CHAPTER 2 - REGULATORY

2.1 – Purpose

This chapter provides you with the statutory and regulatory frameworks and additional information related to your work. It summarizes authorities for inspections; sample collections; advisory, administrative, and judicial actions and discusses your distinct role in these activities. This chapter also includes information on certain regulatory submissions for FDA-regulated products. The Regulatory Procedures Manual (RPM) is the field reference containing specific internal procedures and other guidance related to the work of compliance officers. (You may want to review pertinent sections of the RPM while reading this chapter.)

2.2 – Statutory Authority

Various acts specify the authorities granted to the Secretary of the Department of Health and Human Services (DHHS). This authority is delegated to the commissioner of Food and Drugs, and certain authorities are delegated further by him or her. See Staff Manual Guides, Delegations of Authority, Volume II (1400) for more information.

2.2.1 – Federal Food, Drug, and Cosmetic (FD&C) Act

This act, as amended, and its regulations provide the basic authority for most operations. (Note: Section 2.5.11.1 of this chapter describes authority to detain products under the FD&C Act.)

2.2.1.1 – Selected Amendments to the FD&C Act

The amendments to the FD&C Act are summarized in RPM Chapter 2-2. (https://www.fda.gov/media/77516/download).

2.2.2 – Authority to Sample

Collecting samples is a critical part of the FDA's regulatory activities. Section 702 of the FD&C Act [21 U.S.C. 372(a)] gives the FDA authority to conduct investigations and collect samples. An FDA-482 Notice of Inspection is not always required for sample collections. However, if during a sample collection, you see a need to conduct an inspection and conduct activities, (e.g., examining storage conditions, reviewing records for compliance with laws and regulations, etc.), immediately issue an FDA-482 before continuing your activities. (See IOM 5.1.3.) Sampling authority for biological products that are also drugs is found in both the FD&C Act and the Public Health Service (PHS) Act.

Section 702(b) of the FD&C Act [21 USC 372(b)] requires the FDA to furnish, upon request, a portion of an official sample for examination or analysis to any person named on the label of an article, the owner thereof, or his attorney or agent.

In a precedent case, *United States v. 75 Cases, More or Less, Each Containing 24 Jars of Peanut Butter*, the U.S. Circuit Court of Appeals for the Fourth Circuit held that the taking of samples is authorized under section 702(b) of the FD&C Act [21 U.S.C. 372(b)], since this section *"clearly contemplates the taking of samples."* Sections 704(c) and 704(d) [21 USC 374(c) and 374(d)] also imply an authority to collect samples.

2.2.3 – Authority to Inspect

Section 704 of the FD&C Act [21 U.S.C. 374] provides the basic authority for establishment inspections. This authorizes you, upon presenting appropriate credentials and a written notice (FDA-482, Notice of Inspection), to enter and to inspect at reasonable times, within reasonable limits, and in a reasonable manner, establishments or vehicles being used to process, hold, or transport food, drugs, devices, tobacco products, or cosmetics, for introduction into or in interstate commerce. The statute does not define, in specific terms, the meaning of "reasonable." FDA's establishment inspection procedures maintain this authority extends to what is reasonably necessary to achieve the objective of the inspection.

2.2.3.1 – Food Inspections

Authority to inspect food facilities resides in the general inspectional authority of Section 704 of the FD&C Act [21 U.S.C. 374].

Section 306 of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 ("the Bioterrorism Act") (PL 107-188), created Section 414, “Maintenance and Inspection of Records” in the FD&C Act [21 U.S.C. 350c]. Under this authority, the Secretary may by regulation establish requirements for persons (excluding farms and restaurants) who manufacture, process, pack, transport, distribute, receive, hold, or import food to establish and maintain food records. These records identify the immediate previous sources and the immediate subsequent recipients of food.

In addition, Section 414(a)(1), "Records Inspection," and section 704(a)(1), "Factory Inspection," authorize the Secretary to access and copy all records related to an article of food if: (1) the Secretary has a reasonable belief that an article of food, and any other article of food that the Secretary reasonably believes is likely to be affected in a similar manner, is adulterated and presents a threat of *serious adverse health consequences or death to humans or animals* (SAHCODHA), and (2) the records are necessary to assist the Secretary in making such a determination.

Under Section 414(a)(2), FDA can also access and copy all records related to an article of food if the FDA believes that there is a reasonable probability that the use of, or exposure to, an article of food, and any other article of food that the FDA reasonably believes is likely to be affected in a similar manner, will cause SAHCODHA. The FDA may carry out its authority to inspect all records and other information described in Section 414 in a similar manner as FDA’s authority to perform inspections of facilities (i.e., upon presentation of appropriate credentials and a written notice at reasonable times, within reasonable limits, and a reasonable manner). FDA employees will not invoke this authority during inspections unless the requirements for record access under the Bioterrorism Act are satisfied. Further guidance is available at https://www.fda.gov/food/guidance-documents-regulatory-information-topic-food-and-dietary-supplements/food-defense-guidance-documents-regulatory-information.

The Infant Formula Act of 1980 added new authority to the FD&C Act. Section 412 of the FD&C Act [21 U.S.C. 350a] extends the definition of adulteration to include specific nutritional, quality, and good manufacturing control requirements. Section 412 also mandates a firm make available batch records, quality control records, nutrient test data and methodology, and similar documents for examination and copying. See 21 CFR 106.100 for regulations on infant formula records. Section 704(a)(3) of the FD&C Act [21 U.S.C. 374(a)(3)] gives investigators the right to examine and copy these records.

Section 361(a) of Part G of the PHS Act [42 U.S.C. 264(a)] authorizes the FDA to make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases. FDA regulations at 21 CFR Part 1240, Control of Communicable Diseases, and 21 CFR Part 1250, Interstate Conveyance Sanitation, authorizes inspection, among other measures, to prevent the introduction, transmission, or spread of communicable diseases. This includes investigation of any disease outbreak (not just foodborne) aboard US-flagged vessels (see IOM 8.2.2.3). These regulations also cover the mandatory pasteurization for all milk in final package form intended for direct human consumption; the safety of molluscan shellfish; the sanitation of food service; and food, water, and sanitary facilities for interstate travelers on common carriers.

2.2.3.2 – Drug Inspections

In the case of drug inspections, FDA has explicit authority to address the delay, denial, limiting, or refusal of an inspection, under section 707 of the Food and Drug Administration Safety and Innovation Act (FDASIA), which created Section 501(j) of the FD&C Act [21 U.S.C. 351(j)]. Section 501(j) deems adulterated any drug that is manufactured in an establishment that delays, limits, denies, or refuses to permit entry or inspection. FDA has issued Guidance for Industry with examples of the types of conduct that the FDA considers to be in violation of section 501(j) of the FD&C Act. This guidance also specifies that under certain circumstances, delaying, denying, limiting, or refusing a request for records in advance of or in lieu of an inspection under Section 707 of FDASIA may also result in a manufacturer's drugs being deemed adulterated under the FD&C Act.

2.2.3.3 – Device Inspections

Section 704(a) of the FD&C Act [21 U.S.C. 374(a)] provides the general inspectional authority to inspect medical device manufacturers. The Medical Device Amendments of 1976 provide additional authority to inspect records, files, papers, processes, controls, and facilities to determine whether restricted devices are adulterated or misbranded. The amendments also provide FDA authority, under Section 704(e) [21 U.S.C. 374(e)], to inspect and copy records required under Section 519 or 520(g) of the FD&C Act [21 U.S.C. 360i or 360j(g)]. Section 501(j) of the FD&C Act [21 U.S.C. 351(j)], discussed above in 2.2.3.2 – Drug Inspections, also applies to devices, pursuant to the FDA Reauthorization Act (FDARA) of 2017. Section 704(h)(1) added additional requirements for investigators for inspections of device establishments. These requirements include: pre-announcing the inspection and communication; inspection timeframes; and communication during the inspection. See Guidance Document - Review and Update of Device Establishment Inspection Process and Standards.

2.2.3.4 – Electronic Product Radiation Controls (EPRC) - Examinations and Inspections

The authority for obtaining samples of radiation-emitting electronic products for testing is provided in Section 532(b)(4) of the FD&C Act [21 U.S.C. 360ii(b)(4)].

The authority to inspect factories, warehouses, and establishments wherein electronic products are manufactured or held is provided in Section 537(a) of the FD&C Act [21 U.S.C. 360nn(a)]. This authority is limited. The FDA must find "good cause" that methods, tests, or programs related to radiation safety (such as noncompliance with a standard) may be inadequate or unreliable. If there is no finding of "good cause," inspections must be voluntary unless another authority applies, such as Section 704(a) of the FD&C Act [21 U.S.C. 374(a)] for medical devices. The authority to inspect books, papers, records, and documents relevant to determining compliance with radiation standards is provided in Section 537(b) of the FD&C Act [21 U.S.C. 360nn(b)]. The Electronic Products Radiation Control (EPRC) prohibited acts and enforcement authorities are specified in Sections 538 and 539 of the FD&C Act [21 U.S.C. 360oo and 360pp].

2.2.3.5 – Biologics Inspections

Section 351 of the PHS Act [42 U.S.C. 262] contains provisions for the regulation of biological products. A biological product, as defined in Section 351(i) of the PHS Act [42 U.S.C. 262(i)], also meets the definition of a "drug" or a “device” in Section 201 of the FD&C Act [21 U.S.C. 321]. Section 704 of the FD&C Act [21 U.S.C. 374] and Section 351(c) of the PHS Act [42 U.S.C. 262(c)] authorize the agency to inspect establishments that manufacture biological products. Additionally, Section 510(h) of the FD&C Act [21 U.S.C. 360(h)] applies to biological product establishments because all biological products are also subject to regulation under the drug or device provisions of the FD&C Act. See 21 CFR Part 600, Subpart C for regulations on establishment inspections for biological products.

Section 361(a) of Part G of the PHS Act [42 U.S.C. 264(a)] authorizes inspection and other activities for the enforcement of 21 CFR Part 1270, Human Tissue Intended for Transplantation.

2.2.3.6 – Tobacco Inspections

The Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) of 2009 gives the agency broad authority to regulate the manufacturing, distribution, and marketing of tobacco products. The Tobacco Control Act added Section 905 to the FD&C Act [21 U.S.C. 387e]. Pursuant to Section 905(g) to the FD&C Act [21 U.S.C. 387e(g)], establishments registered under this section shall be subject to inspection under Section 704 of the FD&C Act [21 U.S.C. 374] or 905(h) of the FD&C Act [21 U.S.C. 387e(h)]. See 21 CFR 1107.58 (effective November 4, 2021) for regulations related to certain records that must be available for inspection and copying by duly designated officers or employees.

2.2.3.7 – Bioresearch Monitoring (BIMO) Inspections

Inspectional activities in the Bioresearch Monitoring (BIMO) program involve all product areas and centers. See IOM section 5.14 for BIMO establishment types. In general, the, basic authority for establishment inspections is found in Section 704 of the FD&C Act [21 U.S.C. 374]. Authority for BIMO inspections is detailed in section 704(a)(5) of the FD&C Act [21 U.S.C. 374(a)(5)].

FDA's BIMO program covers Good Laboratory Practices (GLP) (Nonclinical Laboratories) inspections, which includes inspection collaborations between FDA and Environmental Protection Agency (EPA) under the GLP program. As is described in CP 7348.808A, FDA may conduct data audits for EPA under authority delegated from EPA to review records under Sections 8 and 22 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA; 7 U.S.C. 136 et seq.) and/or under Sections 9 and 11 of the Toxic Substances Control Act (TSCA; 15 U.S.C. 2601 et seq.). That understanding is described in an interagency agreement between FDA and EPA. BIMO investigators conducting data audits pursuant to EPA's authority will receive documentation of the delegation of authority from EPA in a "Letter of Entry."]

2.2.4 – Limitations

Section 704(a)(1) of the FD&C Act [21 U.S.C. 374] provides authority for FDA to conduct inspections of factories, warehouses, and establishments in which food, drugs, devices, tobacco products, or cosmetics are manufactured, processed, packed or held, and vehicles being used to transport or hold such food, drugs, devices, tobacco products, or cosmetics, and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. This section does not include a provision to inspect records within those facilities, except for inspections of foods, prescription drugs, nonprescription drugs intended for human use, and restricted devices, or tobacco products, as stipulated in Section 704(a)(1)(B) [21 U.S.C. 374(a)(1)(B)], or inspections of infant formula described in Section 704(a)(3) of the FD&C Act [21 U.S.C. 374(a)(3)].

Keep in mind that several other sections of the act or of regulations also include provisions for inspections and copying of required records. For example, 505(k) provides authority to access and copy records required for new drug applications and abbreviated new drug applications; 512(k)(2) and 512(m)(5) of the FD&C Act [21 U.S.C. 360b(k)(2) and 360b(m)(5)] provide access and copying of records regarding new animal drug and medicated feed permits; HACCP regulations in 21 CFR 123 for fish and fishery products provide for access and copying of required records; and 920(c) provides access, with written notice, to records for investigating potential illicit trade, smuggling, or counterfeiting of tobacco products.

Some firms will allow access to files and other materials for which the FD&C Act does not give mandatory access but retain the right to later refuse. Firm management may propose the following alternatives:

- Inspections to obtain data from these files be made without issuing an FDA-482, Notice of Inspection. You cannot agree to this because the act requires the notice be issued before the inspection.
- When data is provided, you are advised in writing it is being given voluntarily. In this instance accept the written or oral statement and include it as part of the Establishment Inspection Report (EIR).

Firm management may also insist answers to specific questions be provided by the firm's legal department or other administrative officers. In some instances, management may request questions be submitted in writing. Only submit lists of questions if you are specifically instructed to do so by your supervisor.

2.2.5 - Remote Regulatory Assessments (RRAs)

Remote Regulatory Assessments (RRAs) are examinations of an FDA-regulated establishment and/or its records, conducted entirely remotely, to evaluate compliance with applicable FDA requirements. RRAs assist in protecting human and animal health, informing regulatory decisions, prioritizing regulatory activities, and verifying certain information submitted to the Agency. RRAs complement FDA's authority to conduct inspections under section 704(a)(1) of the FD&C Act and other applicable FDA authorities but are not themselves inspections.

Programs across FDA have differing remote regulatory authorities, making participation in RRAs by FDA-regulated establishments either mandatory or voluntary depending on the program and authority.

For more information about RRAs (both mandatory and voluntary RRAs), please refer to the RRA Staff Manual Guide (SMG 6001.1).

The RRA SMG serves as a reference document that includes but is not limited to RRA:

- Purpose, background, scope
- Responsibilities
- Procedures (e.g., selecting, planning, conducting, reporting)

Different programs across the FDA have more specific procedural information that can be accessed through the FDA Remote Regulatory Assessment (RRA) SharePoint Page. Please reach out to your specific program contact(s) as needed for more information.

2.2.6 – Other Acts

See IOM 2.2.10 and IOM 3.2.1.3 for special authorities involving detentions under the Federal Meat Inspection, Poultry Products Inspection, and Egg Products Inspection Acts.

See RPM Chapter 2-2 for selected amendments to the FD&C Act and RPM Chapter 2-3 for other laws. The laws listed below are not referenced in the RPM.

2.2.5.1 - Anabolic Steroids Control Act of 1990

The Anabolic Steroids Control Act amends the Controlled Substances Act by adding Anabolic Steroids to Schedule III of Section 202(c).

2.2.5.2 - Federal Caustic Poison Act

This is primarily a labeling act specifying warnings and precautionary statements required on labeling of certain household caustic preparations.

2.2.3.3 - Poison Prevention Packaging Act

This act provides for special packaging to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting household substances.

2.3 - Evidence

Evidence is quite simply information. While you are out conducting inspections, collecting samples, or conducting other operations, you will be gathering and collecting information or evidence. Evidence is used in judicial cases to show the facts of a matter that is in dispute.

2.3.1 – JIVR (See IOM 4.4.3)

JIVR is an acronym that stands for jurisdiction, interstate commerce, violation(s), and responsibility. It is not a legal term but used within the agency to describe the elements for evidence needed for most charges used by FDA against person(s) as defined by FD&C Act section 201(e).

2.3.1.1 - Jurisdiction

Jurisdiction is the power, right, or authority to interpret and apply the law. Jurisdiction is not defined in the FD&C Act; however, FDA's jurisdiction over a subject (e.g., a product) is determined by acts that the FDA is charged to enforce. In the context of JIVR, jurisdiction is shorthand for evidence that the product is regulated by FDA based on the definitions found in Section 201 of the FD&C Act. See also What does FDA regulate? Exhibit 3-1 in the IOM describes the separation of jurisdiction for foods between FDA and the United States Department of Agriculture (USDA). Exhibit 2-1 contains the definitions of the various commodities and programs that the FDA regulates.

2.3.1.2 – Interstate Commerce

Interstate commerce is an interchange of goods or commodities between one state or territory and any place outside thereof, or commerce within the District of Columbia or within any other territory. Section 201(b) of the Act.

2.3.1.3 – Violation

A violation is an illegal condition (a condition that is contrary to a statute). The most common FD&C Act violations include adulteration and/or misbranding.

2.3.1.4 – Responsibility

Responsibility refers to those who are legally responsible for the violation and who could be named as defendants in a judicial action. There are two types of responsible persons: those who directly perform or cause a prohibited act (see Section 301 of the FD&C Act) and those who have the responsibility and authority either to prevent in the first instance, or promptly to correct, the violation as a result of their position (see U.S. v. Dotterweich and U.S. v. Park). Section 201(e) of the FD&C Act broadly defines the term “person" to include an individual, partnership, corporation, and association.

2.3.2 – Presumption of Regularity

The presumption of regularity is founded on the common-sense idea that courts should assume that government officials “have properly discharged their official duties.” United States v. Chem. Found., Inc., 272 U.S. 1, 15 (1926). The presumption began as a way of filling in minor evidentiary gaps, usually related to procedural or technical formalities. Historically, the same presumption of normality and regularity applied to private parties and corporate officers, as well as to government officials. For example, if a copy of a document with a corporate seal was filed, a court would presume it was an official corporate seal issued by an authorized party unless someone submitted evidence to the contrary. Today, consistent with its historical origins, the presumption serves as a “general working principle” that means courts will “insist on a meaningful evidentiary showing” before entertaining doubts about the integrity of official acts or documents. (National Archives & Records Admin. v. Favish, 541 U.S. 157, 174 (2004))

Presumption of regularity is demonstrated when you follow established procedures in the IOM and other guidance documents.

2.4- Advisory Actions and Other Notices of Violations

Prior Notice means that under most circumstances and consistent with its public protection responsibilities, the FDA will notify or advise persons of violations that appear to exist. In cases of violations of regulatory significance, failure to comply with this notice or advisement may result in the initiation of enforcement action. This affords individuals and firms an opportunity to voluntarily take appropriate and prompt corrective action.

When it is consistent with the public protection responsibilities of the agency, and depending on the nature of the violation, it is the FDA's practice to give individuals and firms an opportunity to take voluntary and prompt corrective action before it initiates an enforcement action.

The FDA is under no legal obligation to provide Prior Notice to individuals or firms before taking enforcement action, except in a few specifically defined areas.

Prior Notice, including exceptions to the practice, is discussed in RPM Chapter 10 - Other Procedures.

2.4.1 - Warning Letters

A Warning Letter is informal and advisory. It communicates the agency's position on a matter, but it does not commit FDA to taking enforcement action. For these reasons, FDA does not consider Warning Letters to be final agency action.

As stated in RPM Chapter 4, Warning Letters are issued to achieve voluntary compliance and to establish Prior Notice. The use of Warning Letters and Prior Notice are based on the expectation that most individuals and firms will voluntarily comply with the law.

The agency's position is that Warning Letters are issued only for violations of regulatory significance that may lead to enforcement action if not promptly and adequately corrected.

See Field Alert 40 (https://fda.sharepoint.com/sites/insideFDA-ORA/Shared Documents/Forms/AllItems.aspx?id=%2Fsites%2FinsideFDA-ORA%2FShared Documents%2FField Investigations%2FField Alerts%2FField Alert 40%2Epdf&parent=%2Fsites%2FinsideFDA-ORA%2FShared Documents%2FField Investigations%2FField Alerts) for information related to interstate commerce documents necessary for a Warning Letter.
There are instances when issuing a Warning Letter is not appropriate, and as previously stated, a Warning Letter is not a prerequisite to taking enforcement action. RPM Chapter 4 (Section 4.-1-1) describes in detail the situations in which the agency will take enforcement action without necessarily issuing a Warning Letter.

2.4.2 - Untitled Letters

An Untitled Letter cites violations that do not meet the threshold for regulatory significance for a Warning Letter. However, it still serves provides prior notice by advising the firm about these violations. Therefore, the format and content of an Untitled Letter should clearly distinguish it from a Warning Letter.

2.4.3 - Regulatory Meetings

A regulatory meeting is a meeting requested by FDA management, at its discretion, to inform responsible individuals or firms about products, practices, processes, or other activities that are in violation of the law. (See RPM Chapter 10.)

Regulatory meetings can be an effective enforcement tool to obtain prompt voluntary compliance and have been used successfully in a variety of different situations.

2.5 - Administrative Actions

Administrative actions are actions that the FDA may take without going through judicial review. The various acts that the FDA enforces provide authority for these actions and specific regulations further explained the regulations. (Chapter 5 of the RPM covers administrative actions in detail.)

2.5.1 - Section 305 Notice/Meeting

The Section 305 Notice is a statutory requirement of the FD&C Act. It provides a respondent with an opportunity to explain why they should not be prosecuted for the alleged violation. Response to the notice may be by letter, personal appearance, or attorney. ORA management must communicate with the local OCI office before pursuing any criminal matter (see RPM 6-5-1).

Under certain circumstances, the agency will refer prosecution (or for further investigation) without first providing the opportunity for presentation of views in accordance with Section 305 [See 21 CFR 7.84(a)(2) and (3)].

2.5.2 - Civil Money Penalties (CMP)

The Civil Money Penalties (CMPs) are monetary penalties that are assessed by the FDA for violations of the FD&C Act or the PHS Act. CMPs are authorized under the FD&C and PHS Acts.

2.5.3 – No-Tobacco-Sale Orders

A No-Tobacco-Sale Order (NTSO) may be pursued against retailers that have a total of five or more repeated violations of certain restrictions within 36 months. Retailers are prohibited from selling regulated tobacco products at the specified locations during the period of the NTSO.

2.5.4 – Disqualification of Clinical Investigators

The FDA may preclude a clinical investigator from receiving investigational drugs, biologics, or devices, and deem them ineligible to conduct any clinical investigation that supports an application for a research or marketing permit for products regulated by FDA. A clinical investigator can be disqualified if they have repeatedly, or deliberately, failed to comply with applicable regulatory requirements, or they have repeatedly, or deliberately, submitted false information to the sponsor or, if applicable, to the FDA, in any required report.

Subchapters 5-10 of the RPM, titled, “Disqualification of Clinical Investigators,” describes the process, including timeframes, for initiating disqualification proceedings – from completion of the inspection to issuance of the Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE) to the clinical investigator.

Criteria for initiation of disqualification proceedings are included in the Compliance Program Guidance Manual (CPGM) 7348.811 for Bioresearch Monitoring: Clinical Investigators, Part V. B.

2.5.5 - Importer Debarment

Importer Debarment is an action taken by the FDA, on the basis of a criminal conviction or conduct, as identified in Sections 306 (b)(3)(A) or (B) of the act, to prohibit an individual, corporation, partnership, or association from:

- Submitting, or assisting in the submission of, certain drug applications or, in the case of individuals only, providing services in any capacity to the sponsor of an approved or pending drug application;
- Importing or offering for import an article of food into the United States;
- Importing or offering for import a drug article into the United States; or
- Being accredited to perform certain functions related to devices through programs administered by the FDA, by other government agencies, or by other qualified nongovernment organizations; and from carrying out activities under agreements with foreign countries to facilitate commerce in devices.

If you observe conduct, or receive an oral or written notice, indicating that a person is violating an active debarment order, please notify your supervisor so that appropriate action can be taken as prescribed in Staff Manual Guide (SMG) 7712 (https://www.fda.gov/media/80036/download). The current FDA debarment list is located on the following agency web page (check both the main list and the updates to the list for the most recent additions): https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/fda-debarment-list-drug-product-applications/fda-debarment-list-updates.

2.5.6 - Food Facility Suspension of Registration (Section 415(b))

The FDA can suspend registration of a facility if it determines that the food produced, processed, packed, received, or held at such facility poses a reasonable probability of serious adverse health consequences or death. A facility that is under suspension is prohibited from distributing food.

Section 415(b) of the FD&C Act, as amended by the Food Safety Modernization Act (FSMA) on January 4, 2011, provides that the FDA may suspend the registration of a food facility if the agency determines that food manufactured, processed, packed, received, or held by a registered facility has a reasonable probability of causing serious adverse health consequences or death to humans or animals. FDA may by order suspend the registration of a facility that:

- Created, caused, or was otherwise responsible for such reasonable probability; or
- Knew of, or had reason to know of, such reasonable probability; and packed, received, or held such food.

2.5.7 - Emergency Permit Control

The commissioner can issue an emergency permit for a temporary period as necessary to protect public health.

Section 404 of the FD&C Act [21 U.S.C. 344] provides for the issuance of temporary permits prescribing the conditions governing the manufacture, processing, or packing of any class of food by reason of

contamination with injurious microorganisms, where such contamination cannot be adequately determined after such articles have entered interstate commerce.

2.5.8 - Mandatory Recall

FDA's mandatory food recall authority was included in the FSMA. The authority allows the FDA to order a responsible party to recall an article of food wherein the FDA determines that there is a reasonable probability that the article of food (other than infant formula) is adulterated under Section 402 of the FD&C Act [21 U.S.C. § 342] or misbranded under Section 403(w) of the FD&C Act [21 U.S.C. § 343(w)] and that the use of or exposure to such article will cause SAHCODHA. Applicable evidence will be evaluated when determining whether there is reasonable probability the adulterated or misbranded food will cause SAHCODHA. See RPM 7-5-3 and Attachment J.

2.5.9 - License Revocation or Suspension

Biologics licenses issued under the PHS Act [42 U.S.C. 264] can be revoked or suspended. Revocation will cancel the firm's license, and without such license, the firm is no longer authorized to introduce, or deliver for introduction, biological products into interstate commerce. If biological products are believed to pose an immediate danger to public health, the Center for Biologics Evaluation and Research (CBER) can place a "suspension" on a biological firm's license. Suspension provides an immediate pause to the introduction, or delivery for introduction, of biological products into interstate commerce. A suspension summary action can be an initial step or an intermediate step to license revocation.

When the license relates to multiple locations, revocation may be limited to one or more of the locations if inspectional findings support that approach. The agency may consider revocation of a biologic license when any of the conditions specified in 21 CFR 601.5 exist. If conditions are met, the agency can either issue a Notice of Intent to Revoke, or Direct Revocation. The Notice of Intent to Revoke provides the license holder an opportunity to address or become compliant before the agency proceeds with the revocation. In cases where willful conduct is involved, the agency can directly revoke a firm's license without providing an opportunity to address compliance status prior to proceeding with the revocation.

Detailed information on these Administrative Actions can be found in Chapter 5 of the RPM in section 5-7.

2.5.10 - Orders of Retention, Recall, or Destruction and Cessation of Manufacturing Related to Human Cell, Tissue and Cellular and Tissue-Based Products (HCT/Ps)

An Order of Retention, Recall, or Destruction of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) may be appropriate in situations where there are significant concerns regarding the source or violative nature of the HCT/P, the adequacy of the screening and/or testing, or a failure of the establishment to fulfill stated commitments to gain control over violative HCT/Ps. The agency may order the retention, recall, and/or destruction of the violative HCT/P; take possession of and/or destroy the

violative HCT/Ps; or order the establishment to cease manufacture until compliance with Part 1271 has been achieved.

Consumer safety officers (CSO) should contact their supervisor if there are significant concerns while an inspection is open and should not wait until the inspection has been completed. The CSO, in conjunction with their supervisor, should ensure that all documentation supporting the violative condition is collected.

An Order of Cessation of Manufacturing may be appropriate in situations where there are significant concerns regarding one or more steps in the manufacture of HCT/Ps, or a failure of the establishment to fulfill stated commitments to gain control over or to bring the areas of manufacturing into compliance with the applicable regulations. During the inspection, if it is determined that an Order of Cessation of Manufacturing is necessary to prevent a potential danger to health, the investigator should collect complete documentation of the violative conditions, including an inventory of products on the premises as of the last day of the inspection. Refer to RPM Subchapter 5-8 "Orders of Retention, Recall, Destruction and Cessation of Manufacturing Related to Human Cells, Tissue, and Cellular and Tissue-Based Products (HCT/Ps)," for procedural instructions for issuance of an order.

2.5.11 - Detention Powers and Criteria for Detention

Detention is an administrative action which protects the public by preventing movement in interstate or intrastate commerce of a food, device, drug, or tobacco product that an authorized FDA representative has reason to believe is adulterated or misbranded, while the agency institutes appropriate action (e.g., seizure or injunction). Import detention is covered separately in IOM Chapter 6 - Imports.

2.5.11.1 – Federal Food, Drug and Cosmetic Act (FD&C Act)

Section 304(g) of the FD&C Act provides the FDA with authority to detain foods, devices, drugs, or tobacco products believed to be adulterated or misbranded. The products may be detained for a reasonable period, not to exceed 20 days, unless extended to no more than 30 days as necessary to institute appropriate action (e.g., seizure or injunction). You should become familiar with this section and the regulations implementing this authority. See 21 CFR 800.55 and 21 CFR 1.980. At present time, the device regulations apply only to devices intended for human use. See FD&C Act section 304(g) [21 U.S.C. 334 (g)].

Section 304(h) of the FD&C Act provides the FDA with the authority to order the administrative detention of any article of food that is found during an inspection, examination, or investigation under the FD&C Act, if FDA has reason to believe that such article is adulterated or misbranded. Become familiar with this section of the FD&C Act and the implementing regulations in 21 CFR Part 1, Subpart K. The FDA's administrative detention authority applies to both food offered for import and food in domestic commerce. FDA's authority to administratively detain food under Section 304(h) is separate and distinct from FDA's authority to refuse admission of imported food under section 801[8](a).

The authority to detain drugs can be found in Section 304(g) of the FD&C Act. The primary criteria are:

- The article(s) meets the definition of drug in section 201(g)(1) of the FD&C Act.
- There is reason to believe the drug(s) are adulterated or misbranded.

Please see RPM Chapter 5, Section 5. Administrative Detention of Drugs for drug detention procedures.

2.5.11.2 – Products Regulated by USDA in Dual Jurisdiction Establishments

Foods regulated by the USDA (i.e., meat, poultry, and processed egg products) located at a dual-jurisdiction facility and meeting the jurisdictional requirements of Section 304 of the FD&C Act and believed to be adulterated or misbranded, can be detained under USDA authority.

2.5.11.2.1- Federal Meat Inspection Act

Federal Meat Inspection Act (FMIA) Sections 402 and 409(b) provide the FDA with the authority to detain meat products subject to the FMIA, found outside a USDA inspected plant, if the FDA has reason to believe the products are adulterated or misbranded under the FD&C Act. The detention may not exceed 20 days and the items detained shall not be moved by any person from the place of detention until released by the FDA representative.

2.5.11.2.2 - Poultry Products Inspection Act

Poultry Products Inspection Act (PPIA) Sections 19 and 24(b) provide the FDA with the authority to detain poultry products subject to the PPIA found outside a USDA inspected plant, if the FDA has reason to believe the products are adulterated or misbranded under the FD&C Act. Detention may not exceed 20 days and the items detained shall not be moved from the place of detention until released by the FDA representative.

2.5.11.2.3 - Egg Products Inspection Act

Egg Products Inspection Act (EPIA) Sections 19 and 23(d) provide the FDA with the authority to detain egg products subject to the EPIA, found outside an USDA inspected plant, if the FDA has reason to believe the products are in violation of the EPIA Act. Detention may not exceed (20 days and the items detained shall not be moved from the place of detention until released by the FDA representative.

2.6 - Procedural Steps for Execution of a Detention at a Firm

The procedures to be followed in both ordering and terminating a detention differ depending on the applicable authority and product. You must consult with your supervisor before detaining any food from a dual jurisdiction facility under Section 304 of the FD&C Act, or under the detention authorities in FMIA, PPIA, or EPIA. If upon consultation, you and your supervisor determine that a detention is the appropriate action, then you should initiate a request with them seeking approval from the affected district office. It's imperative that before detaining any food that you have the approval of the Division

Director in whose district the article of food is located, or from an official senior to the division director, prior to detaining any food under Section 304(h) of the FD&C Act. You must also have the approval of the Division Director or an official senior to the Division Director before detaining any device, drug, or tobacco product under Section 304(g). If prior written approval is not feasible, prior oral approval must be obtained and confirmed in writing as soon as possible.

2.6.1 - Detention Procedure

After assuring that the criteria for detention are met, immediately advise your supervisor of the situation.

The information you furnish be adequate to fully complete the following blocks appearing on Detention Order, FDA 2289: 2, 4, 5, 7, 8, 10, 11, 13, 15, 19, 20, 21, 22, 24 and 26. See Exhibit 2-2. See IOM 2.6.2.1.

2.6.1.1 - Considerations

If the article of food to be detained is in transit aboard a conveyance (e.g., railcar, truck, or ship), be aware that detention of food aboard a conveyance may impact other activities of commerce that are dependent upon the ongoing operation of the conveyance.

FDA may allow the detained food to be removed from the conveyance to a storage facility. However, consult with your supervisor on this matter because the determination of whether the food can be moved from the conveyance to another location should be made based on considerations about the nature of the contaminant, security, preservation of the food, and accessibility to the food during the period of detention.

For all detentions, follow the guidance in IOM Section 4.3.3 to determine when FDA may examine a package that is in the possession, control, or custody of a common carrier. Guidance on resealing a conveyance is also found in IOM section 4.3.3.3.

If your supervisor instructs you to detain the article, proceed as directed in IOM 2.6.2.3, and 2.6.2.4.

2.6.1.2 - Executing the Detention

When you have been authorized to place a detention, proceed as follows:

- If the article is a food, indicate the conditions that are to be maintained while the article is detained by checking the appropriate method in Block 28 on the Detention Order (Form FDA 2289). After a device, drug, or food is detained, it may not be moved, unless specific procedures are followed. Consult your supervisor for guidance.
    - For detention of food under section 304(h), determine the storage conditions required (e.g., refrigeration), and whether movement to another facility is necessary to either provide the storage conditions required or for security purposes. Consult your supervisor for guidance. Indicate conditions that are to be maintained while the article of food is detained in the “Remarks” section of the detention notice (Block #26). If

applicable, also indicate that the movement of the food to another facility during detention has been authorized in writing by the FDA Division Director or an FDA official senior to such director, pursuant to 21 CFR 1.380 and 1.381.
    - Maintain surveillance on detained products, including the in-transit products, during their transfer and after the products are placed in storage if possible.
    - Ensure the custodian (i.e., the person in possession of the article when detained) places or maintains the detained product under the proper storage conditions.
    - If neither of the above items are possible, you should then place product under detention and move it to a proper storage facility. Notify the custodian of the place of storage (use Block 16 on the FDA-2289) and advise your supervisor of the necessity for including this information in the letter to the custodian and/or owner of the article.
- Personally inform the immediate custodian, at the highest management level, that the article is under FDA detention. If the article is a device, inform the custodian that the record-keeping requirements of 21 CFR 800.55(k)40 are in effect. If the article is a drug, inform the custodian that the record-keeping requirements of 21CFR 1.980(k) are in effect.
- Prepare the Form FDA-2289, as instructed in IOM 2.7.2.3.1, and issue page 1, the original, to the custodian named. Point out the appeal rights of the owner of the article, which are listed on the back of page 1 of the FDA-2289, and the right to appeal, with or without requesting an informal hearing.
- Affix Detention Tags, FDA-2290, to the article in a manner to assure visibility. If necessary, a label other than the Detention Tag may be used to identify an article(s) of food that has been detained, provided the label includes all the information listed on the current FDA-2290.

2.6.2 - Detention Order (Form FDA 2289)

The Detention Order (Form FDA 2289) is a pre-numbered, five-part, snap-out form, constructed and arranged to serve as the Detention Order, as a report of the action and as a notice to the custodian of an opportunity for an informal hearing.

2.6.2.1 - Preparation of Detention Order Notice

Print or type the information in the appropriate blocks of the Form FDA 2289. The first page blocks--which must be filled for detentions of foods in accordance with 21 CFR 1.382 are those numbered 1, 3, 6, 9, 10, 11, 12, 15, 16, 17, and 18. In blocks 17 and 18, indicate the name and title of the person who approved the detention order, and the manner in which the approval was obtained. For devices or drugs, mark 24 and 26 as N/A. For meat, poultry, or egg products not being detained under the authority of section 304(h) of the FD&C Act, mark 17 and 18 as N/A. Complete block 2. Once page 1 is completed, signed, and issued to the custodian of the product, it becomes an official document, and the detention period begins.

Immediately complete the additional pages of the Form FDA 2289 (pages 2 through 5) and submit them to your supervisor, for processing the action. Blocks to be filled in on these pages are items 13, 14, and 19 through 28. These blocks should be completed as appropriate (e.g., if samples were collected) or according to the product being detained (e.g. device, drug, or food) if the pertinent information can be readily determined. See IOM Exhibit 2-2.

Specific instructions for completing the FDA 2289 are provided on the last pages of the form. Pages 2-5 of the form are identical and completion of these constitutes your report on the detention, unless directed otherwise by your supervisor. Promptly submit these pages to your supervisor when you return to the office. Use FDA Form 2289c to elaborate on items wherever necessary. List any recommendations you made to the custodian for special storage of the product, such as its need to be refrigerated, frozen, etc.

2.6.2.2 - Distribution of FDA-2289

Distribution of FDA-2289 - The five-part, snap-out form is distributed as follows:

- Page 1, original - Give to custodian and, if applicable, give a copy of page 1 to the owner of the product. Give the two-sided text page listing statutory references to the owner of the article.
- Page 2, 3, 4 - Turn in to your district immediately using the fastest means possible.
- Page 5 - Retain in your possession.

2.6.2.3 - Detention Tag FDA-2290

This tag is a warning and identification device intended to be affixed to the detained products. Reference:
https://fda.sharepoint.com/sites/insideFDA-Administrative/FDA%20Forms/Forms/AllItems.aspx?id=%2Fsites%2FinsideFDA%2DAdministrative%2FFDA%20Forms%2FFDA%2D2290%5F508%289%2E14%29%2Epdf&parent=%2Fsites%2FinsideFDA%2DAdministrative%2FFDA%20Forms

2.6.2.3.1 - Preparation

As soon as you have issued the Detention Notice, fill out Detention Tags FDA 2290, following the instructions below. The information on the 2289 should be copied onto the FDA 2290, but where there is not sufficient room, you may shorten or copy enough information to make it clear what is intended in the block. See IOM Exhibit 2-3.

2.6.2.3.2 - Use of Tag

Complete and affix tags so that they are visible on several sides of the lot being detained. Use sufficient tags to give adequate warning that the lot is under U.S. FDA Detention and must not be used, moved, or tampered with, in any manner.

Each tag has a self-locking pin, the point of which should be firmly inserted in an appropriate seam, border, flap, or other area of the container or product, and pulled sharply downward to engage the top curve of the pin. Do not simply lay tags on the articles. Secure them to the containers or products. If the locking pin cannot be used, tape or tie the tag firmly onto the container or item. If using the pdf version of the Detention Tag, use tape to affix the tag to the product. Print multiple copies so that you can affix tags in several locations as needed to clearly and fully identify the lot.

Advise the custodian that Detention Tags have been affixed, the reason for the detention, and that the merchandise may not be moved without written permission of the agency. In-process devices may be completed without permission. See 21 CFR 800.55(h)(2)[53] for instructions on devices. See 21 CFR 1.980(h)(2) for instructions on drugs. See 21 CFR 1.381(c) for detention of foods.

2.6.2.4 - Termination of Detention

When final action has been taken on the detention, you will be authorized to terminate the detention. This will occur when one of the following conditions has been met.

1. For articles of food under detention, the article of food has been destroyed under appropriate supervision.
2. For drugs or devices, the product has been brought into compliance or destroyed under appropriate supervision. For meat, poultry, or egg products detained under authority of the FMIA[55], PPIA[56], or EPIA[57], the product has been brought into compliance, denatured or destroyed under appropriate supervision.
3. For meat, poultry, and egg products detained under authority of the FMIA, PPIA, or EPIA, the USDA, state, county, or local authorities have accepted jurisdiction and control of the article.
4. For meat, poultry, and egg products detained under authority of the FMIA, PPIA, or EPIA, it has been determined there is no significant violation of the FD&C Act, or of the EPIA, whichever is applicable, and the USDA has been notified that the FDA intends to terminate the detention.
5. Twenty calendar days have expired (or, if an additional 10-calendar-day detention period has been ordered, 30 calendar days have expired), counting from the day and hour of detention of the product. In this circumstance, no action is necessary on the part of the district.
6. A seizure action under section 304(a) of the FD&C Act has been instituted in court, and the goods have been seized by the U.S. Marshals pursuant to a court-issued warrant; or injunction action under section 302 of the FD&C Act has been instituted in court.
7. The division director or the Office of Regulatory Affairs program directors order the termination.

2.6.2.4.1 - Removal of Detention Tags

As soon as you are authorized to terminate the detention, proceed to where the detained material is stored, then personally remove and completely destroy all detention tags. Do not merely throw them in the trash.

2.6.2.4.2 - Issuance of Detention Termination Notice FDA 2291

Once you have removed all detention tags, inform the custodian that the article is no longer under detention. Immediately prepare a Detention Termination Notice by filling out blocks 1 through 12, and the bottom of the form to include name, title, and signature. Give the original (page 1) to the custodian. This action terminates the detention.

Complete the "Remarks" section to elaborate on pertinent information such as supervision, reconditioning, destruction accomplished, etc. The Detention Termination Notice, FDA 2291, together with Detention Notice, FDA 2289, will, unless instructed otherwise, constitute the complete report on the detention. See IOM Exhibit 2-4.
https://www.fda.gov/files/inspections,%20compliance,%20enforcement,%20and%20criminal%20investigations/published/Chapter-5---Administrative-Actions.pdf

2.6.3 - Sampling

When sampling is directed, official samples of articles involved in this type of operation are collected, prepared, and submitted in the same manner as any other regulatory samples. In the case of food detained under Section 304(h) of the FD&C Act[59], consult with your supervisor to determine whether the suspected contaminant in articles of food that have been detained makes it necessary to follow sampling procedures that may be different from those followed for routine regulatory samples.

2.6.4 - Supervision of Reconditioning, Denaturing, Or Destruction

Methods and procedures for reconditioning, denaturing, or destruction will be proposed to the division by the owner of the devices, drugs, or meat, poultry, or egg products. For food detained under Section 304(h) of the FD&C Act[60], destruction will likely be the only option, and it can only be done after the FDA approves in writing a request to modify the detention order. For all detentions, do not take any action on reconditioning, denaturing, or destruction unless you are authorized by your supervisor. Division officials will determine the adequacy of the proposed method. If satisfactory, you will be advised of the procedure and authorized to monitor the action.

When the operation is satisfactorily completed, and when authorized, terminate the detention as indicated in IOM 2.6.2.6.

The results of the reconditioning, denaturing, or destruction may be described in the "Remarks" section on the Detention Termination Notice, FDA 2291, if desired. See IOM Exhibit 2-4.

2.6.5 - Reporting

Except in unusual situations, or unless instructed otherwise by your supervisor, the Detention Order, Form FDA 2289, the Detention Order Termination, Form FDA 2291, and the Collection Report provide all information required to report the action from detention to termination.

2.7 - Denaturing

The purpose of denaturing is to prevent salvage or diversion of violative materials for human consumption. When products must be destroyed through a procedure other than incineration or direct entry into a landfill or compost operation, they are typically denatured using a chemical agent, rendering them undesirable to attempt to salvage or later sell for human consumption.

2.7.1 - Diversion to Animal Feed

The indiscriminate use of contaminated food for livestock may constitute a hazard to such livestock, as well as humans. Due to this concern, all diversion requests of this nature should be forwarded to the Center for Veterinary Medicine (CVM), Division of Compliance for review, to determine if the product may be converted to animal feed.

2.7.1.1 - Rodent or Bird Contaminated Foods

Diversion of rodent- or bird-contaminated foods for animal feed is authorized only when the contaminated product is treated by heat to destroy *Salmonella* organisms. In the case of wheat and other grains containing rodent excreta, a suitable heat process may be used, or the product is examined bacteriologically and proven not to contain *Salmonella*.

2.7.1.2 - Moldy Food

If processors insist on salvage of moldy grain or foods for animal feed use, it must be done under proper supervision, and provide for:

- Treatment by dry heating to destroy viable spoilage microorganisms (generally, this will result in grain having a toasted color and odor), and
- Evidence it does not contain mycotoxins, and
- Evidence, by animal feeding studies, the product is safe for animal use.

2.7.1.3 - Pesticide Contamination

Foods contaminated by pesticide residues should not be diverted to animal food use unless a determination is made that assures illegal residues will not be present in the food animal or their food products, (e.g., meat, milk, eggs).

2.7.2 - Decharacterization for Non-Food or Feed Purposes

Choose the method(s) by considering the type of the denaturant, the physical properties of the diverted material, and the ultimate use of the product.

2.7.3 - Reconditioning and Destruction

Sections 304 and 801 of the FD&C Act [21 U.S.C. 334 and 381] provide the legal basis for the reconditioning or destruction of goods under domestic seizure or import detention.

Reconditioning and destruction are the means whereby goods are brought into compliance with the law, or permanently disassociated from their intended use. Manpower may not be expended on supervision of reconditioning and destruction of goods except under administrative controls, detention, or emergency and disaster operations. See IOM 8.1.5.8 for operations in disasters.

FDA does not seek or condone the destruction of books or other publications. FDA policy and practice tries to be sensitive to the potential First Amendment issues associated with the regulation of books and

other printed materials that function as labeling of a product. See Compliance Policy Guide 140.100. In the context of judicial enforcement, disposition of any labeling subject to the court's jurisdiction is determined by the court. In a voluntary compliance situation, the disposition is the prerogative of the manufacturer, distributor, wholesaler, or retailer. Agency policy does not authorize field employees to director limit the options for disposition of violative labeling or other printed materials in such circumstances. Good judgment should always be exercised in such matters.

Section 536(b) of the FD&C Act [21 U.S.C. 360ii (b)] provides authority for electronic products to be reconditioned if FDA determines they can be brought into compliance with radiation performance standards. Therefore, reconditioning of radiation-emitting products must be approved by the Center for Devices and Radiological Health (CDRH), OHT8: Office of Radiological Health, prior to implementation to assure compliance with performance standards. If a foreign manufacturer conducts the reconditioning, the division should notify both the importer/consignee and the foreign manufacturer's agent of all FDA actions.

2.8 - Judicial Actions

2.8.1 - Information

An Information is a legal document filed in misdemeanor actions identifying the defendants and setting forth the charges. The Information is forwarded to the appropriate U.S. attorney, who then files the legal instruments. A trial date is set by the court. Ideally, trial preparation is a collaboration between representatives of the U.S. attorney's office, Office of the Chief Counsel (OCC), the division, and the involved FDA center.

2.8.2 - Grand Jury Proceedings

The Department of Justice (DOJ) must proceed by indictment in all felony cases. Evidence in possession of the government is presented to a grand jury that decides if it is sufficient to warrant prosecution. If the grand jury returns a "True Bill", and the defendant pleads not guilty at the arraignment, preparation for trial begins.

2.8.3 - Seizure

Seizure is a judicial civil action directed against specific offending goods, in which goods are "arrested." Authority for seizure is found in Section 304 of the FD&C Act. Originally designed to remove violative goods from consumer channels, it was intended primarily as a remedial step; however, this sanction often has a punitive and deterrent effect.

For more information on seizure actions consult RPM Chapter 6-1 “Seizures.”

2.8.3.1 – Division Recommendation

The division considers all evidence, including any establishment inspection, sample collection, and analytical results, as an inspection progresses. The Investigations Branch communicates with the

Compliance Branch during the inspection, and if the division determines a seizure is the best course of action, the compliance officer sets up a Preliminary Assessment Call (PA call). The investigator typically participates in the PA call and works closely with the compliance officer. If during the PA call there is consensus that a seizure action should be pursued, the process described in the RPM is initiated (See link above).

2.8.3.2 - Department of Justice

The Food and Drug Division of the HHS OCC reviews and forwards the seizure action to the U.S. attorney assigned to the judicial district in which the violative goods are located, through the seizing district. The U.S. attorney files a Complaint for Forfeiture addressed to the U.S. district court, setting forth the facts of the case and calling for the "arrest" of the goods. This complaint is filed with the appropriate district court.

2.8.3.3 - U.S. District Court

The court orders the arrest of the goods by issuing a motion and warrant to the U.S. Marshals Service, directing the seizure of the goods.

2.8.3.4 – Seizure of Goods by the Marshal and Investigator's Role

A Deputy U.S. Marshal (deputy marshal) seizes the goods, which then become the property of the court. You may be asked to assist in the seizure. If so, submit a memorandum to your division office covering this activity. This often includes documenting a detailed list of all product names, amount of each product seized, and location of each product. The investigator should work with the compliance officer prior to assisting the deputy marshal to determine the activities that must be documented.

2.8.3.5 - Claimant and Options

Any person who has an interest in the goods may appear as claimant or to step in to intervene and claim the goods.

2.8.3.6 - Abandonment

If no claimant appears within a specified time, (return date), then the U.S. attorney requests a Default Decree of Condemnation and Forfeiture, in which the court condemns the goods and directs the U.S. Marshals Service to destroy or otherwise dispose of the goods. Usually, the division assists in determining the method of disposal. You may be asked to help in the actual disposition. However, primary responsibility for disposition of seized lots following a default decree lies with the U.S. Marshals Service. Your role may include accompanying a deputy marshal to witness the operation. Although you are there in an advisory capacity, assist as needed to assure compliance with the court order. Promptly submit a written report of your observations upon completion of the operation. (See IOM 8.1.2.1 and 8.1.9.2)

2.8.3.7 – Proposed Actions to Come into Compliance from Claimant

A claimant may propose the goods be destroyed or reconditioned to bring them into compliance. After the FDA agrees to the method of reconditioning, the court issues a Decree of Condemnation permitting destruction or reconditioning under the supervision of the FDA, after a bond is posted. The investigator will typically observe the destruction and/or reconditioning as defined in the court order. If the reconditioning process does not appear to comply with the order, you should immediately advise the claimant and your supervisor. Submit a detailed report upon conclusion of the operation. In instances where the operation is prolonged, you should submit interim progress reports. Include the following information in your report of the operation:

- Identification of the case (sample number, court number, FDA number, product, and claimant).
- Description of the method of reconditioning or destruction. Collect pertinent written methods, labels, etc.
- Disposition of rejects; explanation for unaccounted goods.
- Findings of field examinations.
- Exhibits and samples collected. Do not pay for samples collected during reconditioning operations conducted under a consent decree.
- Expenses, including time spent in supervision and travel, mileage, per diem, and incidental expenses.

2.8.3.8 - Contested Seizure

A claimant may file an answer to the complaint and deny the allegations. The issues then go to trial. See Court Room Testimony section below (Reference section).

2.8.4 - Injunction

An injunction is a civil restraint issued by the court to prohibit violations of the FD&C Act. Injunction is designed to stem the flow of violative products in interstate commerce, and to correct the conditions in the establishment.

Injunction actions must be processed within strict time frames. Therefore, you may be requested to conduct an inspection to determine the current condition of a firm and to obtain specific information required for the injunction.

An injunction is ongoing. For more information on how to manage injunctions refer to RPM 6.2.

2.8.4.1 – Injunction Recommendation

The division considers all evidence, including inspections, samples, and analytical results. The Investigations Branch communicates with the Compliance Branch during the inspection, and if the division determines an injunction is the best course of action, the compliance officer sets up a Preliminary Assessment Call (PA call). The investigator typically participates in the PA call and works closely with the compliance officer. If during the PA call there is consensus that an injunction should be pursued, the process described in the RPM is initiated (See RPM 6-2-9).

2.8.4.2 - Temporary Restraining Order (TRO), Preliminary Injunction and Permanent Injunction

See RPM 6-2-3 for detailed definitions of these terms.

A temporary restraining order (TRO) is a court-enforced order entered to control an emergency situation. A TRO seeks immediate temporary relief. The TRO may be subject to a hearing prior to its expiration. Generally, a TRO lasts 10 days, but can be extended 10 days prior to hearing (a total of 20 days). If a hearing is held, the U.S. attorney presents evidence to support the injunction. This is not a courtroom trial described in 2.8.4.3.

A preliminary injunction may be issued by a judge based on a motion from the government requesting one prior to a trial. The judge may or may not grant a hearing depending on the actions of the defense.

A permanent injunction is a final decree from the court declaring actions that must be taken to correct the continuing violations. It may be entered by the court following a trial, hearing, or without a hearing, if no one contests the DOJ petition.

2.8.4.3 – Processing the Injunction

If the center(s) and OCC concur with the injunction recommendation, OCC sends a referral letter to the DOJ. If DOJ concurs, it will then issue a letter, containing a proposed consent decree, to the respective firm. If the firm signs the consent decree, the complaint is entered into the court. If the firm does not sign it, a trial begins in the U.S. court. (See Court Room Testimony section below.) If the court rules in favor of the government, a court-ordered injunction is filed. The terms of the injunction specify the steps to be taken to correct the violations at issue. See RPM 6.2.3 for details on the differences in the process and timeframes between a preliminary and permanent injunction. Unless there is a trial and the court rules in the firm's favor, or the case is withdrawn by the government, the outcome of an injunction case is either a court-ordered injunctive relief or a consent decree signed by the firm. In either case, the firm must comply with the terms of the court's order.

2.8.4.4 - Division Follow-up

It is the agency's responsibility to assure the terms of an injunction are met. This may include inspections to assure compliance. You must review the court order (injunction or consent decree) prior to inspection to assure that the firm is not only meeting the requirements of the regulations but is also meeting any additional requirements set forth by the court.

If during the inspection the investigator determines that the terms of the consent decree are not being followed, the supervisor and compliance officer should be notified immediately. Often the terms of the injunction require the firm to pay for the cost of supervision. If so, the investigator must document the hours spent inspecting at the firm, as well as any applicable costs related to

flights, mileage, lodging, and per diem, so that the compliance branch can appropriately charge the firm for the cost of supervision. (see RPM 6-2-14)

2.8.5 - Prosecution

Prosecution is a criminal sanction directed against a firm and/or responsible individuals. Prosecutions can be pursued at one of two levels: misdemeanor or felony and Misdemeanor prosecutions. A prosecution is punitive, with the view of punishing past behavior and obtaining future compliance.

2.8.6 - Court Room Testimony

If the seizure, injunction, or prosecution is contested, the case goes to trial. If required to testify, the investigator will work with the U.S. attorney and OCC to prepare.

2.8.6.1 - Courtroom Testimony

You may be called to testify in court before a judge, jury, or grand jury; or at a deposition before opposing counsel. Effective testimony is a result of quality investigative skills, the ability to prepare factual and informative investigative reports, and thorough preparation.

As a fact witness, you are required to testify from memory, but you are allowed to refer to notes, reports, and memoranda, as necessary to refresh your recollection. For this reason, and because they are available to opposing counsel; your notes, reports and the like must be accurate, organized, and complete.

There is little difference in giving testimony in court, in a deposition or before a grand jury. In a deposition, testimony is given upon interrogation by opposing counsel, under oath, and before a court reporter. Use guidance from your (the government's) attorney in preparing for a deposition. Once completed, the deposition is available to all persons interested in the case and is available for use at trial.

In a grand jury, testimony is given under oath to a group of jurors who determine whether sufficient evidence exists to charge an individual or party with a felony (See IOM 2.2.7.3).

2.8.6.2 - Testimony Preparation

Keep in mind you must have approval to testify. The authority to testify is found in 21 CFR 20.1. The following suggestions may be helpful in preparing to provide testimony in court, before a grand jury or at a deposition:

- Carefully and thoroughly review your notes, inspection reports, and all information about samples collected.
- Be neat in your personal appearance; dress conservatively in business attire and be well groomed.

- When you take the witness stand, sit erectly in your chair, look around the room to familiarize yourself with the court surroundings, but also try to assume a feeling of comfort and ease.
- Tell the truth. You are not there to convince, only to answer. If asked, do not hesitate to admit that you have discussed your testimony in advance with the U.S. attorney's office.
- Do not volunteer information. Do not interject comments that you have not been asked to make, as comments could be inadmissible and could result in a mistrial.
- Be sure you fully understand the question before you answer. If you don't understand the question, request clarification.
- Take your time. Give each question ample thought, as well as the time needed, to understand and formulate your answer.
- Do not answer questions too quickly. Give your attorney time to raise an objection in case it is a question you should not answer.
- Answer questions clearly and loudly enough so that everyone can hear you. Look at and address your remarks to the jury so that all jury members will be able to hear and understand you.
- Speak directly and authoritatively. Do not use ambiguous phrases such as, "I guess so, “or "I believe," etc.
- However, in instances where you genuinely lack the information or facts with which to answer, it is quite acceptable and advisable to reply, "I don't know."

If you are testifying virtually, you should also ensure that you have a plain, undistracting background and that your internet connection will be uninterrupted. Plan to test your internet connection and assure that the platform being used (e.g., Zoom, Teams, etc.) is installed and operating on your laptop before you connect for the testimony.

2.9 – Compliance Achievement for Voluntary Corrective Actions

The FDA uses a blend of industry voluntary corrections and regulatory actions to help achieve industry compliance. See FMD 86 and RPM 10-2.

A voluntary corrective action is defined as the observed voluntary repair, modification, or adjustment of a violative condition or product. For purposes of this definition, violative means the product or condition does not comply with the Acts FDA enforces or their associated regulations.

Voluntary destruction, in lieu of seizure of small lots of violative goods, shall be encouraged in instances where the proposed method is adequate. Supervision of voluntary segregation and denaturing of violative goods shall not be provided, except where it can be accomplished quickly and effectively, using minimal inspectional resources, and in a manner consistent with procedures outlined in this subchapter. The most extensive actions in this area usually occur in disaster situations. Follow instructions in IOM 8.1.5.8 Disaster/Emergency Response.

Do not engage in actual destruction, reconditioning, repair, modification, etc. of goods. This is the responsibility of the owner or dealer. You are a witness only. Samples of violative goods should be

collected prior to voluntary destruction if needed to support subsequent action against the responsible individuals. Take photographs where applicable. See IOM 5.7.6.1 and IOM 2.6.4, 2.6.4.1/2 for reporting requirements.

2.9.1 - Destruction

Before you supervise destruction, be sure management is aware the action is voluntary and that you are acting only as a witness. See IOM 2.6.4.

Personally witness all destructions, making certain destroyed goods are rendered totally unsalvageable for use as a food, drug, device, etc. Keep in mind your own personal as well as public safety. Exercise proper precautions in dealing with potentially dangerous substances and situations. Comply with local ordinances regarding the disposition of garbage and trash.
Note that certain products should not be disposed of in a conventional manner (e.g., sanitary landfill, flushing down the drain, etc.), especially if they contain chemicals that are banned (e.g., chloroform, methapyrilene, hexachlorophene, PCB, etc.), and have been classified by the EPA as hazardous and toxic substances. These products may require a special method of disposal by a licensed hazardous disposal facility. Any possible hazardous or toxic substance (carcinogen, mutagen, etc.) should not be disposed of without prior consultation by the firm with the EPA and/or the regulating state authority. Refer to 21 CFR Part 25 and the National Environmental Protection Act for guidance regarding the environmental impact of voluntary destructions.

2.9.1.1 - DEA Controlled Drugs

The FDA has a memorandum of understanding (MOU) with the Drug Enforcement Administration (DEA) (see MOU 225-15-11)). The FDA and DEA have a written policy to permit FDA representatives, in certain situations, to witness the destruction of DEA-controlled drugs. The procedures and instructions to follow when these drugs are destroyed are:

2.9.1.1.1 - DEA Approval

The FDA and the DEA have a mutual, written policy concerning witnessing the destruction of drugs under the distribution control of DEA. This policy dictates that FDA, upon receiving a request to witness such destruction, will advise the DEA regional office about the request and obtain approval for the action. If approval is requested by telephone and verbally approved, the approval should be reflected in writing for the record.

2.9.1.1.2 - Procedure

The necessity for FDA personnel to witness destruction of DEA-controlled drugs typically occurs in one of two situations:

- when you are already present at the firm in question, and you encounter DEA-controlled drugs, and you are requested to witness destruction; or
- when DEA-controlled drugs are to be destroyed at the same time the FDA is witnessing destruction of other drugs, not under DEA control.

If you are in a firm either conducting an inspection or witnessing destruction of drugs under FDA's distribution control, and the firm requests you to also witness destruction of DEA-

controlled drugs, do not commit yourself. Telephone your supervisor for instructions. You will be advised whether to proceed after your division communicates with DEA. In all other situations, refer the requester to DEA.
If the request to witness the destruction is approved, observe the destruction, and prepare DEA Form DEA 41. Instructions for completing it are included with the form.

2.9.2 - Reconditioning

The supervision of voluntary segregation of violative goods without the regulatory safeguards of seizure should be avoided. Voluntary segregation and destruction of violative lots should be encouraged; but under no circumstances should you supervise the voluntary segregation and salvage of unfit goods, regardless of the nature of the violation or the size of the lot. Be sure management is aware that the segregation is its responsibility. Collect samples where indicated, and/or advise the dealer or owner of their responsibilities under the law. If the dealer decides to voluntarily destroy any lot, refer them to the National Environmental Protection Act (NEPA). See IOM 2.6.2.

2.9.3 – Reporting Voluntary Correction

Report any voluntary correction of a problem unrelated to a division recommendation for regulatory action.

2.9.3.1 - Documenting Voluntary Destruction

Prior to supervising voluntary destruction, prepare a statement on the firm's letterhead, or on an FDA 463a Affidavit, providing the following information.

- Voluntary nature of the action, with you as a witness.
- Name of the product, including applicable code marks.
- Condition of the lot.
- Amount.
- Method of destruction.
- Signature of responsible individual.

2.9.4 - Compliance Achievement Reporting

Voluntary corrective actions should be described in the EIR and reported into the Compliance Achievement Reporting System (CARS) in the Field Accomplishments and Compliance Tracking System (FACTS) (Exhibit 5-15) per division standard operating procedures (SOP). Reportable items include:

- Voluntary destruction of any violative product by the person in possession of it.
- Destruction of violative products by a cooperating food or health official, where such product was discovered by and reported to such official by the FDA, or when those officials were doing work for the FDA under contract. Do not report formal condemnation by cooperating officials in the usual course of their independent work.
- Voluntary destruction of manufacturer's raw materials during an inspection.
- Capital Improvements such as significant improvements correcting a violative condition including, for example new equipment, rodent-proofing, etc. Typically, these corrections cannot

be verified during the inspection where they are observed and should be reported at follow-up inspections where actual improvement has been accomplished and is the result of a previous FDA observation. It should not be reported in CARS when it resulted from a seizure, injunction, or prosecution.

- Correction of GMP deficiencies when, during an inspection, the investigator observes that good manufacturing practice (GMP) deficiencies have been corrected since the previous inspection. These corrections are based on the previous FDA-483 and any communication following the previous inspection identifying significant deficiencies not listed in FDA-483. Corrections reported should be specific to observations made during inspections and reported when completed.
- Formula or label correction made based on a sample analysis, consumer complaint, etc.
- Additional employment of personnel for quality improvement or improved quality control.
- Initiation of an education and/or training program among employees or producers, or other general industry movement to improve conditions.

Do not report:

- Recalls, although voluntary, because they are already recorded elsewhere.
  Corrections that are not directly attributable to the efforts of the FDA, or to states under contract to the FDA.
- Corrections as a result of a seizure, injunction, or prosecution.
- *Medical Devices Only:* Use Form FDA 2473a to report corrections related to field compliance testing of diagnostic X-Ray equipment, as directed by the Compliance Program.

2.10 – Regulatory Submissions

This subchapter provides information on the procedures for obtaining information and filing applications with the agency. The filing and registration requirements are directed by the FD&C Act and its implementing regulations. They are filed, in most cases, by industry (e.g., drug registration, Low Acid Canned Food (LACF) registration and process filing, new drug applications, etc.).

Although these regulatory submissions are typically submitted to the various centers, it is important that you are introduced to these applications. Issues identified by the centers during the application review process can lead to follow-up assignments for ORA. In addition, while conducting a surveillance assignment, you may find that an establishment has not filed a regulatory application or is not following an application submission. The filing itself can provide information on what regulations are applicable to an establishment when the inspection is conducted.

Complete, accurate and up-to-date establishment registration and listing information is essential to promote safety. FDA relies on establishment registration and listing information for several key programs, including:

- Establishment inspections (foreign and domestic)
- Post market surveillance
- Counterterrorism
- Recalls
- Drug quality reports

- Adverse event reports
- Monitoring of drug shortages and availability
- Supply chain security
- Import admissibility decisions and export decisions
- Identification of products that are marketed without an approved application
- Establishment of user fees

2.10.1 – Human Foods

The FD&C Act was amended in 2002 requiring "any facility engaged in manufacturing, processing, packing, or holding food for consumption in the United States be registered with the Secretary." See 21 U.S. Code § 350d. For more information see the FDA/CFSAN website on food firm registration.

2.10.1.1 - Low Acid Canned Food (LACF) / Acidified Foods (AF) Food Canning Establishment (FCE) Registration

Food Canning Establishments (FCE) (foreign and domestic) engaged in the manufacturing of Low Acid Canned Food/Acidified Foods (LACF/AF) offering their products for interstate commerce within the United States are required by 21 CFR Parts 108, 113, and 114 to register their facility with the FDA. Registration details can be found on the FDA Website at Establishment Registration & Process Filing for Acidified and Low-Acid Canned Foods (LACF) | FDA.

2.10.1.2 - FCE Process Filing of LACF/AF Processors

Processors must submit scheduled process information for their LACF/AF products. Details can be found on the FDA website at Establishment Registration & Process Filing for Acidified and Low-Acid Canned Foods (LACF): Paper Submissions | FDA.

2.10.1.3 – Cosmetics

Cosmetics registration is voluntary. Details on registration for cosmetic establishments can be found on the FDA website at Voluntary Cosmetic Registration Program | FDA.

2.10.1.4 – Color Certification Program

Color additives are subject to FDA approval before use in many FDA-regulated products that come in contact with human or animal bodies for a significant period of time. FDA will also certify batches of color additives. Details about color certification can be found on the FDA website at Color Certification | FDA.

2.10.1.5 – Infant Formula

Prior to introducing or delivering for introduction a new infant formula into interstate commerce, persons responsible for manufacturing or distribution of it must register with the FDA. Details about registration can be found on the FDA website at Infant Formula Registration & Submissions | FDA.

2.10.1.6 - Interstate Certified Shellfish (Fresh and Frozen Oysters, Clams, and Mussels) Shippers

FDA maintains the Interstate Certified Shellfish Shippers List (ICSSL). The list includes firms that may ship molluscan shellfish in interstate commerce under the National Shellfish Sanitation Program (NSSP). Details about the listing and the program can be found on the FDA website at Interstate Certified Shellfish Shippers List | FDA.

2.10.1.7 - Interstate Milk Shippers (IMS)

FDA maintains the Interstate Milk Shippers List (IMSL). The list includes firms that may ship Grade A milk and milk products in interstate commerce under the National Milk Safety Program. Details about the listing and the program can be found on the FDA website at Interstate Milk Shippers List | FDA.

2.10.1.8 - Premarket Notification of New Dietary Ingredients.

Firms are required to notify FDA prior to using a new dietary ingredient not marketed before October 15, 1994. https://www.fda.gov/food/dietary-supplements-guidance-documents-regulatory-information/dietary-supplement-labeling-guide-chapter-vii-premarket-notification-new-dietary-ingredients

2.10.1.9 - Qualified Facility Attestation

A business that meets the definition of a "qualified facility" is subject to modified requirements of the preventive controls' rules. These modified requirements can be met by submitting a form to FDA, attesting to the business's status as a qualified facility and attesting that the facility is implementing preventive controls to address hazards associated with its food or is in compliance with non-Federal food safety laws and regulations. https://www.fda.gov/food/registration-food-facilities-and-other-submissions/qualified-facility-attestation

2.10.1.10 - Shell Egg Registration

Shell egg facilities are required to register with FDA.
https://www.fda.gov/food/registration-food-facilities-and-other-submissions/shell-egg-producer-registration

2.10.1.11 - Structure/Function Claim Notification for Dietary Supplements Electronic Submissions.

The Federal Food, Drug, and Cosmetic Act (the Act) requires that the manufacturer, packer, or distributor who wishes to market a dietary supplement notify FDA regarding the statement on the label or in the labeling of its product, pursuant to § 403(r)(6) of the Act.https://www.fda.gov/food/registration-food-facilities-and-other-submissions/structurefunction-claim-notification-dietary-supplements-electronic-submissions

2.10.2 – Human Drugs

The FD&C Act and its regulations require the filing of certain forms by firms that produce human drugs and drug-related products. The requirements and procedures for these are described below.

2.10.2.1 - Registration and Listing

Owners or operators of drug manufacturing establishments are required to register their establishments with the FDA. Registrants are also required to list each drug manufactured at their establishment(s) intended for commercial distribution and to submit updated drug listing information to the FDA twice each year, in June and in December, notifying FDA if this information has changed.

Registration and listing are required whether interstate commerce is involved or not.

- Drug Establishment Registration - The guidance document on electronic submissions for drug establishments' registrations and drug product listings is available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/guidances/ucm072339.pdf.
  General information and questions can be addressed by phone: 301-210-2840 or e-mail: eDRLS@fda.hhs.gov. See IOM Exhibit 5-12 for types for drug operations that require registration and listing.
- Outsourcing Facility Registration - The guidance documents on electronic submissions for outsourcing facilities' registration and drug product reporting is available at: https://www.fda.gov/media/87570/download and https://www.fda.gov/media/90173/download.
  General information and questions concerning outsourcing facilities' registrations and product reporting can be addressed by: Compounding@fda.hhs.gov.

21 CFR 207.69 defines the requirements for the official contact and the United States agent for registration and listing information.

Since many products and components are manufactured overseas, particular attention should be made to verify that the U.S. Agent as defined in 207.69(b) is correct and has the defined responsibilities such as when there is need to initiate product recalls or facilitate a foreign inspection.

207.69(b) U.S. Agent: Registrants of foreign establishments subject to this part must designate a single United States agent. The United States agent must reside or maintain a place of business in the United States and may not be a mailbox, answering machine or service, or other place where a person acting as the United States agent in not physically present. The United States agent is responsible for:

(1) Reviewing, disseminating, routing, and responding to all communications from the FDA including emergency communications;

(2) Responding to questions concerning those drugs that are imported or offered for import to the United States;

(3) Assisting the FDA in scheduling inspections; and

(4) If the FDA is unable to contact a foreign registrant directly or expeditiously, the agency may provide the information and/or documents to the United States agent.

2.10.2.2 - Investigational New Drug Application (IND)

An Investigational New Drug (IND) application must be submitted to the FDA by a drug sponsor before beginning tests of a new drug on humans. The IND contains the plan for the study and is supposed to give a complete picture of the drug, including its structural formula, animal test results, and manufacturing information. Detailed instructions for the submission of INDs can be found in 21 CFR Part 312.

Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA.

More information on the IND Process.

2.10.2.3 - New Drug Application (NDA)

A New Drug Application is an application requesting FDA approval to market, in interstate commerce, a new drug for human use. The application must contain, among other things, data from clinical studies needed for FDA review from specific technical viewpoints, including chemistry, pharmacology, biopharmaceutics, statistics, anti-infectives, and microbiology. Detailed instructions for the submission of NDAs can be found in 21 CFR Part 314.

The goals of the NDA are to provide enough information to enable the FDA reviewer to reach the following key decisions:

- Whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks.
- Whether the drug's proposed labels and labeling are appropriate, and what they should contain.
- Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.
-

The documentation required in an NDA should be adequate enough to tell the drug's whole story, including its ingredients, the drug’s behavior in the body, the results of animal studies, the nature and results of clinical tests or studies, and information about the drug’s manufacturing, processing and packaging.

More information on New Drug Applications.

2.10.2.4 - Abbreviated New Drug Application (ANDA)

An Abbreviated New Drug Application (ANDA) contains data that is submitted to the FDA for the review and potential approval of a generic drug product. Once approved, an applicant may

manufacture and market the generic drug product to provide a safe, effective, lower-cost alternative to the brand-name drug it references.
ANDAs are for products with the same or very closely related active ingredients, dose form, strength, administration route, use, and labeling as a product already shown to be safe and effective. An ANDA includes all the information on chemistry and manufacturing controls found in a new drug application (NDA), but is not required to include data from studies in animals and humans. It must, however, contain evidence that the duplicate drug is bioequivalent to the previously approved drug. Information concerning the submission of ANDAs can be found in 21 CFR Part 320. For more information, visit ANDA.

2.10.3 – Animal Foods and Drugs

Requirements for registration and filing of various applications by firms that manufacture animal drugs, feeds, and other veterinary products are required by the FD&C Act.

2.10.3.1 - Registration and Listing

Owners or operators of all drug establishments, not exempt under Section 510(g) of the FD&C Act [21 U.S.C. 360 (g)] or Subpart D of 21 CFR 207, who engage in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs, are required to register. Also, they must submit a list of every drug in commercial distribution; however, such listing information may instead be submitted by the parent, subsidiary, and/or affiliate company for all establishments when operations are conducted at more than one establishment, and there exists joint ownership and control among all the establishments. Owners and operators of establishments engaged in manufacture or processing of drug products must register and list their products.

The owner or operator of an establishment must register within five days after beginning of the operation and submit a list of every drug in commercial distribution at that time. Owners and operators of all establishments engaged in drug activities described in 21 CFR 207.3(a)(8) shall register annually. The guidance document on electronic submissions for drug establishment registration and drug product listing is available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072339.pdf.

For information on registered animal drug firms, contact CVM's Registration Monitor (HFV-212), 7519 Standish Place, Rockville, MD 20855, or 240-402-6816. You may make inquiries on the registration status of individual firms through CVM's Registration Monitor or through the Medicated Feed webpage at Medicated Feeds.

For information on animal drug listing, CVM maintains its own database for animal drug listing found at Animal Drugs @ FDA. You may also make inquiries for information via email at MedicatedFeedsTeamMail@fda.hhs.gov.

2.10.3.2 - Medicated Feed Mill License (FML)

An approved medicated feed mill license is required for facilities that manufacture feed using Category II, Type A medicated articles; liquid and free-choice medicated feed containing a Category II drug; or liquid and free-choice medicated feed containing a Category I drug that follow an approved proprietary formula and/or specifications.

Licensed mills are required to operate in compliance with current GMP described in 21 CFR 225 and must undergo a pre-approval inspection prior to licensure. Licensed mills must also register as drug establishments with FDA per 21 CFR 207. Registration is completed electronically each year between October 1 and December 31. Information on how to complete registration and check registration status can be found on CVM's Medicated Feeds webpage.

For general information and questions, an email can be sent to the Medicated Feeds Team at MedicatedFeedsTeamMail@fda.hhs.gov.

2.10.3.3 - New Animal Drug Application (NADA)

A new animal drug is defined, in part, as any drug intended for use in animals other than man--including any drug intended for use in animal feed but not including the animal feed--the composition of which is such that the drug is not generally recognized as safe and effective for the use under the conditions prescribed, recommended, or suggested in the labeling of the drug (21 U.S.C. Section 321(v)). Manufacturers of new animal drugs must complete a New Animal Drug Application (NADA) and receive approval prior to distribution.

New Animal Drug Applications must be submitted on a form FDA 356. The applications must be signed by the applicant or by an authorized attorney, agent, or official. The application must be filled out completely, in triplicate, and submitted to the address below.

FDA 356 which can be obtained from:

Food and Drug Administration
Center for Veterinary Medicine (HFV-12)
7500 Standish Place
Rockville, MD 20855

Completed NADAs should be mailed to:

Food and Drug Administration
Center for Veterinary Medicine (HFV-199)
7500 Standish Place
Rockville, MD 20855

General information or questions can be answered by calling 240-276-9300 or more information is available at NADA.

2.10.3.4 - Abbreviated New Animal Drug Application (ANADA)

The Generic Animal Drug and Patent Term Restoration Act amended the FD&C Act to provide for the approval of generic copies of previously approved animal drug products. The generic product may be approved by providing evidence that it contains the same active ingredients, in the same concentration, as the approved article, and is bioequivalent. The information is submitted to the FDA in the form of an Abbreviated New Animal Drug Application or ANADA.

An ANADA must be submitted to FDA on the form FDA 356V. The format and content of the application must be in accordance with the policies and procedures established by FDA's C VM. The application must be filled out completely in triplicate and submitted to the address below.

ANADA's may also use the form FDA 356 which can be obtained from:

Food and Drug Administration
Center for Veterinary Medicine (HFV-12)
7500 Standish Place
Rockville, MD 20855

Completed legible applications should be mailed to:

Food and Drug Administration
Center for Veterinary Medicine (HFV-199)
7500 Standish Place
Rockville, MD 20855

Assistance and additional information can be obtained by calling 240-402-5674. More information is available at ANADA.

2.10.4 – Medical Devices

The FD&C Act, its amendments, and the regulations promulgated under the Act, require the filing of certain forms and the submission of certain data by those involved in the production (and in some cases the use) of medical devices and radiological products. Within the CDRH, the Division of Industry and Consumer Education (DICE) has been charged with responsibility for providing information and assistance to industry in complying with these requirements. The general requirements are discussed below, as several issues are unique to CDRH submissions.

2.10.4.1 – Device Registration and Listing

Section 510 of the FD&C Act [21 U.S.C. 360] and 21 CFR 807 describe the establishment registration, device listing, and premarket notification requirements, and also specify conditions under which establishments are exempt from these requirements.

Manufacturers of finished devices (including device specification developers, reprocessors of single-use devices), repackers and relabelers, contract sterilizers, foreign exporters, and initial importers of medical devices, are required to register their establishments by submitting their registration and

listing information via the FDA Unified Registration and Listing System (FURLS)/Device Registration and Listing Module (DRLM). After initial submission, annual registration is accomplished by reviewing previously submitted registration and listing information via FURLS/DRLM. Component manufacturers are not required to register if the components are only sold to registered device establishments for assembly into finished devices. Registration and listing are required, however, if the component is labeled for a health care purpose and sold to medical or clinical users. Optical laboratories, clinical laboratories, dental laboratories, orthotic and prosthetic appliance assemblers, hearing aid dispensers, and others who, using previously manufactured devices, perform a service function for physicians, dentists, other licensed practitioners, or their patients, are exempt from establishment registration if they are located in the United States. X-ray assemblers are exempt from establishment registration. An exemption from registration does not exempt an establishment from inspection under Section 704 of the FD&C Act [21 U.S.C. 374].

Each establishment required to register, except initial importers of medical devices, must list their devices. Device listing and updates to listing information are accomplished via FURLS/DRLM.
All foreign manufacturers are required to notify the FDA of the name, address, telephone, and fax numbers, and e-mail address of their United States agent.

Medical device establishments are required to register and list, even if interstate commerce is not involved. Foreign establishments must register, list, and identify a United States agent prior to exporting to the United States. See IOM Exhibit 5-13 for the types of medical device operations that require registration and listing.

An establishment must initially register by paying the annual registration user fee and submitting their registration and listing information via FURLS/DRLM. Step-by-step instructions explaining how to pay the annual registration user fee, register an establishment, and list a device can be found on our website at https://www.fda.gov/medical-device/how-to-study-and-market-your-device/device-registration-and-listing.

General registration and listing information and questions about FURLS/DRLM can be addressed by sending an e-mail message to reglist@cdrh.fda.gov. Policy questions can be addressed by sending an email to device.reg@fda.hhs.gov.

2.10.4.2 - Premarket Notification - Section 510(k)

The Medical Device Amendments of 1976 require medical device manufacturers to notify the CDRH at least 90 days before commercially distributing a device. This is known as a “Premarket Notification”, or a 510(k) submission. Commercial distribution, for practical purposes, means the device is held for sale. These 510(k) requirements do not apply to Class I devices unless the device is intended for a use that is of substantial importance in preventing impairment of human health, or that presents a potential unreasonable risk of illness or injury. See Section 510(l) of the FD&C Act [21 U.S.C. 360(l)]

A manufacturer must submit a Premarket Notification to the FDA in any of the following situations:

- Introducing a device into commercial distribution, for the first time, when a predicate device exists.
- Introducing a new device or product line, for the first time, which may already be marketed by another firm.
- Introducing a device into commercial distribution when there is a modification to a previously cleared device that could significantly affect safety and/or effectiveness. Such changes or modifications may relate to design, material, chemical composition, energy source, manufacturing method, or intended use.
- Introducing a device into commercial distribution when the device exceeds the limitations of exemption per the .9 section of the associated regulation. (For example, 21 CFR 888.9 describes limitations of exemptions from Section 510(k) for Orthopedic Devices.)
-

These requirements do not apply to Custom Devices. A Custom Device is a device made exclusively for, and to meet the special needs of, an individual physician or health professional; or for use by an individual patient named in the order of a physician or dentist (such as specially designed orthopedic footwear). A "custom device" is not generally available in finished form for purchase and is not offered through labeling or advertising for commercial distribution.

Refer to IOM Exhibit 5-13 for the types of medical devices that require 510(k) submissions. The investigator should document, for CDRH review, failures to submit required 510(k)s.

2.10.4.3 - Premarket Approval

Class III devices are required to undergo Premarket Approval (PMA) in accordance with the provisions of Section 515 of the FD & C Act [21 U.S.C. 360e]. A PMA is initiated with the submission of an application to the FDA. Prior to approval of a PMA application, or a PMA supplemental, the FDA may inspect the applicant's facilities and records as pertinent to the PMA.

Compliance Program 7383.001 *Medical Device PMA Preapproval and PMA Postmarket Inspections* provides instructions to FDA field and CDRH staff for PMA preapproval, PMA postmarket inspections, and regulatory activities associated with PMAs.

Requests for PMA inspections will be made by CDRH Office of Regulatory Programs, DRP2: Division of Establishment Support, Regulatory Inspections and Audits Team. These assignments will require a comprehensive assessment of the firm’s quality management system for compliance with the appropriate regulations.

2.10.4.4 - Investigational Device Exemption/Humanitarian Device Exemption (IDE/HDE)

2.10.4.4.1 - Investigation Device Exemption (IDE)

The IDE regulation in 21 CFR 812 contains requirements for sponsors, Institutional Review Boards (IRBs), and clinical investigators. Additional requirements are found in 21 CFR 50, Informed Consent; and 21 CFR 56, IRB's. All sponsors of device clinical investigations must have an approved IDE, unless specifically exempted by the regulation. Sponsors who have an

approved IDE are exempt from requirements regarding labeling, registration and listing, premarket notification, performance standards, premarket approval, GMPs (except the design control provisions), banning of devices, restricted devices, and color additives.

Provisions for obtaining an IDE, and the sections of the regulations, with which sponsors, investigators, and IRBs must comply, differ according to the risks posed by the device. Sponsors of nonsignificant risk devices must obtain IRB approval and are subject to a limited number of provisions; sponsors of significant risk (See 21 CFR 812.3(m)) investigations are subject to the entire regulation.

There are investigations, described in 21 CFR 812.2(c), which are exempt from the IDE regulation. Exempted investigations apply to devices and diagnostics that meet the criteria in the regulation. These devices, however, are still subject to other regulatory requirements of the FD&C Act, such as labeling, premarket approval of Class III devices, and GMPs (as stated in the preamble to the IDE regulation).

A sponsor who knows a new device is not "substantially equivalent" to a pre-amendment device, or who is not sure if a device is "substantially equivalent" without conducting a clinical investigation, must obtain an approved IDE to conduct the clinical investigation. After collecting clinical data, a sponsor who desires to market a device must either submit a premarket notification (510k) or a premarket approval application to the FDA. A premarket notification may be submitted if the sponsor believes the data supports a finding of substantial equivalence. Certain radiation-emitting electronic devices that are investigational are also subject to radiological health regulations, as found in 21 CFR 1000 through 1050.

Transitional devices must have an approved IDE to be investigated. Sponsors, monitors, IRBs, investigators, and non-clinical toxicological laboratories will be covered under the BIMO Program. FDA has the authority to inspect and copy records relating to investigations. Records identifying patients by name will be copied only if there is reason to believe adequate informed consent was not obtained, or if investigator records are incomplete, false, or misleading.

2.10.4.4.2 – Humanitarian Device Exemption (HDE)

A Humanitarian Device Exemption (HDE) is a device approved under Section 520(m) of the FD&C Act [21 U.S.C. 360j(m)]. The HDE standard for approval is exempt from the requirement of establishing a reasonable assurance of effectiveness that would otherwise be required under Sections 514 and 515 of the FD&C Act but is not exempt from the requirement for a reasonable assurance of safety. FDA approval of an HDE application authorizes an applicant to market a humanitarian use device in accordance with approved labeling and indication(s) for use, subject to certain profit and use restrictions set forth in Section 520(m) of the FD&C Act. HDE approval for a device is initiated with the submission of an application to the FDA. Refer to IOM Section 2.9.2.4, Premarket Approval.

2.10.4.5 - Classification of Devices

All medical devices subject to the FD&C Act will be classified as either Class I, Class II, or Class III medical devices.

Manufacturers who have questions regarding the classification of a device can write CDRH under Section 513(g) of the FD&C Act [21 U.S.C. 360c (g)] and request a response regarding the status of the device.

2.10.5.6.1 - CLASS I

Class I - General Requirements- Devices for which general controls (i.e., the controls in Section 501, 502, 510, 516, 518, 519 and 520 of the FD&C Act [21 U.S.C. 351, 352, 360, 360f, 360h, 360i, and 360j]) provide reasonable assurance of safety and effectiveness.

2.10.5.6.2 - CLASS II

Class II - Special Control Requirements - Devices for which the general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness of the device, and for which there is sufficient information to promulgate special controls, necessary to provide such assurance.

2.10.5.6.3 - CLASS III

Class III - Premarket Approval Requirements - Devices which:

- Cannot be placed into Class I or II because insufficient information exists to provide assurance of safety and effectiveness, and cannot be placed into Class II because too little data exists to support the promulgation of special controls, and
- Are purported or represented to be for use in supporting or sustaining human life, or for a use that is of substantial importance in preventing impairment of human health, or
- Presents a potentially unreasonable risk of illness or injury.

Unless they are determined substantially equivalent to devices distributed prior to the 1976 Medical Device Amendments, devices proposed for marketing after May 28, 1976, fall automatically into Class III. Class III medical devices marketed before May 28, 1976, and the substantially equivalent devices marketed after that date, remain subject to the premarket notification requirements until required to have an approved PMA. Petitioners can request to have such devices reclassified into Class I or II. Transitional devices, those regulated as new drugs before May 28, 1976, are automatically assigned to Class III.

2.10.6 – Biologics

The requirements for the registration and licensing of biological products fall under both the (PHS) and the FD&C Act.

2.10.6.1 - Registration and Listing

CBER provides industry with registration and listing forms, including Form FDA 2830, Blood Establishment Registration and Product Listing; and Form FDA 3356, *Establishment Registration and*

Listing for Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). Instructions for completing these documents are found on the reverse side of these forms along with establishment and product definitions. Registration forms are available through your district office, and through CBER's Office of Communication, Manufacturers Assistance and Technical Training Branch, and from its website. Registration and listing is required whether interstate commerce is involved or not. (See IOM 5.13.3)

For questions regarding a firm's registration, CSOs should refer to Document JA-000081, "OBPO Registration and Listing Inquiries." CSOs can refer industry questions to: Industry.Biologics@fda.hhs.gov. See also IOM 5.13.3.

2.10.6.1.1 - Human Blood and Blood Products

1. **Who must register** - Section 510 of the FD&C Act and 21 CFR 607 delineate the requirements and exemptions relating to the registration of establishments engaged in the collection, manufacturing, preparation, or processing of human blood or blood products. Registration and listing are required whether or not interstate commerce is involved. Fixed blood collection sites must register if they have supplies or equipment that requires quality controls or compliance with an expiration date, (e.g., copper sulfate, centrifuges, etc.), or is being used to store donor records. Temporary collection sites--to which all blood collection supplies are brought on the day of collection and are completely removed from the site at the end of the collecting period (except beds, tables, and chairs) -- and blood mobiles are not required to register. All military blood bank establishments are required to register. (MOU with Department of Defense [Federal Cooperative Agreements Manual] Regarding Licensure of Military Blood Banks.) Brokers who take physical possession of blood products, such as in storage, pooling, labeling, or distribution, are required to register. Blood establishments located outside of the United States that import or offer for import blood products into the United States are required to register with the FDA. They must also provide the name of the U.S. agent, the name of each importer, and the name of each who imports or offers for import these blood products.
2. **When to register** - Establishments must register within five days after beginning operations and must submit a list of blood products that they distribute commercially. They must register annually thereafter.
3. **How to register** - Owners or operators of blood establishments must register using the Form FDA 2830. Refer to Compliance Policy Guide (CPG) 230.110 for additional information on registration. These persons may complete and submit line or may submit a paper form.
4. **Where to mail completed paper forms** -
   Food and Drug Administration
   Center for Biologics Evaluation and Research
   Division of Blood Applications (HFM-370)
   1401 Rockville Pike, 200N
   Rockville, MD 20852-1448
5. **For general information and questions:**
   Phone: 301-827-3546
   Email: bloodregis@cber.fda.gov

Mail:
Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Avenue, WO7, G112
Silver Spring, MD 20993-0002

2.10.6.1.2 - Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/PS)

1. **Who must register** – Any establishment that manufactures HCT/Ps that are regulated solely under the authority of section 361 of the Public Health Service Act (42USC264) (the PHS Act) must register and list with CBER whether or not the HCT/P enters into interstate commerce (21 CFR 1271.1). Establishments that manufacture HCT/Ps regulated as drugs, devices and/or biological products under Section 351 of the PHS Act and/or the Federal Food, Drug and Cosmetic Act, must register and list with CBER following procedures in subpart B, 21 CFR 1271.21 thru 1271.37. Registration and listing are required if the establishment recovers, processes, stores, labels, packages, or distributes any human cell or tissue; or screens or tests the cell or tissue donor. Establishments exempted from registration are listed in 21 CFR 1271.15. Establishments that only have HCT/Ps under premarket review (IND/IDE/BLA/PMA) do not have to register and list until the HCT/P has been licensed, approved, or cleared by the FDA.
2. **When to register** - Establishments must register within five days after beginning operations and must submit a list of each HCT/P manufactured.
3. **How to register** - To register, a Form FDA 3356 must be completed.
4. **Where to mail completed forms** -
   Food and Drug Administration
   Center for Biologics Evaluation and Research
   Attention: Tissue Establishment Registration Coordinator
   10903 New Hampshire Avenue, WO7, G112
   Silver Spring, MD 20993-0002

   Or forms may be submitted by FAX according to form instructions.
   Alternatively, establishments may now submit the information electronically via the Electronic Human Cell and Tissue Establishment Registration (eHCTERs) page.
5. **For general information and questions:**
   Phone: 301-827-6176 (Tissue Establishment Registration Coordinator)
   Email: tissuereg@cber.fda.gov
   Mail:
   Food and Drug Administration
   Center for Biologics Evaluation and Research, HFM-775,
   1401 Rockville Pike, 200N,
   Rockville, MD 20852-1448

2.10.6.2 - Biologic License

Section 351 of the Public Health Service Act requires individuals or companies who manufacture biological products for introduction into interstate commerce to hold a license for the products.

Biologics licenses are issued by CBER and the Center for Drug Evaluation and Research (CDER) (21 CFR 601.4).

Applicants must inform the FDA about each change in the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling established in the approved license application (21 CFR 601.12).

Major changes require supplement submission and approval prior to distribution of products made using the change (21 CFR 601.12(b)). Certain changes require supplement submissions at least 30 days prior to distribution of the product made using the change, and other minor changes need only be described in an annual report (21 CFR 601.12(c) and (d)).
Where to send reports –

For licensed biological products regulated by CBER:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center (HFM-99),
10903 New Hampshire Avenue, WO7, G112,
Silver Spring, MD 20993-0002

For licensed biological products regulated by CDER:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drugs (OND) (Specify OND Review Division)
5901-B Ammendale Road

2.10.7 – Tobacco

The FD&C Act and its amendment under the Family Smoking Prevention and Tobacco Control Act require manufacturers or importers of tobacco products to submit certain information to the FDA, including: Tobacco Health Documents, Establishment Registration and Product Listing, and Ingredient Listing. New tobacco products subject to further requirements include the following: any tobacco product that was not commercially marketed in the United States as of February 15, 2007 (including those products in test markets); or any tobacco product that has been modified (including a change in design, or change to any component, any part, or any constituent, including a smoke constituent, or change in the content, delivery or form of nicotine, or any other additive or ingredient) t in which the modified product was commercially marketed in the United States after February 15, 2007. The general requirements for new tobacco products are discussed below. On March 15, 2022, the President signed legislation to amend the FD&C Act to extend FDA's jurisdiction to products "containing nicotine from any source," not just nicotine derived from tobacco. See Consolidated Appropriations Act, 2022, Public Law 117-103, Division P, Subtitle B. The changes to the law took effect April 14, 2022, thus FDA considers "tobacco products" to encompass both tobacco-derived nicotine and non-tobacco-derived nicotine products.

2.10.7.1 – Premarket Requirements

A Premarket Tobacco Product Application (PMTA) can be submitted by any person seeking an FDA marketing order for any new tobacco product, under Section 910(b) of the Federal Food, Drug, and

Cosmetic (FD&C) Act. A PMTA must provide scientific data that demonstrates a tobacco product is appropriate for the protection of public health. To reach such a decision and to authorize marketing, the FDA considers (per Section 910(c)(4)), among other things:

- The risks and benefits to the population as a whole, including people who would use the proposed new tobacco product, as well as non-users
- Whether or not people who currently use any tobacco product would be more, or less likely, to stop using such products if the proposed new tobacco product were available;
- Whether or not people who currently do not use any tobacco products would be more, or less, likely to begin using tobacco products if the new product were available
- The methods, facilities, and controls used to manufacture, process, and pack the new tobacco product

2.10.7.2 – Postmarket Requirements

Postmarket requirements oblige applicants to establish and maintain records and make reports that the FDA requires as necessary to determine, or facilitate a determination of, whether or not there may be grounds to withdraw or temporarily suspend a marketing granted order. Postmarket reporting requirements for all tobacco products that receive a marketing granted order are set forth in § 1114.41, and the FDA may require additional reporting under the terms of a marketing granted order.

2.10.7.3 – Substantially Equivalent

The term 'substantially equivalent' or 'substantial equivalence' means, with respect to a tobacco product being compared to the predicate tobacco product, that the Secretary, by order, has found that the tobacco product either a) has the same characteristics as the predicate tobacco product; or b) has different characteristics and the information submitted contains clinical data (if deemed necessary by the Secretary) demonstrating that it is not appropriate to regulate the product under this section because the product does not raise different questions of public health. (In subparagraph (a) above, the term 'characteristics' means the materials, ingredients, design, composition, heating source, or other features of a tobacco product.)

A tobacco product may not be found to be substantially equivalent to a predicate tobacco product that has been removed from the market at the initiative of the Secretary, or to a predicate tobacco product that has been determined by a judicial order to be misbranded or adulterated.
General information regarding industry submissions, or the process, can be found at:
https://www.fda.gov/tobaccoproducts/compliance-enforcement-training/manufacturing.

2.11 – References

2.11.1 – Definitions involving Districts

Program Alignment created program specific divisions in which most field CSOs are assigned to work. However, geographical districts still exist, and references are made to them in assignments, correspondence, and various procedures described in this manual and used throughout the FDA. Geography-related terms are described below.

2.11.1.1 – Home District

Home district is the term used for the FDA district office that an establishment or firm is associated with. This is based upon the geographical area responsibilities of the district. Most often, the home district will be the office retaining original records associated with a firm, such as sample collection reports, analyst worksheets, establishment inspection reports, and correspondence. Check with your supervisor for your program division procedures for maintaining original records.

2.11.1.2 – Seizing District

Seizing district is the district in which a seizure was actually accomplished. The seizing district is not necessarily the collecting district, (as in the case of in-transit samples).

2.11.1.3 – Supervising District

Supervising district is the district that exercises supervision over reconditioning lots in connection with seizure actions.

2.11.2 – FDA/ORA Manual and Reports

The most used FDA and ORA manual and reports you may need to reference are linked below.

- Compliance policy guides,
- Compliance program guidance manuals,
- Enforcement reports,
- Field Managements directives,
- Guide to International Inspections and Travel
- Inspection Technical Guides
- International Cooperative Agreements
- Investigations Operations Manual
- Laboratory Manual
- Laboratory Information Bulletins
- Regulatory Procedures Manual
- Recalls and Safety Alerts
- Staff Manual Guides
- State and Federal Cooperative Agreements
- Federal Memorandums of Understandings

2.11.3 – Forms and Other Publications

The FDA Online Public Forms Catalog contains a list of FDA forms and the information necessary to order them.

Paper copies of the forms may be ordered electronically from the Program Support Center. To submit a forms request, or for other questions concerning FDA forms, see https://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/ucm236184.htm.

The DHHS Program Support Center at 16071 Industrial Drive, Gaithersburg, MD 20877, also maintains a limited selection of FDA forms and publications. To inquire about printing, please contact the center at: pscpublishing@psc.hhs.gov.

FDA's intranet Electronic Forms Catalog is a repository of internal forms related to field operations. For example, you can find seals, affidavits, FDA-482, Notice of Inspection, and other forms that document activities related to investigations, inspections, and sample collection and analysis. Forms are organized alphabetically, as well as by form number.

2.11.4 – Regulatory References and the General Public

The public must make a request under the Freedom of Information Act (FOIA) in order to obtain certain FDA documents that require redaction. See IOM 1A.3.4 (FOIA) and IOM 1A.3.5 (internal FDA documents) for additional information on FOIA. For guidance for the public on how to file an FOIA request, see https://www.fda.gov/RegulatoryInformation/FOI/HowtoMakeaFOIARequest/default.htm.

Many FDA documents are available to the public without a FOIA request. To obtain forms, direct the public to the FDA Public Use Forms web page. The public can purchase paper editions of various agency manuals, such as the Food Code and Compliance Program Manuals, if ordered by National Technical Information Service (NTIS) item number from the NTIS. Instruct the person in search of a publication to first locate the NTIS item number by calling the NTIS sales department at 888-584-8332. Next, enter the NTIS item number in the search box at the NTIS website at www.ntis.gov, and follow directions on ordering the publication. For additional information on NTIS publications, refer the public to the following contact information:

National Technical Information Service
Technology Administration
U.S. Department of Commerce
Alexandria, VA 22312
Order Desk: 703-605-6050
customerservice@ntis.gov

2.11.5 – Laws Enforced by FDA

The Food and Drugs Act of 1906 was the first of more than 200 laws, constituting one of the world's most comprehensive and effective networks of public health and consumer protections. Details about the laws that the FDA enforces can be found on the web at Laws Enforced by FDA. Information about, and links to, the FD&C Act can be found at FD&C Act.

2.11.6 – Regulations

The Code of Federal Regulations (CFR) is a codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the federal government. The CFR is divided into 50 titles that represent broad areas subject to federal regulation. Each title is divided into chapters, which usually bear the name of the issuing agency. Each chapter is further subdivided into

parts covering specific regulatory areas. For example, the specific regulation covering drug GMPs appears as "21 CFR 211", that is, Title 21, Part 211. Regulations enforced by the FDA are found in volumes 1-8 of Title 21, parts 1-1299. They are updated as of April 1 of each year. Both the Federal Register and the CFR must be used together to determine the latest version of a given rule.

2.11.7 - United States Code (U.S.C.)

“The United States Code is a consolidation and codification by subject matter of the general and permanent laws of the United States. It is prepared by the Office of the Law Revision Counsel of the United States House of Representatives.” U.S.C. Use FDA’s to obtain cross references for sections of the FD&C Act and the U.S.C.

2-1 - Definitions

The following definitions are from the Food, Drug and Cosmetic Act. Additional definitions can be found in 21 USC 321 (FD&C Act Definitions).

- The term “food” means (1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.
- The term “drug” means (A) articles recognized in the official United States Pharmacopoeia,[1] official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or *any supplement to any of them; and (B) articles intended for use in the diagnosis, cure,* mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C). A food or dietary supplement for which a claim, subject to sections 343(r)(1)(B) and 343(r)(3) of this title or sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim. A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 343(r)(6) of this title is not a drug under clause (C) solely because the label or the labeling contains such a statement.
- The term “device” (except when used in paragraph (n) of this section and in sections 331(i), 343(f), 352(c), and 362(c) of this title) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—
  (A) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
  (B) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  (C) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term “device” does not include software functions excluded pursuant to section 360j(o) of this title.
- The term “cosmetic” means (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles; except that such term shall not include soap.
- The term “raw agricultural commodity” means any food in its raw or natural state, including all fruits that are washed, colored, or otherwise treated in their unpeeled natural form prior to marketing.
- The term “food additive” means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to

evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include—

(1) a pesticide chemical residue in or on a raw agricultural commodity or processed food; or
(2) a pesticide chemical; or
(3) a color additive; or
(4) any substance used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to this chapter, the Poultry Products Inspection Act [21 U.S.C. 451 et seq.] or the Meat Inspection Act of March 4, 1907, as amended and extended [21 U.S.C. 601 et seq.];
(5) a new animal drug; or
(6) an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement.

- The term "color additive" means a material which—
  (A) is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source, and
  (B) when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction with other substance) of imparting color thereto;

  except that such term does not include any material which the Secretary, by regulation, determines is used (or intended to be used) solely for a purpose or purposes other than coloring.
  - The term "color" includes black, white, and intermediate grays.
  - Nothing in subparagraph (1) of this paragraph shall be construed to apply to any pesticide chemical, soil or plant nutrient, or other agricultural chemical solely because of its effect in aiding, retarding, or otherwise affecting, directly or indirectly, the growth or other natural physiological processes of produce of the soil and thereby affecting its color, whether before or after harvest.

The term "animal feed", as used in paragraph (w) [2] of this section, in section 360b of this title, and in provisions of this chapter referring to such paragraph or section, means an article which is intended for use for food for animals other than man and which is intended for use as a substantial source of nutrients in the diet of the animal, and is not limited to a mixture intended to be the sole ration of the animal.

2-2 FDA 2289 - Detention Order

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DETENTION ORDER

1a. DIVISION ADDRESS

1b. PHONE NUMBER

1c. NAME OF DIVISION DIRECTOR

1d. EMAIL ADDRESS

1e. FAX NUMBER

2. NAME OF CUSTODIAN

TO:

3. DETENTION ORDER NUMBER

DO

4. TITLE OF CUSTODIAN

5. TELEPHONE NUMBER

6. DATE AND HOUR DETAINED

a.m.

p.m.

7. FIRM NAME

8. ADDRESS *(Street, City, State, ZIP Code)*

9. MAXIMUM DETENTION

DAYS

Pursuant to *(Check applicable Section(s))* ☐ Section 304(h) of the Federal Food, Drug and Cosmetic Act (FD&C Act), ☐ Section 304(g) of the FD&C Act, ☐ Sections 402 and 409b of the Federal Meat Inspection Act, ☐ Sections 19 and 24(b) of the Federal Poultry Inspection Act, and/or ☐ Sections 19 and 23(d) of the Federal Egg Products Inspection Act, the article(s) listed in blocks 10 - 12 below on this form must not be used, moved, altered or tampered with in any manner during the detention period without the written permission of an authorized representative of the Secretary of the U.S. Department of Health and Human Services, except that, pursuant to Section 304(g)(2)(B) of the FD&C Act, 1) a device may be moved and processed under 21 CFR 800.55(h)(2), and 2) a drug may be moved and processed under 21 CFR 1.980(h)(2). An article of food detained pursuant to Section 304(h) of the FD&C Act shall not be consumed, moved, altered or tampered with in any manner during the detention period, unless the detention order is first modified under 21 CFR 1.381(c).

10. NAME OF DETAINED ARTICLE(S)

11. SIZE OF DETAINED LOT

12. DETAINED ARTICLE(S) LABELED *(Include Master Carton Label)*

15. REASON FOR DETENTION

16. DETAINED ARTICLE(S) STORED AT *(Name, Address, ZIP Code)*

17. NAME AND TITLE OF PERSON WHO APPROVED THE DETENTION ORDER

18. APPROVAL OF DETENTION ORDER ☐ Written ☐ Verbal

20. STORAGE OF DETAINED ARTICLES *(Select appropriate – Per 21 CFR1.393(b)(7), the detained articles must be stored by only these methods.)*
☐ N/A ☐ Refrigerated at ____ ° F ☐ Frozen ☐ Ambient ☐ Other *(For non-temperature related storage conditions; specify)*:

NAME OF FDA EMPLOYEE *(Type or print)*

TITLE *(FDA Employee)*

SIGNATURE *(FDA Employee)*

FORM FDA 2289 (01/22) **DETENTION ORDER** **1**

PSC Publishing Services (301) 443-6740 EF

■ See Instructions following page 5 in this electronic form version.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DETENTION ORDER

1a. DIVISION ADDRESS

1b. PHONE NUMBER

1c. NAME OF DIVISION DIRECTOR

1d. EMAIL ADDRESS

1e. FAX NUMBER

2. NAME OF CUSTODIAN

TO:

3. DETENTION ORDER NUMBER

DO

4. TITLE OF CUSTODIAN

5. TELEPHONE NUMBER

6. DATE AND HOUR DETAINED

a.m.

p.m.

7. FIRM NAME

8. ADDRESS *(Street, City, State, ZIP Code)*

9. MAXIMUM DETENTION

_____ DAYS

Pursuant to *(Check applicable Section(s))* ☐ Section 304(h) of the Federal Food, Drug and Cosmetic Act (FD&C Act),
☐ Section 304(g) of the FD&C Act, ☐ Sections 402 and 409b of the Federal Meat Inspection Act,
☐ Sections 19 and 24(b) of the Federal Poultry Inspection Act, and/or ☐ Sections 19 and 23(d) of the Federal Egg Products Inspection Act,
the article(s) listed in blocks 10 - 12 below on this form must not be used, moved, altered or tampered with in any manner during the detention period without the written permission of an authorized representative of the Secretary of the U.S. Department of Health and Human Services, except that, pursuant to Section 304(g)(2)(B) of the FD&C Act, 1) a device may be moved and processed under 21 CFR 800.55(h)(2), and 2) a drug may be moved and processed under 21 CFR 1.980(h)(2). An article of food detained pursuant to Section 304(h) of the FD&C Act shall not be consumed, moved, altered or tampered with in any manner during the detention period, unless the detention order is first modified under 21 CFR 1.381(c).

10. NAME OF DETAINED ARTICLE(S)

11. SIZE OF DETAINED LOT

12. DETAINED ARTICLE(S) LABELED *(Include Master Carton Label)*

13. APPROXIMATE VALUE OF LOT

14. SAMPLE NUMBER

15. REASON FOR DETENTION

16. DETAINED ARTICLE(S) STORED AT *(Name, Address, ZIP Code)*

17. NAME AND TITLE OF PERSON WHO APPROVED THE DETENTION ORDER

18. APPROVAL OF DETENTION ORDER ☐ Written ☐ Verbal

19. NAME AND ADDRESS OF ARTICLE(S) OWNER

20. NAME AND ADDRESS OF INITIAL SHIPPER OR SELLER

21. NAME AND ADDRESS OF SUBSEQUENT SHIPPERS OR SELLERS *(Continue in Remarks, if necessary)*

22. NAME OF CARRIERS

23. DATE LOT SHIPPED

24. NAME AND ADDRESS OF PACKING PLANT

25. DATE LOT RECEIVED

26. PACKING PLANT USDA NUMBER

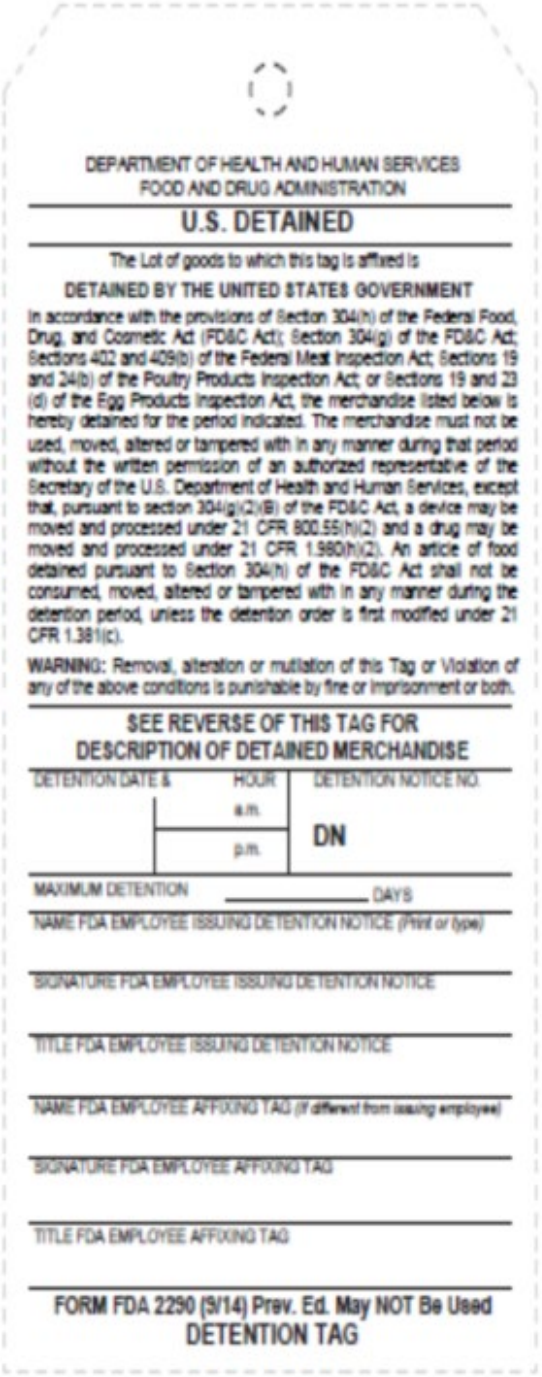
27. DESCRIPTION OF SAMPLE

28. STORAGE OF DETAINED ARTICLES *(Select appropriate – Per 21 CFR1.393(b)(7), the detained articles must be stored by only these methods.)*
☐ N/A ☐ Frozen ☐ Other *(For non-temperature related storage conditions; specify)*: _____
☐ Refrigerated at _____ ° F ☐ Ambient

NAME OF FDA EMPLOYEE *(Type or print)* | TITLE *(FDA Employee)* | SIGNATURE *(FDA Employee)*

FORM FDA 2289 (01/22) DETENTION ORDER 2

2-3 – FDA 2290 – Detention Tag



DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

U.S. DETAINED

The Lot of goods to which this tag is affixed is

DETAINED BY THE UNITED STATES GOVERNMENT

In accordance with the provisions of Section 304(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); Section 304(g) of the FD&C Act; Sections 402 and 409(b) of the Federal Meat Inspection Act; Sections 19 and 24(b) of the Poultry Products Inspection Act; or Sections 19 and 23 (d) of the Egg Products Inspection Act, the merchandise listed below is hereby detained for the period indicated. The merchandise must not be used, moved, altered or tampered with in any manner during that period without the written permission of an authorized representative of the Secretary of the U.S. Department of Health and Human Services, except that, pursuant to section 304(g)(2)(B) of the FD&C Act, a device may be moved and processed under 21 CFR 800.55(h)(2) and a drug may be moved and processed under 21 CFR 1.980(h)(2). An article of food detained pursuant to Section 304(h) of the FD&C Act shall not be consumed, moved, altered or tampered with in any manner during the detention period, unless the detention order is first modified under 21 CFR 1.381(c).

WARNING: Removal, alteration or mutilation of this Tag or Violation of any of the above conditions is punishable by fine or imprisonment or both.

SEE REVERSE OF THIS TAG FOR DESCRIPTION OF DETAINED MERCHANDISE

DETENTION DATE &	HOUR	DETENTION NOTICE NO.
	a.m.	DN
	p.m.	

MAXIMUM DETENTION _____ DAYS

NAME FDA EMPLOYEE ISSUING DETENTION NOTICE *(Print or type)*

SIGNATURE FDA EMPLOYEE ISSUING DETENTION NOTICE

TITLE FDA EMPLOYEE ISSUING DETENTION NOTICE

NAME FDA EMPLOYEE AFFIXING TAG *(If different from issuing employee)*

SIGNATURE FDA EMPLOYEE AFFIXING TAG

TITLE FDA EMPLOYEE AFFIXING TAG

FORM FDA 2290 (3/14) Prev. Ed. May NOT Be Used
DETENTION TAG

U.S. DETAINED

NAME OF DETAINED ARTICLE

DETAINED ARTICLE LABELED

SIZE OF DETAINED LOT

SEE REVERSE

FORM FDA 2290 (3/14)

2-4 – FDA 2291- Detention Termination

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DETENTION TERMINATION NOTICE

1a. Division Address

1b. Phone Number

1c. Name of Division Director

TO: 2. NAME OF CUSTODIAN

3. DETENTION NOTICE NUMBER
DN

4. TITLE OF CUSTODIAN

5. DATE AND HOUR DETAINED
a.m.
p.m.

6. FIRM NAME

7. DATE AND HOUR DETENTION TERMINATED
a.m.
p.m.

8. ADDRESS (Street, city, and State)

9. ZIP CODE

The merchandise listed below which, pursuant to Sections 402 and 409(b) of the Federal Meat Inspection Act; Sections 19 and 24(b) of the Poultry Products Inspection Act; Sections 19 and 23(d) of the Egg Products Inspection Act; or Sections 304(g) or 304(h) of the Federal Food, Drug, and Cosmetic Act, was detained on the above date and bears the above detention number, is hereby released and the detention is terminated.

10. NAME OF DETAINED ARTICLE

11. SIZE OF DETAINED LOT

12. DETAINED ARTICLE LABELED (Include Master Carton Label)

NAME OF FDA EMPLOYEE (Type or print)

TITLE (FDA Employee)

SIGNATURE (FDA Employee)

FORM FDA 2291 (1/22) DETENTION TERMINATION NOTICE 1

PSC Graphics (301) 443-1090

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DETENTION TERMINATION NOTICE

1a. Division Address

1b. Phone Number

1c. Name of Division Director

TO:

2. NAME OF CUSTODIAN

3. DETENTION NOTICE NUMBER

DN

4. TITLE OF CUSTODIAN

5. DATE AND HOUR DETAINED

a.m.

p.m.

6. FIRM NAME

7. DATE AND HOUR DETENTION TERMINATED

a.m.

p.m.

8. ADDRESS (Street, city, and State)

9. ZIP CODE

The merchandise listed below which, pursuant to Sections 402 and 409(b) of the Federal Meat Inspection Act; Sections 19 and 24(b) of the Poultry Products Inspection Act; Sections 19 and 23(d) of the Egg Products Inspection Act; or Sections 304(g) or 304(h) of the Federal Food, Drug, and Cosmetic Act, was detained on the above date and bears the above detention number, is hereby released and the detention is terminated.

10. NAME OF DETAINED ARTICLE

11. SIZE OF DETAINED LOT

12. DETAINED ARTICLE LABELED (Include Master Carton Label)

REMARKS

NAME OF FDA EMPLOYEE (Type or print)

TITLE (FDA Employee)

SIGNATURE (FDA Employee)

FORM FDA 2291 (1/22) DETENTION TERMINATION NOTICE 2