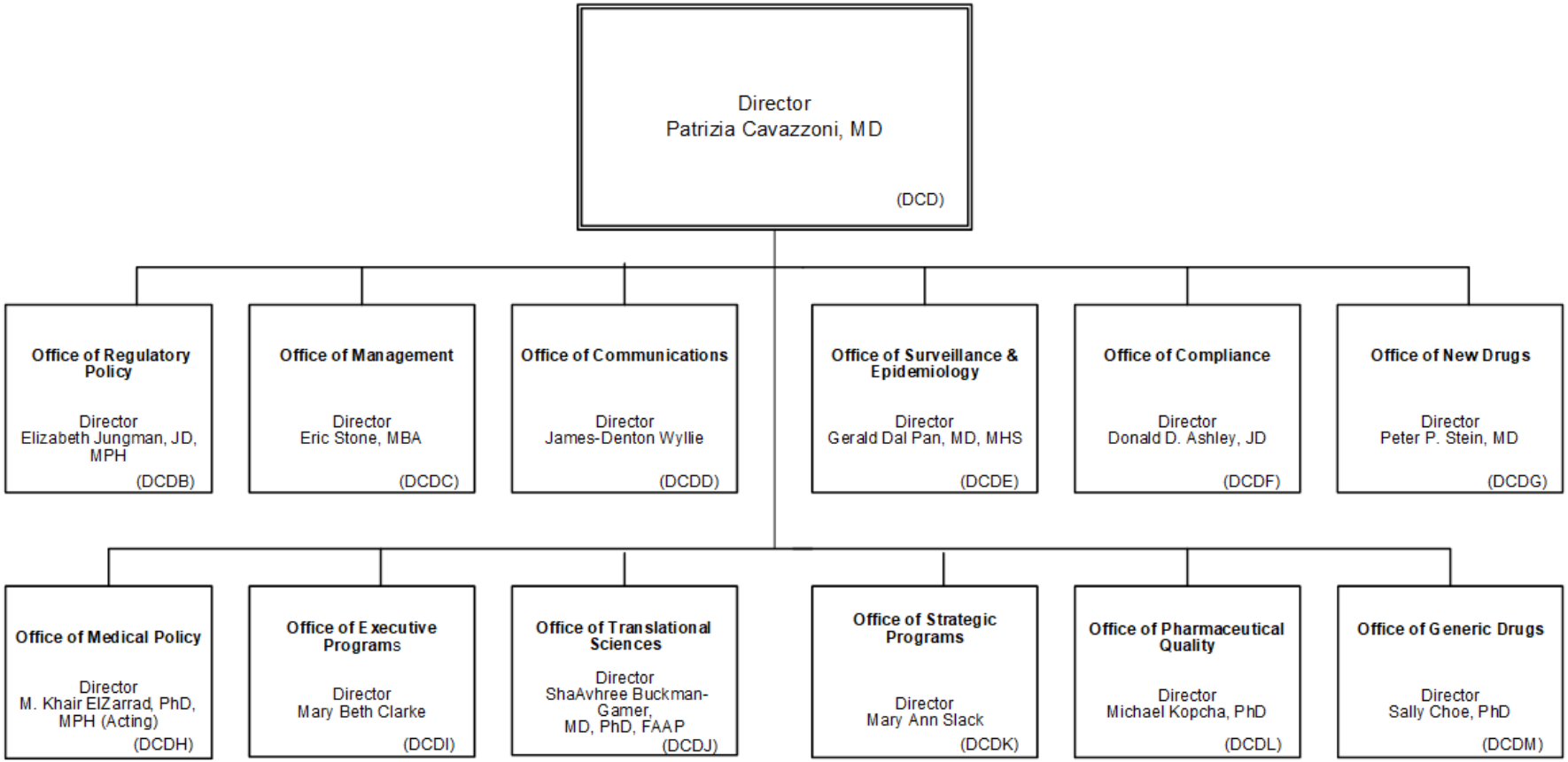

**Legend**:
--- Direct report to DHHS General Counsel

June 2021

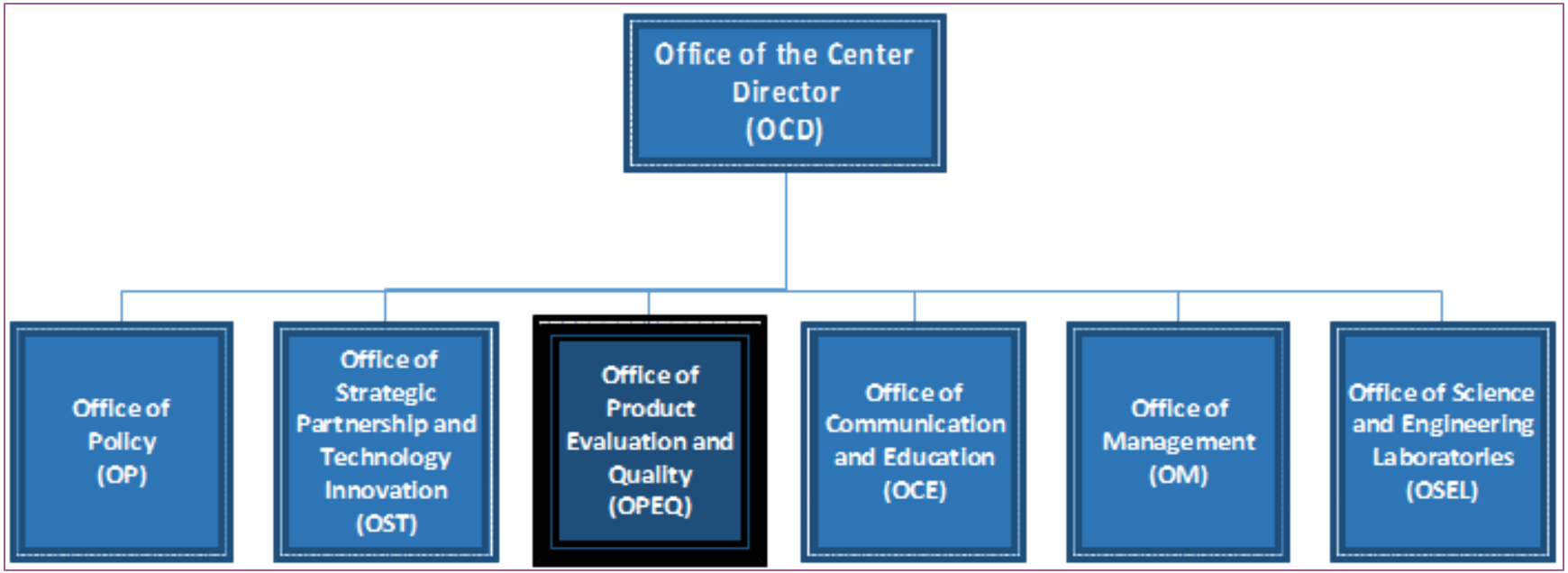
# Department of Health and Human Services
# Food and Drug Administration
# Center for Biologics Evaluation and Research



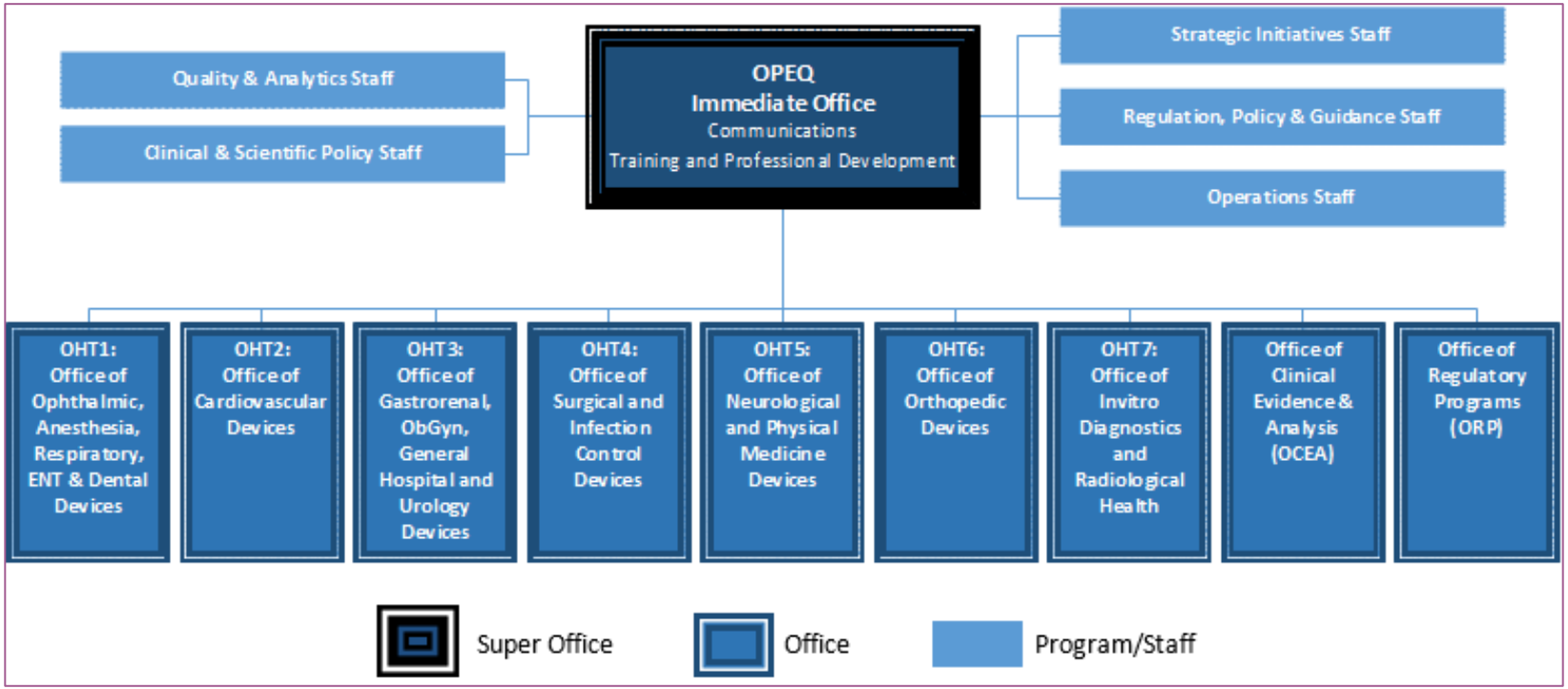
# Food and Drug Administration
# Center for Drug Evaluation and Research



# Current CDRH Structure



# Current CDRH Office (cont.)



# Devices Regulated By CBER

U.S. FOOD & DRUG ADMINISTRATION

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## Intercenter Agreement Between the Center for Biologics Evaluation and Research and the Center for Devices and Radiological Health

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Jurisdictional Information

Combination Product Contacts

RFD Jurisdictional Decisions

Jurisdictional Updates

Intercenter Agreements

Jurisdictional Transfers

In 1982, an agreement detailed the working relationships between the organization previously identified as the Bureau of Medical Devices (BMD), the Bureau of Radiological Health (BRH) and the Bureau of Biologics (BoB) to identify the responsibilities of each for medical device activities.

Since then there have been several major organizational changes within the Food and Drug Administration (FDA). In 1982, BMD and BRH were joined administratively to form the Center for Devices and Radiological Health (CDRH). Also in 1982, BoB and the Bureau of Drugs were merged to form the Center for Drugs and Biologics (CDB), with biological products regulated by the Office of Biologics Research and Review (OBRR). In 1987, however, CDB was split into two major Centers, with biological products regulated by the Center for Biologic Evaluation and Research (CBER).

There also have been major advances in medical device technology and significant changes in the applications for existing technologies. New categories of in vitro diagnostics products have been developed to detect evidence of transfusion transmitted agents that were not recognized in 1982; use of "cellular" biologicals has continued to evolve as a therapeutic practice; and monoclonal antibodies are used in conjunction with medical devices for therapeutic purposes. Thus, this agreement has been updated to include medical devices which were not specified in the previous agreement and developing medical devices and device technologies for which there are no previous jurisdictional guidelines.

This document, which supersedes all prior agreements, outlines the working relationships that exist between CBER and CDRH for certain categories of medical devices or specified medical devices.

Submissions and inquiries should be made directly to the lead Center identified

Content current as of:
02/16/2018

# FDA HQ and the Field

# FDA Law and Policies

# Overview

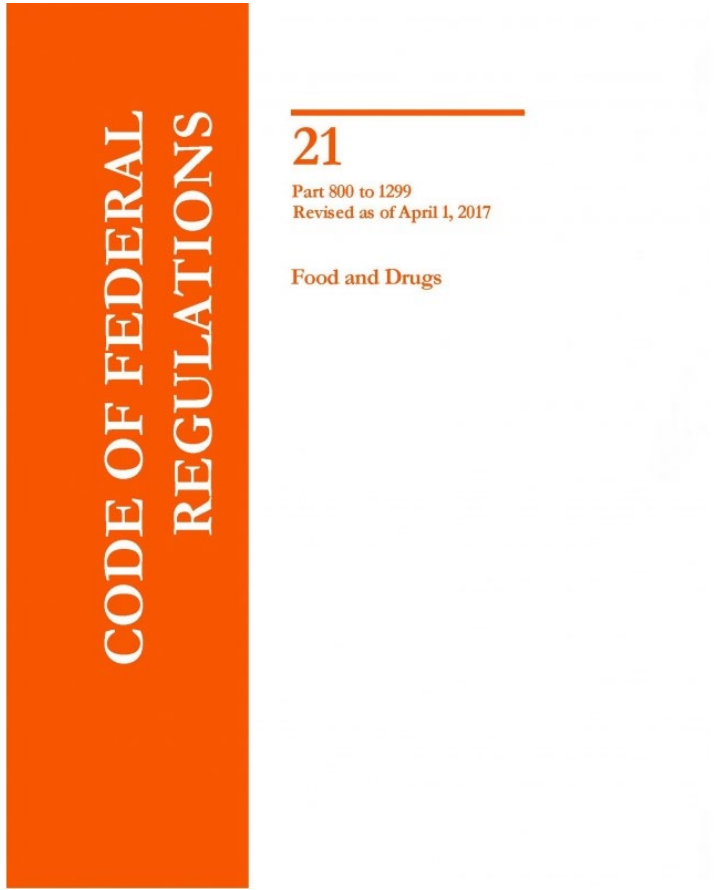
1. U.S. Constitution
2. **Statutes**
3. **Regulations**
4. **Federal Register Notices**
5. Advisory Committees
6. **Guidance Documents**
7. Regulatory Procedures Manual (RPM)
8. **Compliance Policy Guides (CPGs)**
9. **Staff Manual Guides**
10. Memorandum of Understanding (MOUs)
11. **Enforcement Actions and Letters**
12. **Informal Statements and Advice**

# Statutes

- The Federal Food, Drug, and Cosmetic Act (1938)
  - New Drug Approval (NDA)
  - Abbreviated New Drug Application (ANDA)
- The Public Health Service Act (1944)
  - Biologic License Application (BLA)
  - Abbreviated Biologic License Application (aBLA)

# Regulations

- Created under the authority granted to an agency by Congress (as required or authorized by statute)
- Created in accordance with the Administrative Procedure Act of 1946 (APA); procedures may be impacted by Executive Orders, memoranda issued by the President, and FDA's own regulations



# “Notice and Comment Rulemaking”

- The bulk of agency rulemaking is done under APA Informal § 553 Rulemaking, also known as “Notice and Comment Rulemaking”
- Basic requirements of Informal Rulemaking:
  - **Notice of the proposed rulemaking**
    - Published in the Federal Register (FR)
  - **Opportunity for public comments**
    - Public comments are available on the public docket to view at regulations.gov
  - Publication of the **final rule** in the FR, after consideration of comments

FEDERAL REGISTER

The Daily Journal of the United States Government

# Exemptions from Informal Rulemaking

- 21 CFR 10.40 discusses FDA's promulgation of regulations for the efficient enforcement of the law
- § 10.40(e)(1) provides that the requirements of notice and public procedure do not apply "When the Commissioner determined for good cause that they are ***impracticable, unnecessary, or contrary to the public interest***"
- There are other exemptions:
  - Rule of "agency organization, procedure, or practice"
  - "Interpretative rules" that add little substantive interpretation of the law
  - "General statements of policy"
- Agencies may run into difficulties in the courts trying to invoke these exemptions if the proposed action has a major impact on the public
- Congress may require an agency to follow a specific public participation procedure

# Advisory Opinions & Preambles

- Federal Register preambles:
  - Under 21 C.F.R. § 10.85(d)(1), preambles to proposed or final rules constitute ***advisory opinions***, which represent the formal position of FDA. FDA cannot generally take regulatory action against someone who relies on an FDA advisory opinion (21 C.F.R. § 10.85(e))
- Once a rule is finalized, it is added to the Code of Federal Regulations (CFR)
  - Final rules adopted through notice-and-comment procedure sets forth substantive, binding requirements
  - These rules can be challenged in court before FDA tries to enforce them
- FDA's regulations can be found in Title 21 of the Code of Federal Regulations

# Guidance Documents

- **What is a Guidance Document? – 21 C.F.R. § 10.115(b)**
  - "Guidance documents are documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of policy on a regulatory issue."
  - "Guidance documents include, but are not limited to, documents that relate to: The design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation of approval of submissions, and inspection and enforcement policies."
  - "Guidance documents do not include: Documents relating to internal FDA procedures, agency reports, general information documents provided to consumers or health professionals, speeches, journal articles and editorials, media interview, press materials, warning letters, memoranda of understanding, or other communications directed to individual persons or firms."

# Compliance Policy Guides (CPGs)

- The FDA CPGs manual consists of statement or explanations of compliance policy to FDA staff.
- Provide interpretations of FDA statutory or regulatory requirements as agreed upon by ORA and program center or offices.
- FDA may issue CPGs for many reasons, including new legislation, regulations, guidances, court decision, and similar legal, scientific, and public health factors.
- CPGs are guidance documents prepared for FDA staff as defined in the GGP regulations found in 21 C.F.R. § 10.115.

| Chapter 3 | Devices |
|---|---|
| Sub Chapter 300 | General / Processes |
| 305 (Revoked) | Anesthesiology |
| 310 | Cardiovascular |
| 315 | Dental |
| 320 | Ear, Nose, and Throat |
| 325 | Gastoent. and Urology |
| 335 | General Hospital |
| 345 | Obst. and Gynecology |
| 350 | Ophthalmics |
| 355 | Orthop. and Phy. Med. |
| 370 | Immunology |
| 390-398 | Radiology |

# Good Guidance Practices

- **21 C.F.R. § 10.115 – Good Guidance Practices (GGP's)**
  - "The agency may not use documents or other means of communication that are excluded from the definition of guidance document to informally communicate new or different regulatory expectations to a broad public audience for the first time. These GGP's must be followed whenever regulatory expectations that are not readily apparent from the statute or regulations are first communicated to a broad public audience."
  - "Guidance documents do not establish legally enforceable rights or responsibilities. They do not legally bind the public or FDA."
  - "An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both."
  - "Although guidance documents shall not be binding on the Secretary, the Secretary shall ensure the employees of the Food and Drug Administration do not deviate from such guidances ***without appropriate justification and supervisory concurrence***."
    - Section 701(h)(I)(B) of the FD&C Act

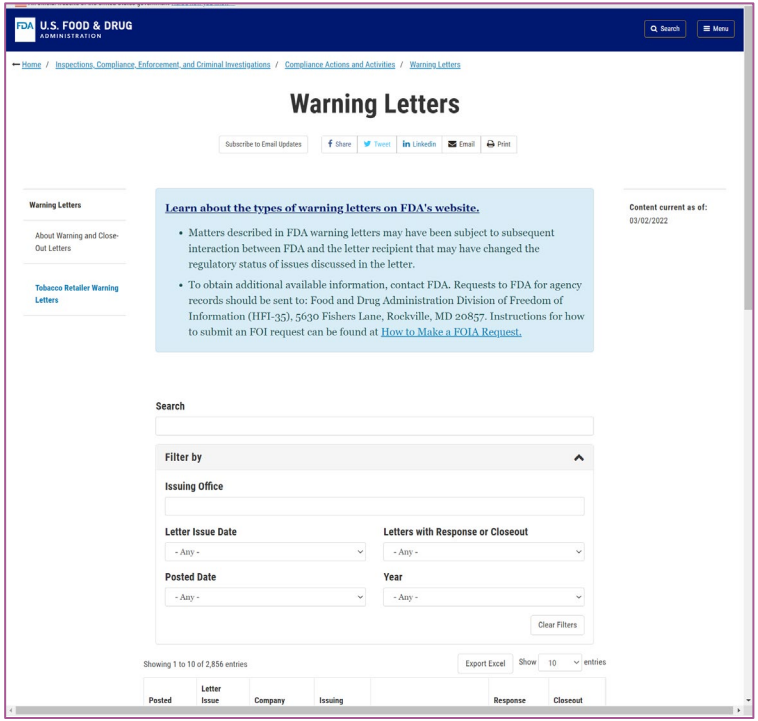
# “Must” vs “Should” in Guidances

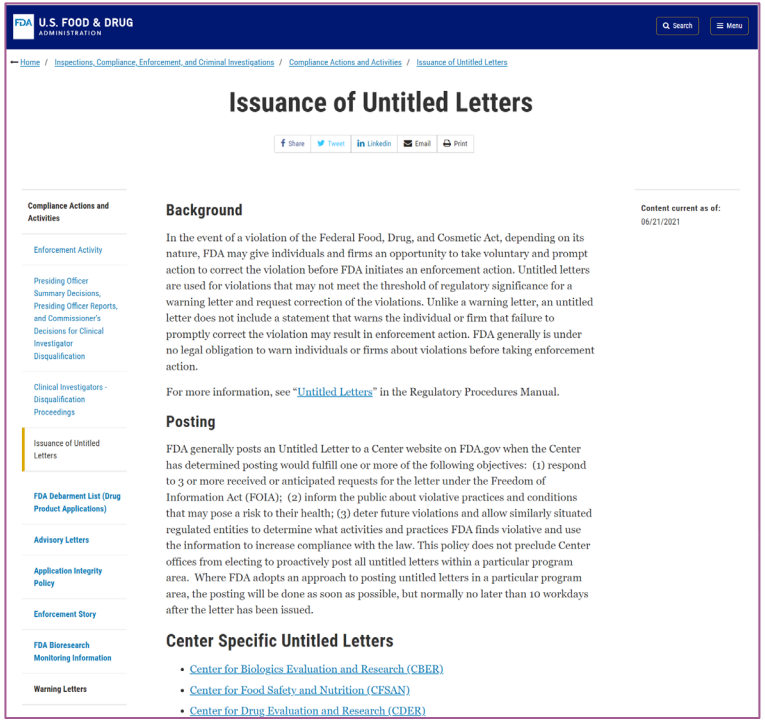
- 21 C.F.R. § 10.115(i)(2)
  - “Guidance documents must not include mandatory language such as “shall,” “must,” “required,” or “requirement,” unless FDA is using these words to describe a statutory or regulatory requirement.
- “Draft” vs “Final” Guidances
  - Draft Guidance, ***when finalized***, will represent the FDA’s current thinking on a topic.
- January 2018 Department of Justice (DOJ) Memo from Former Associate Attorney General Rachel Brand prohibits DOJ from:
  - Using noncompliance with “guidance documents as a basis for proving violations of applicable law in” affirmative civil enforcement cases
  - Using “its enforcement authority to effectively convert agency guidance documents into binding rules”

# Staff Manual Guides

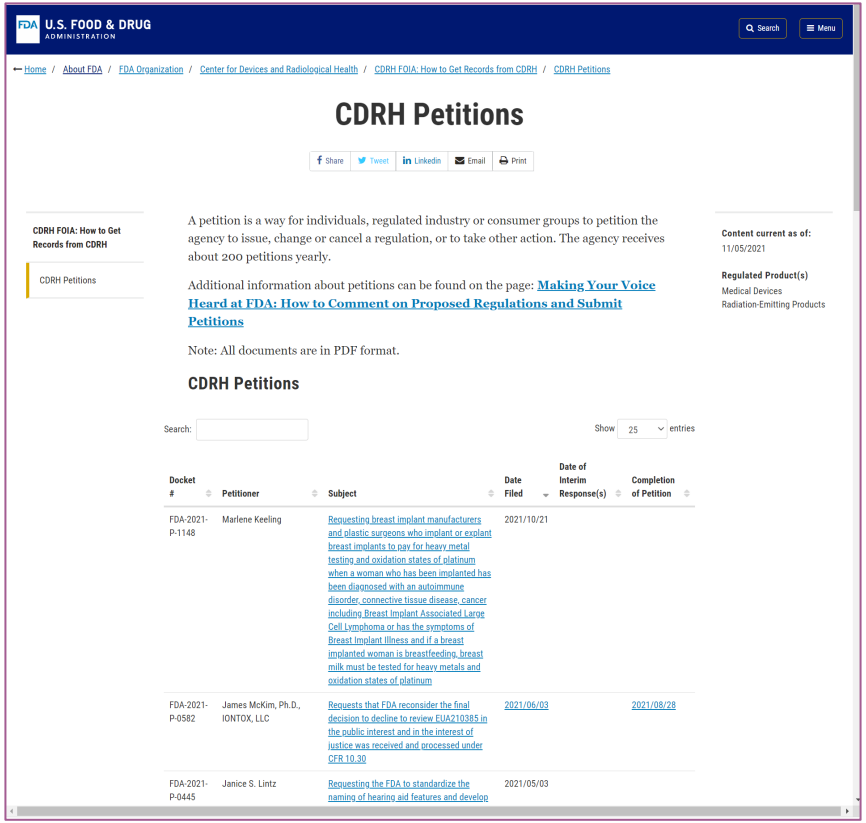
- Does not confer rights or bind FDA or the public
- Describes FDA internal procedures and directive related to:
  - organization and functions
  - delegations of authority
  - administrative and program policies
  - responsibilities and procedures
- Select Staff Manual Guides are publicly available on FDA's website and can otherwise be requested through a Freedom of Information Act request

# Enforcement Actions & Letters



# Citizen Petition Responses



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## CDRH Petitions

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CDRH FOIA: How to Get Records from CDRH

CDRH Petitions

A petition is a way for individuals, regulated industry or consumer groups to petition the agency to issue, change or cancel a regulation, or to take other action. The agency receives about 200 petitions yearly.

Additional information about petitions can be found on the page: **Making Your Voice Heard at FDA: How to Comment on Proposed Regulations and Submit Petitions**

Note: All documents are in PDF format.

**Content current as of:** 11/05/2021

**Regulated Product(s)**
Medical Devices
Radiation-Emitting Products

### CDRH Petitions

Search:

Show 25 entries

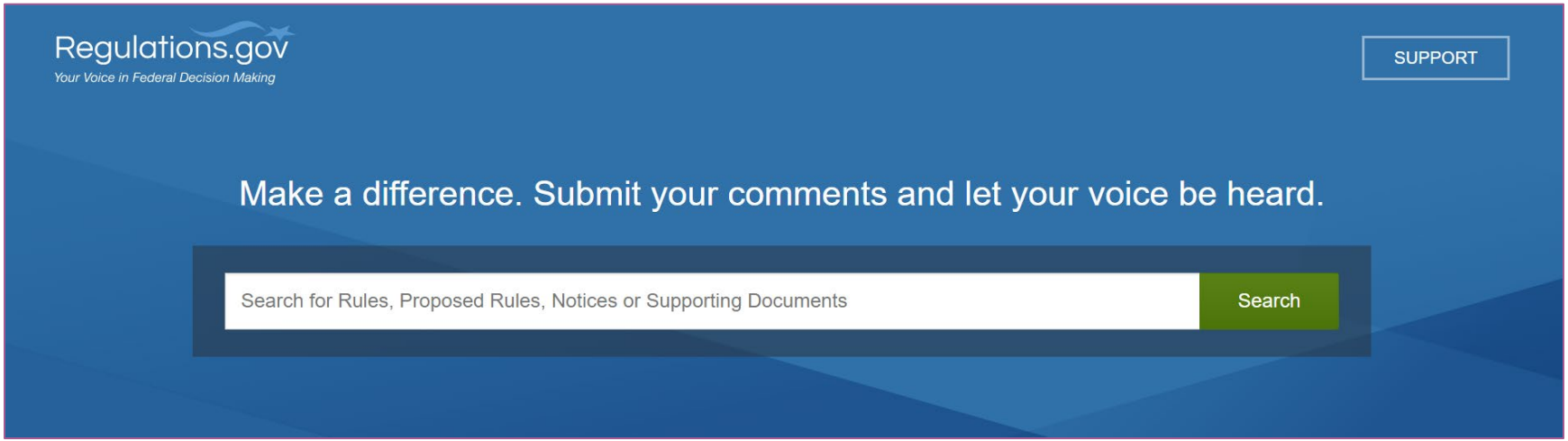
| Docket # | Petitioner | Subject | Date Filed | Date of Interim Response(s) | Completion of Petition |
|---|---|---|---|---|---|
| FDA-2021-P-1148 | Marlene Keeling | Requesting breast implant manufacturers and plastic surgeons who implant or explant breast implants to pay for heavy metal testing and oxidation states of platinum when a woman who has been implanted has been diagnosed with an autoimmune disorder, connective tissue disease, cancer including Breast Implant Associated Large Cell Lymphoma or has the symptoms of Breast Implant Illness and if a breast implanted woman is breastfeeding, breast milk must be tested for heavy metals and oxidation states of platinum | 2021/10/21 | | |
| FDA-2021-P-0582 | James McKim, Ph.D., IONTOX, LLC | Requests that FDA reconsider the final decision to decline to review EUA210385 in the public interest and in the interest of justice was received and processed under CFR 10.30 | 2021/06/03 | | 2021/08/28 |
| FDA-2021-P-0445 | Janice S. Lintz | Requesting the FDA to standardize the naming of hearing aid features and develop | 2021/05/03 | | |

# Informal Statements and Advice

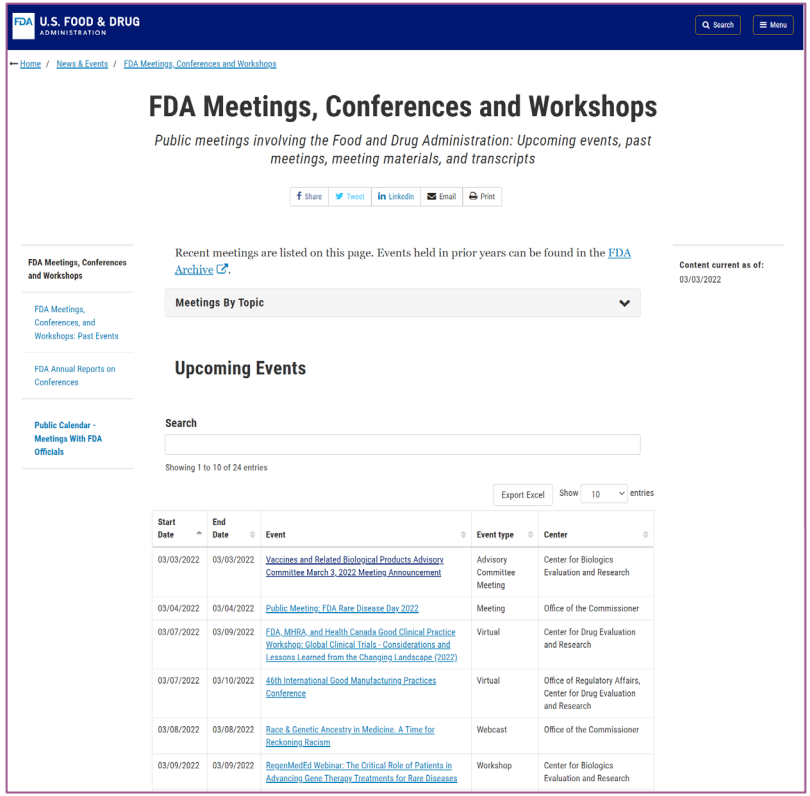
- Provided by FDA employees orally, or in writing, but not under 21 C.F.R. § 10.85 (advisory opinions)
- Represents the judgment / opinion of a specific employee at a specific time
- An informal statement –
  - Not an “advisory opinion”
  - Does not necessarily represent the formal position of FDA
  - Does not bind or otherwise obligate or commit FDA to the views expressed

# Participating in FDA Policy Making

# Comments on Proposed Regulations and Draft Guidance



# FDA Meetings and Workshops



U.S. FOOD & DRUG ADMINISTRATION

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## FDA Meetings, Conferences and Workshops

*Public meetings involving the Food and Drug Administration: Upcoming events, past meetings, meeting materials, and transcripts*

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**FDA Meetings, Conferences and Workshops**

FDA Meetings, Conferences, and Workshops: Past Events

FDA Annual Reports on Conferences

**Public Calendar - Meetings With FDA Officials**

Recent meetings are listed on this page. Events held in prior years can be found in the FDA Archive.

**Content current as of:** 03/03/2022

**Meetings By Topic**

### Upcoming Events

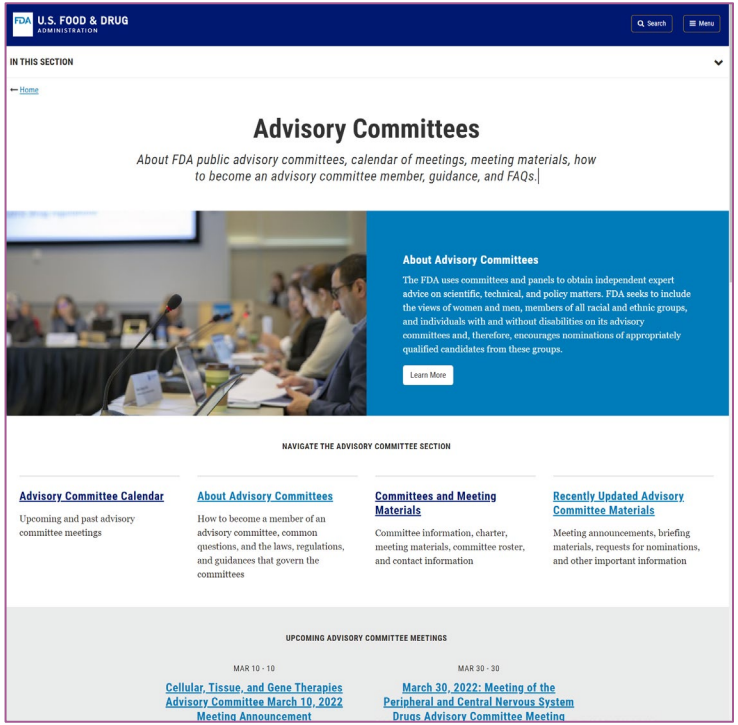
**Search**

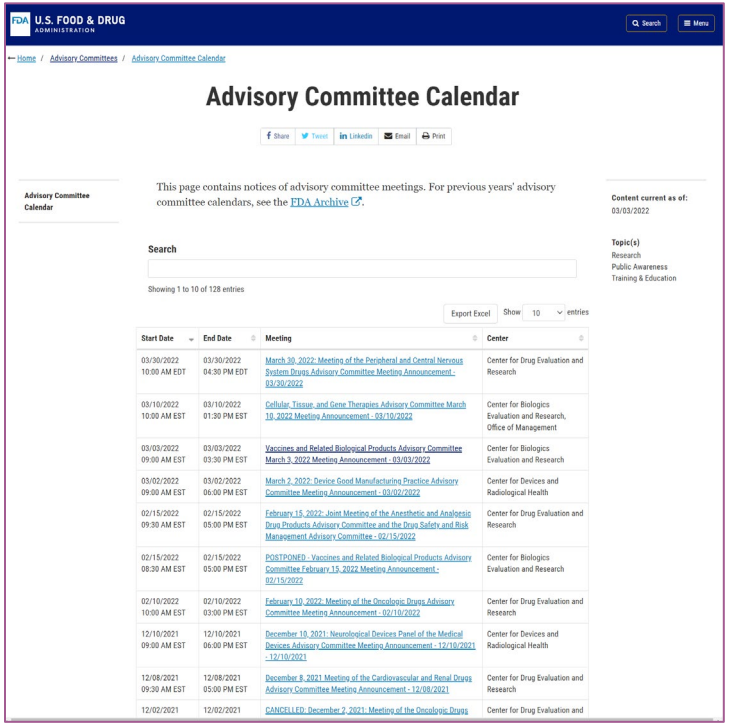
Showing 1 to 10 of 24 entries

Export Excel Show 10 entries

| Start Date | End Date | Event | Event type | Center |
|---|---|---|---|---|
| 03/03/2022 | 03/03/2022 | Vaccines and Related Biological Products Advisory Committee March 3, 2022 Meeting Announcement | Advisory Committee Meeting | Center for Biologics Evaluation and Research |
| 03/04/2022 | 03/04/2022 | Public Meeting: FDA Rare Disease Day 2022 | Meeting | Office of the Commissioner |
| 03/07/2022 | 03/09/2022 | FDA, MHRA, and Health Canada Good Clinical Practice Workshop: Global Clinical Trials - Considerations and Lessons Learned from the Changing Landscape (2022) | Virtual | Center for Drug Evaluation and Research |
| 03/07/2022 | 03/10/2022 | 46th International Good Manufacturing Practices Conference | Virtual | Office of Regulatory Affairs, Center for Drug Evaluation and Research |
| 03/08/2022 | 03/08/2022 | Race & Genetic Ancestry in Medicine. A Time for Reckoning Racism | Webcast | Office of the Commissioner |
| 03/09/2022 | 03/09/2022 | RegenMedEd Webinar: The Critical Role of Patients in Advancing Gene Therapy Treatments for Rare Diseases | Workshop | Center for Biologics Evaluation and Research |

# Advisory Committee Meetings



# Citizen Petitions

An opportunity for interested parties to initiate an administrative proceeding by petitioning FDA to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action.

*21 C.F.R. § 10.25(a)*

# Prescription Drug User Fee Act (PDUFA) and Biosimilar User Fee Act (BsUFA) negotiations

**PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2018 THROUGH 2022**



**BIOSIMILAR BIOLOGICAL PRODUCT REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2023 THROUGH 2027**

# Judicial Review & Lobbying Congress

# Product Specific Proceedings

# Dispute Resolutions; Appeals

- Adjudicative process for resolving disputes that arise during the course of regulatory proceedings.
  - Request review of a disputed issue by the immediate supervisor, and up the chain of command.
  - Request review by the appropriate advisory committee.

# Ombudsman

## FDA's Office of the Ombudsman

Assisting in resolving disputes between companies or individuals and FDA offices.


### Who We Are, What We Do

An ombudsman is someone who looks into and addresses complaints and disputes involving an organization. But the role of the ombudsman here at the Food and Drug Administration (FDA) involves much more.

FDA's ombudsman function is handled at two levels:

- a separate office within the Office of the Commissioner (FDA Office of the Ombudsman)
- designated ombudsmen within specific product centers (drugs, devices, biologics, tobacco) and office of regulatory affairs

Companies can turn to the FDA Office of the Ombudsman for:

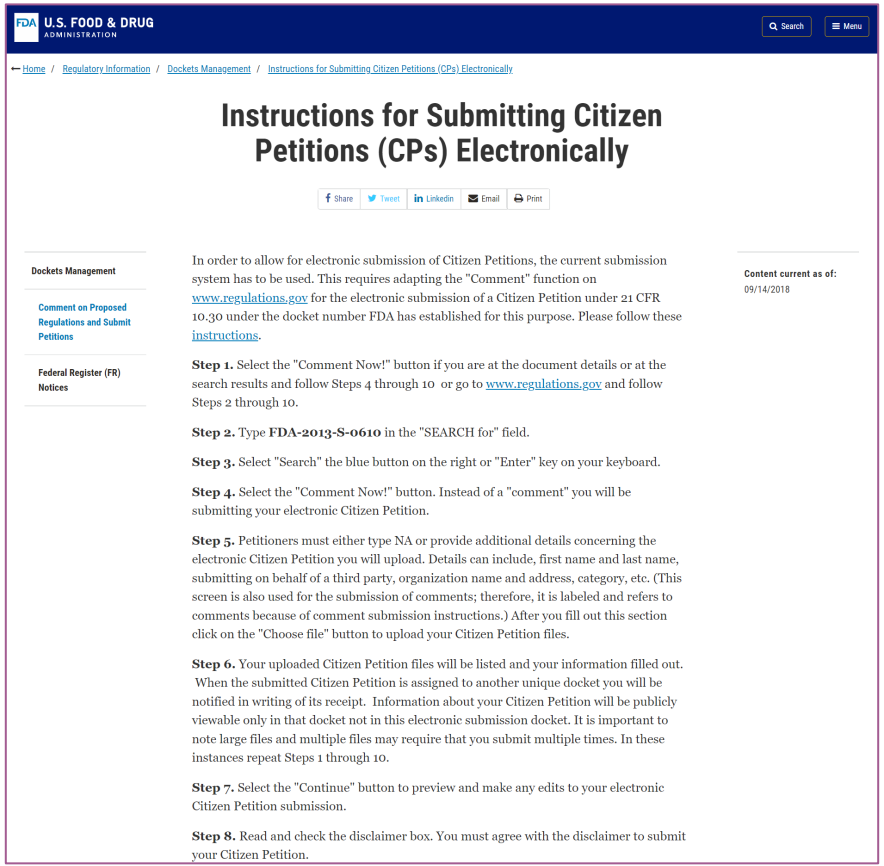
- dispute resolution
- mediation
- breaking up "log jams" with the agency
- guidance and assistance in solving problems with the agency or with FDA-regulated products
- general regulatory questions or concerns

### Cases We Handle

The following types of cases are routinely handled by the FDA Office of the Ombudsman:

- Disputes from regulated industry regarding agency product center actions, or lack of action, and those issues that cut across center jurisdictions
- Disputes from regulated industry related to interactions with agency field offices, including inspection and compliance issues
- Concerns from small businesses, including those referred by the U.S. Small Business Administration
- Inquiries about the agency's handling of Freedom of

# Citizen Petitions



U.S. FOOD & DRUG ADMINISTRATION

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## Instructions for Submitting Citizen Petitions (CPs) Electronically

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Dockets Management

Comment on Proposed Regulations and Submit Petitions

Federal Register (FR) Notices

In order to allow for electronic submission of Citizen Petitions, the current submission system has to be used. This requires adapting the "Comment" function on www.regulations.gov for the electronic submission of a Citizen Petition under 21 CFR 10.30 under the docket number FDA has established for this purpose. Please follow these instructions.

**Step 1.** Select the "Comment Now!" button if you are at the document details or at the search results and follow Steps 4 through 10 or go to www.regulations.gov and follow Steps 2 through 10.

**Step 2.** Type **FDA-2013-S-0610** in the "SEARCH for" field.

**Step 3.** Select "Search" the blue button on the right or "Enter" key on your keyboard.

**Step 4.** Select the "Comment Now!" button. Instead of a "comment" you will be submitting your electronic Citizen Petition.

**Step 5.** Petitioners must either type NA or provide additional details concerning the electronic Citizen Petition you will upload. Details can include, first name and last name, submitting on behalf of a third party, organization name and address, category, etc. (This screen is also used for the submission of comments; therefore, it is labeled and refers to comments because of comment submission instructions.) After you fill out this section click on the "Choose file" button to upload your Citizen Petition files.

**Step 6.** Your uploaded Citizen Petition files will be listed and your information filled out. When the submitted Citizen Petition is assigned to another unique docket you will be notified in writing of its receipt. Information about your Citizen Petition will be publicly viewable only in that docket not in this electronic submission docket. It is important to note large files and multiple files may require that you submit multiple times. In these instances repeat Steps 1 through 10.

**Step 7.** Select the "Continue" button to preview and make any edits to your electronic Citizen Petition submission.

**Step 8.** Read and check the disclaimer box. You must agree with the disclaimer to submit your Citizen Petition.

**Content current as of:**
09/14/2018

# Regulatory Hearings

- Formal Evidentiary Public Hearing (21 C.F.R. Part 12)
- Public Hearing Before a Board of Inquiry (21 C.F.R. Part 13)
- Public Hearing Before a Public Advisory Committee (21 C.F.R. Part 14)
- Public Hearing Before the FDA Commissioner (21 C.F.R. Part 15)
- Regulatory Hearing Before the FDA (21 C.F.R. Part 16)

# Formal Adjudications

- An “adjudication” is the process by which an agency formulates an “order” meaning the “final disposition, whether affirmative, negative, injunctive, or declaratory in form, of an agency in a matter other than rule making but including licensing.” (5 U.S.C. § 551(6) & (7))
- Adjudication results in an order that usually applies to a specific entity or set of facts.
- Formal adjudication refer to statutorily-mandated proceedings (e.g., review and approval of a New Drug Application)

# Judicial Review

- The Administrative Procedure Act provides the right to court review of "final" agency decisions, based on the "administrative record" before the agency.
- Pursuant to Section 706(2), federal courts may hold unlawful and set aside agency action, findings, and conclusions found to be, among other things:
  - Arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, contrary to constitutional right, power, privilege, or immunity.
  - In excess of statutory jurisdiction, authority, or limitations, or short of statutory right, or
  - Without observance of procedure required by law.

# Obtaining and Protecting Information under the Freedom of Information Act (FOIA)

# Disclosable Information

FOIA allows members of the public to request access to records that FDA normally does not post publicly.

# Exemptions from Mandatory Disclosure

There exist 9 statutory exemptions from disclosure, including:

#4: Trade secret or confidential commercial or financial information

#5: Privileged inter- or intra-agency communication

#6: Individual personal privacy

#7(a): Interfere with enforcement proceedings

# Discretionary Disclosure on Request

- Federal agencies generally have discretion under FOIA to decide whether to invoke the applicable FOIA exemptions. FOIA exemptions are not "mandatory bars to disclosure."
- However, other considerations exist, such as applicability of the Trade Secrets Act for "business" information.

# Preventing Disclosure of Information Submitted to FDA

- FDA is required to notify a party of a FOIA request (21 C.F.R. § 20.61).
- The party has 5 days to object to disclosure.
- If FDA decides to disclosure, FDA must give notice to the party.
- The party may then bring a “Reverse FOIA” case in district court to seek relief from disclosure.

# Thank you

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