Chapter 5 - Inspections

Chapter 5 - Inspections 1

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5-1 FORM FDA 482 NOTICE OF INSPECTION

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION	1. DISTRICT OFFICE ADDRESS & PHONE NO. 1431 Harbor Bay Parkway Alameda, CA 94502 (510)337-6700

TO			
	2. NAME AND TITLE OF INDIVIDUAL Helen E. Castro, President		3. DATE 07/28/13
	4. FIRM NAME ABC Bread Company	5. HOUR	7:30 a.m.
	6. NUMBER AND STREET 579 Main Street		p.m.
	7. CITY AND STATE & ZIP CODE Richmond, CA 94805		8. PHONE NO. & AREA CODE (510)123-4567

Notice of Inspection is hereby given pursuant to Section 704(a)(1) of the Federal Food, Drug, and Cosmetics Act [21 U.S.C. 374(a)][1] and/or Part F or G, Title III of the Public Health Service Act [42 U.S.C. 262-264][2]

As a small business that is subject to FDA regulation, you have the right to seek assistance from the U.S. Small Business Administration (SBA). This assistance includes a mechanism to address the enforcement actions of Federal agencies. SBA has a National Ombudsman's Office that receives comments from small businesses about Federal agency enforcement actions. If you wish to comment on the enforcement actions of FDA, CALL (888) 734-3247. The website address is www.sba.gov/ombudsman.

FDA has an Office of the Ombudsman that can directly assist small business with complaints or disputes about actions of the FDA. That office can be reached by calling (301) 796-8530 or by email at ombuds@oc.fda.gov.

For industry information, go to www.fda.gov/oc/industry.

9. SIGNATURE(S) *(Food and Drug Administration Employee(s))*	10. TYPE OR PRINT NAME(S) AND TITLE(S) *(FDA Employee(s))*
Sidney H. Rogers	Sidney H. Rogers, Investigator

[1] **Applicable portions of Section 704 and other Sections of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374] are quoted below:**

Sec. 704(a)(1) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, tobacco products, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, tobacco products, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any person (excluding farms and restaurants) who manufactures, processes, packs, transports, distributes, holds, or imports foods, the inspection shall extend to all records and other information described in section 414, when the standard for records inspection under paragraph (1) or (2) of section 414(a) applies, subject to the limitations established in section 414(d). In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs, nonprescription drugs intended for human use, restricted devices, or tobacco products are manufactured, processed, packed, or held, inspection shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs, nonprescription drugs intended for human use, restricted devices, or tobacco products which are adulterated or misbranded within the meaning of this Act, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data (other than data as to qualifications of technical and professional personnel performing functions subject to this

(Continued on Reverse)

Act), and research data (other than data relating to new drugs, antibiotic drugs, devices, and tobacco products and subject to reporting and inspection under regulations lawfully issued pursuant to section 505 (i) or (k), section 519, section 520(g), or chapter IX and data relating to other drugs, devices, or tobacco products, which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(j)). A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.

Sec. 704. (a)(2) The provisions of the third sentence of paragraph (1) shall not apply to (A) pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not, either through a subsidiary or otherwise, manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail; (B) practitioners licensed by law to prescribe or administer drugs, or prescribe or use devices, as the case may be, and who manufacture, prepare, propagate, compound, or process drugs, or manufacture or process devices solely for use in the course of their professional practice; (C) persons who manufacture, prepare, propagate, compound, or process drugs, or manufacture or process devices solely for use in research, teaching, or chemical analysis and not for sale; (D) such other classes of persons as the Secretary may by regulation exempt from the application of this section upon a finding that inspection as applied to such classes of persons in accordance with this section is not necessary for the protection of the public health.

Sec. 704. (a)(3) An officer or employee making an inspection under paragraph (1) for purposes of enforcing the requirements of section 412 applicable to infant formulas shall be permitted, at all reasonable times, to have access to and to copy and verify any records (A) bearing on whether the infant formula manufactured or held in the facility inspected meets the requirements of section 412, or (B) required to be maintained under section 412.

Sec. 704(b) Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, tobacco product, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary.

Sec. 704. (c) If the officer or employee making any such inspection of a factory, warehouse, or other establishment has obtained any sample in the course of the inspection, upon completion of the inspection and prior to leaving the premises he shall give to the owner, operator, or agent in charge a receipt describing the samples obtained.

Sec. 704. (d) Whenever in the course of any such inspection of a factory or other establishment where food is manufactured, processed, or packed, the officer or employee making the inspection obtains a sample of any such food, and an analysis is made of such sample for the purpose of ascertaining whether such food consists in whole or in part of any filthy, putrid, or decomposed substance, or is otherwise unfit for food, a copy of the results of such analysis shall be furnished promptly to the owner, operator, or agent in charge.

Sec. 704(e) Every person required under section 519 or 520(g) to maintain records and every person who is in charge or custody of such records shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and to copy and verify, such records.

Section 704 (f)(1) An accredited person described in paragraph (3) shall maintain records documenting the training qualifications of the person and the employees of the person, the procedures used by the person for handling confidential information, the compensation arrangements made by the person, and the procedures used by the person to identify and avoid conflicts of interest. Upon the request of an officer or employee designated by the Secretary, the person shall permit the officer or employee, at all reasonable times, to have access to, to copy, and to verify, the records.

Section 512 (l)(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A), and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m) (4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

[2] Applicable sections of Parts F and G of Title III Public Health Service Act [42 U.S.C. 262-264] are quoted below:

Part F – Licensing – Biological Products and Clinical Laboratories and* * * * * *

Sec. 351(c) "Any officer, agent, or employee of the Department of Health and Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation

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5.1 – General Inspection Information

This chapter will provide you with inspection guidance. It consists of both a general section and sections related to specific product categories. You should become familiar with the material in both the general section and your product specific area.

5.1.1 – Definition / Purpose of Inspections

An inspection, as described in Section 704(a)(1) of the Food Drug & Cosmetic (FD&C) Act [21 U.S.C. 374], involves duly designated officers or employees of the FDA physically entering (at reasonable times and in a reasonable manner), establishments subject to regulation under the Act to determine compliance with applicable FDA requirements (See IOM 3.2.3). There are three general categories of inspections:

- **Surveillance (also called routine) inspections**, which are conducted to generally determine or monitor a firm's compliance with regulatory requirements.
- **Pre-approval, pre-market, or pre-license inspections**, which are conducted, when necessary, as part of the review of an application to market a new product.
- **For-cause inspections**, which are prompted when there is reason to believe a facility has serious manufacturing problems, or to investigate a specific problem/product complaint that has come to FDA's attention.

5.1.2 – Inspectional Approach

Your inspectional approach may vary depending on the reason or basis for the inspection. You should determine, during your preparation, what type of approach will work best and prove most effective for the assignment. This may mean focusing your examination on a specific location within the facility or on a particular phase of manufacturing associated with a potential concern. (For example, if you are following up on a complaint alleging records are not being contemporaneously recorded during production activities, you may want to observe the manufacturing conditions immediately after displaying FDA credentials and issuing the FDA 482, Notice of Inspection, before holding your introductory meeting or walkthrough of the plant.)

5.1.3 - Authority to Enter and Inspect (Domestic, Foreign)

(See IOM 3.2 for detailed information about your statutory authority to enter and inspect firms.)

Keep in mind that it is your obligation to fulfill the requirements described below in IOM 5.1.4. A failure to do so may prevent use of evidence and information obtained during the inspection.

Note, too, that you may occasionally be accompanied on your inspection by other officials. These may be state or local officials who have their own inspectional authority, or other officials who do not have authority to enter the firm. You should obtain permission from the firm's most responsible individual if officials without inspectional authority wish to accompany you during your inspection. You should document in your establishment inspection report (EIR) instances in which any non-FDA officials accompany you during your inspection, and whether they entered under their own authority, or through the permission of an individual at the firm. Be sure to identify, by name and title, the responsible individual giving permission. (See IOM 5.5.1 and 5.3.4.6.2 for more).

5.1.4 - Responsibilities of Investigators

Section 704 of the FD&C Act sets requirements on how you should conduct inspections.

Accordingly, it is your responsibility to conduct all inspections at reasonable times, within reasonable limits, and in a reasonable manner. Proceed with professionalism, using ethical behavior, diplomacy, tact, and consideration. You are expected to dress neatly, professionally and in a manner that is appropriate for your assigned duties. When possible, you should conduct your inspection on consecutive business days. If there will be breaks in the inspection, you should

advise firm management promptly and tell them when the inspection will resume (see IOM 5.5.1.1). During the inspection, you should update the firm management periodically to discuss your findings and any objectional conditions per IOM 5.5.12.1.

It is also your responsibility to understand the authority the FDA has under the Act and any associated regulations, as certain authorities pertain to specific products. (IOM Chapter 3.2.3 describes FDA's authority to inspect different product commodities, while IOM Chapter 3.2.4 describes the limitations of those authorities.)

Above all, remember that during any inspection in which you find or collect evidence of conditions indicating a reasonable probability that the associated products will cause imminent and serious adverse health consequences or death, you should notify your supervisor immediately.

5.1.4.1 – FDA Credentials

Display your FDA credentials to the most responsible individual onsite at the time you arrive to initiate the inspection at the firm[1] or the facility you are inspecting. The most responsible individual may also be the top management official for the firm. The top management official refers to the most responsible individual for the overall company, corporation, business, etc. However, the top management official may or may not be present during an inspection. (See IOM 5.5.1.) In a team inspection, remember that all FDA participants must display their individual credentials. Team leaders should ensure all participants have valid credentials before entering the firm.

NOTE: Although management may examine your credentials and record their number, as well as your name, do not permit your credentials to be photocopied. Federal Law (18 U.S.C. 701) prohibits photographing, counterfeiting, or misusing official credentials. Additionally, do not permit a firm to take your fingerprints. If the firm insists on taking your fingerprints, contact your supervisor.

5.1.4.2 – Forms

This section summarizes several forms you may use, as required, during most inspections. It is important to issue the correct form to the correct person. The Act specifically directs you to issue forms to "the owner, operator, or agent-in-charge."

5.1.4.2.1 - Written Notice

After showing your credentials, issue the original, properly executed, and signed FDA 482, Notice of Inspection, to the most responsible individual at the firm. Keep a copy for submission with your report. A Notice of Inspection is not required to be issued during foreign inspections (refer to 5.5.8); however, credentials should still be presented to the most responsible individual at the firm.

In a team inspection, all FDA participants must sign the FDA 482. If an FDA employee or employees join a team inspection *after* the issuance of the FDA 482, a new FDA 482 must be issued and signed, but only by the new participant(s).

If any errors are noted while issuing the FDA 482, you should make any necessary additions, deletions, or corrections, but be sure to notate them in this way: strike-throughs for deletions, brackets [ ] for additions, and initials and dates next to all changes.

5.1.4.2.2 – Written Observations

Upon completing the inspection but before leaving the premises, provide the most responsible individual at the time of closeout (this would be the top management official if they are present) with your inspectional findings on an FDA 483, Inspectional Observations; an FDA 483a, Foreign Supplier Verification Program (FSVP)

[1] The terms firm and establishment are often used interchangeably. In the context of this chapter the terms mean the specific location being inspected. In some circumstances, a "firm" may be an individual (for example, a clinical investigator).

Observations (for FSVP inspections); or an FDA 4056, Produce Farm Inspection Observations (for produce safety inspections). (For more details, see Section 704(b) of the FD&C Act [21 U.S.C. 374(b)] and IOM 5.5.10 and 5.5.11.6. For details on the FDA 4056 see Exhibit 5-17)

5.1.4.2.3 – Receipts

When you collect any physical sample during an inspection, you must issue an FDA 484, Receipt for Samples, to the most responsible individual (or top management official if present). As with written observations, the original receipt is to be issued to the most responsible individual, upon completion of the inspection and prior to leaving the premises, with a copy to be kept for submission with your report. (See Section 704(c) of the FD&C Act [21 U.S.C. 374(c)], IOM 5.5.13.5, and 4.2.5 for more information on issuing the FDA 484.)

5.1.4.2.4 - Written Demands or Requests for Information

This section does not address requests for records under Section 704(a)(4) of the FD&C Act [21 U.S.C 374(a)(1) which provides FDA authority to obtain records "in advance of or in lieu of an inspection". Please talk to your supervisor if you intend to obtain records under 704(a)(4).

There are several methods of requesting records. These may include a request for information based upon the following: Low Acid Canned Food (LACF) or Acidified Food (AF) regulations, FDA 482d, Request for FSVP Records, 703 written requests, and requests for records under the Bioterrorism Act (for more, see IOM 3.2.3.1 and 5.8.1.1).

Per CPG Sec. 160.300, any evidence associated with Requests for Records under Section 703 of the FD&C Act [21 U.S.C. 373], in other words obtained in response to a specific written request under Section 703, cannot be used in a criminal prosecution of the person from whom the evidence was obtained. With supervisory approval, in certain circumstances, you may decide to issue a 703 written request when the significance of the evidence is crucial to protecting the public health. (See IOM 4.4.4.2 for more information, including procedures for requesting records under Section 703 authority.)

5.1.4.3 – Business Premises

IOM 5.1.3. describes FDA's authority to inspect firms operating at a business location. A few unique business premise situations are described below.

5.1.4.3.1 – Premises Used for Living Quarters

All inspections where the premises are also used for living quarters must be conducted with a warrant for inspection, unless the inspection qualifies as one of the following:

- **Owner Agreeable** – The owner or operator is fully agreeable and offers no resistance or objection whatsoever. In this case, clearly document in the EIR that you are inspecting a residence and that the owner was agreeable.
- **Physically Separated** – The actual business operations to be inspected are physically separated from the living quarters by doors or other building construction, such that there is a distinct division of the premises into two physical areas: one for living quarters and the other for business operations. Do not enter the living quarters.

In both cases, proceed as any other inspection with the appropriate presentation of credentials and issuance of a Notice of Inspection.



Special note: For personal safety precautions, it is recommended that at least two credentialed FDA employees are present when conducting inspections in a residence.

5.1.4.3.2 – Facilities where Electronic Products are Used or Held

Section 537(a) of the FD&C Act [21 U.S.C. 360nn] provides the FDA with the authority to inspect the facilities of such manufacturers in certain circumstances. However, this authority is limited. The agency must find "good cause" that methods, tests, or programs related to radiation safety (such as noncompliance with a standard) may be inadequate or unreliable. (IOM 3.2.3.1 describes the authority for these inspections in detail.

IOM 10.15.2 describes important radiation hazard safety considerations.

5.1.4.3.3 – Multiple Occupancy Inspections

You are required per Section 704(a)(1) of the FD&C Act [21 U.S.C 374(a)(1)] to issue a Notice of Inspection, FDA 482, to each firm inspected.

5.1.4.3.4 – Multi-Site Establishments

When firms have operations located in different sites or buildings, you should use your best judgment to determine when multiple FDA 482 forms need to be issued. For sites located a fair distance apart, it is preferable to issue an FDA 482 to the most responsible individual at each site. A helpful rule of thumb: If the sites or buildings are within walking distance, your original Notice of Inspection should be considered sufficient to cover both sites. During your initial interview with management, after you issue the FDA 482, make sure you clearly indicate to firm management the facility and sites you intend to inspect. Remember that while the Act requires the issuance of a Notice of Inspection, it does not prohibit issuing multiple notices, if management so requests. As with all our work, your good judgment and knowledge of the official establishment inventory (OEI) and the FD&C Act, are necessary in deciding what to do.

5.1.4.4 – Products Imported Under the Provisions of Section 801(d)(3) of the FD&C Act (Import for Export)

Products otherwise not permitted entry into the United States may be imported under the authority commonly called “Import for Export.”

The FDA Export Reform and Enhancement Act of 1996 (PL 104-134 and 104-180) amended the FD&C Act by adding Section 801(d)(3) of the FD&C Act [21 U.S.C. 381(d)(3)] ("Import Export") which permits the importation of unapproved drug and medical device components, food additives, color additives, and dietary supplements intended for further incorporation or processing into products destined for export from the United States. Section 801(d)(3) was subsequently amended by Section 322 of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Act), Public Law 107-188, which specified certain requirements an importer must satisfy in order to import a product under this Section. (See IOM 6.1.4.6 for more.)

5.1.4.4.1 – Requirements for Bioterrorism Act

These requirements must all be met by the importer/owner:

- A statement confirming the intent to further process such article, or incorporate such article into a product to be exported,
- The identification of all entities in the chain of possession of the imported article,
- A certificate of analysis "as necessary to identify the article" (unless the article is a device), and
- The execution of a good and sufficient bond providing for liquidated damages in the event of default, in accordance with U.S. Customs.

In addition, the initial owner or consignee must keep records showing the use of the imported articles and must be able to provide upon request a report showing the disposition or export of the imported articles. An article imported under this section, and not incorporated or further processed, must be destroyed, or exported by the owner or consignee. Failure to keep records or to make them available to the FDA, making false

statements in such records, failure to export or destroy imported articles not further incorporated into finished products, and introduction of the imported article or final product into domestic commerce are all Prohibited Acts under Section 301(w) of the Act [21 U.S.C. 331(w)].

Filers making entry under the Import for Export provisions must identify entry/line submissions with the intended use code Import for Export and Affirmation of Compliance "IFE" (Import for Export), and supply FDA with written documentation stating the product is entered under the Import for Export provisions. A Certificate of Analysis (as necessary) and identification of all involved entities must be submitted in writing to the import program division. The import program division will ensure all written documentation has been uploaded to the entry/line. The Office of Import Operations (OIO) will make IFE entry information and documentation available to the home program division of the initial owner or consignee through the "*Import for Export - IFE*" section in OSAR Firm 360 and ORADSS report "*IMP046 Import for Export Entry Lines and Documents.*"

5.1.5 – Confidential and Trade Secret Information

You have certain responsibilities under the FD& C Act Section 301(j) [21 U.S.C. 331(j)]; Sections 319 and 359 of the Public Health Service Act; and Section 1905 of the Federal Confidential Statute (Privacy Act) (18 U.S.C. 1905) regarding protection of confidential material obtained during your official duties. See IOM 2.3.

The FDA has the authority to inspect most types of records including, trade secret and other confidential records. The authority does not extend to certain records such as financial data, sales data (other than shipment data), pricing data, personnel data (other than data as to qualification of technical and professional personnel performing functions subject to this chapter), and research data (other than data required to be maintained under regulations or the Act).

Manufacturers may mark information within submitted records as "confidential" or "trade secret." You may advise manufacturers they may mark as confidential those records they deem proprietary to aid the FDA in determining which information may be disclosed under Freedom of Information Act (FOIA). The firm choosing to mark or not mark a document does not change whether the information may be subject to release under the Act. (See 21 CFR 20.61(d).)

Some firms often contend that their entire process and formulas are "trade secrets." However, the term "trade secret" should only be used to cover the manufacturing process and/or quantitative-qualitative formulation that is truly unique to the firm (see 21 CFR 20.61(a)). Confidential information, in particular, includes commercial or financial information customarily kept private, or at least closely held, by the submitter. (See 21 CFR 20.61(b).)

Therefore, and per 21 CFR 20.27, a firm's act of simply "marking records submitted to the FDA as confidential, or with any other similar term, raises no obligation by the FDA to regard such records as confidential, to return them to the person who has submitted them, to withhold them from disclosure to the public, or to advise the person submitting them when a request for their public disclosure is received or when they are in fact disclosed." The same applies to other designations that appear to be frivolous, as outlined at 21 CFR 20.61(f)(5).

Any designations whether in part or in whole by the submitter must clearly meet the definitions of "trade secret" or "confidential commercial" information. Furthermore, justification of why this information should be withheld may be requested as needed by agency information disclosure staff.

Additionally, "data and information submitted or divulged to the FDA which fall within the definitions of trade secret or confidential commercial or financial information are not available for public disclosure" (21 CFR 20.61(c)) and will be held in confidence by the FDA unless release is required or authorized by regulation, statute, or court order. (See also 21 CFR 20.28.)

Sharing of information (regardless of the manner) must comply with the Freedom of Information Act (FOIA); other applicable laws, such as the Privacy Act and the Trade Secret Act; and FDA procedures and regulations. For more on

other potentially relevant laws, see 21 CFR Part 20 Subpart–D - Exemptions, other CFR disclosure references, and RPM Chapter 3, Commissioning and Information Sharing.

Use care so that any information collected is protected from release during the inspection. This includes proactively guarding against accidental release. For example, do not leave records exposed on the seat of your GOV and do not review records on public transit where someone may view them without your knowledge (for example, peering over your shoulder). Unauthorized disclosure of confidential, commercial, or financial information, trade secrets, or personal privacy information could be a civil or criminal violation and may carry legal or other consequences for the disclosing official. (See IOM 2.3.)

If non-public information is inadvertently, or accidentally, disclosed, follow ORA's Addressing Inadvertent Disclosures SOP. Immediately report the loss or theft of any device or equipment capable of storing data to the FDA Cybersecurity and Information Operations Coordination Center at CIOCC@fda.hhs.gov. Any information disclosure questions should be directed to the Division of Information Disclosure Policy (DIDP) at ORAinfoshare@fda.hhs.gov.

(See also IOM 5.5.9.3 concerning information sharing with persons invited by the firm to participate in the inspection.)

5.1.6 – Common Reasons for Inspections

Your assignment should provide you with information conveying the inspection basis or type of inspection to be conducted. If there is no inspection basis provided, ask your supervisor for the purpose of the inspection.

Some reasons for inspections include:

- Surveillance inspection (also called routine or workplan inspections)
- Recall follow-up
- Consumer complaint follow-up
- Follow-up to a whistleblower complaint
- Follow-up to a compliance action, such as a warning letter or seizure

The purpose of the inspection will often provide you with an area to focus on during the inspection. For example, during a recall follow-up inspection, you will likely focus on the firm's recall activities and procedures. But, regardless of the purpose of the inspection, if you observe issues in other areas that may result in product adulteration or misbranding, you should follow-up on those items diligently, too, as time permits.

5.2 – Pre-Inspection Activities

Information contained in the subsections under 5.2 is general in nature and may apply to multiple programs. For commodity specific content, refer to subchapters for the individual programs.

Good preparation helps ensure that your inspection proceeds smoothly and that all issues are covered. However, there may be times when you will not be able to conduct a thorough review of all materials or inspection information prior to an inspection, including, for example, in the event of an urgent public health emergency when you may need to travel unexpectedly to an inspection site without time for preparatory research or review. In these cases, you should plan to review the materials described in this section as soon as the situation is resolved, or you are able.

Before the start of any inspection, you should conduct several activities. Begin by reviewing the establishment's history, to include any previous EIRs, complaints, registrations, and listings, recalls, personal safety alerts, etc. The purpose of this review is to determine the location of the establishment, obtain an overview of its operations and products and understand its compliance history.

Conducting a consumer complaint review will help you identify any complaints that require follow-up during your inspection, including any with the status "Surveillance information for next EI" that will need to be addressed and closed. (See IOM 5.2.3)

You should also review the establishment file to determine if there are any prior safety issues noted, (for example, any, documented investigator safety incidents or suggestions for specific personal protective equipment needed prior to the start of the inspection (See IOM 5.3). Plan to review the eNSpect assignment to determine if the Personal Safety Alert (PSA) Indicator is set to “yes” for this specific firm. If so, the reason or reasons for the PSA should be listed in the Endorsement section for the previous inspection and should be accompanied by a memo to the establishment file. Note, too, that for some firms, the PSA may be in the hardcopy establishment file, and not captured in Online Search and Retrieval (OSAR). (For more, see IOM 10.3.2, Personal Safety Alerts). If you discover that there has, in fact, been a past personal safety incident, you should discuss the details with your supervisor and develop a Personal Safety Plan prior to the start of the inspection. (See IOM 10.3, Personal Safety.)

You should become familiar with the reporting requirements for the specific assignment, as well as the requirements of IOM 5.7 (Reporting).

If the inspection is a directed assignment from an FDA center, OII headquarters, or another program division, read the assignment and attached materials to ensure you understand the assignment.

If the inspection is being conducted in part or solely as a follow-up to a recall or consumer complaint, refer to Chapter 7 (Recalls) or Chapter 8 (Investigations) of the IOM for additional guidance.

You should also plan to review the applicable compliance programs prior to the start of your inspection. In addition, the centers have issued numerous guidance documents for industry, which you should also become familiar with. These documents are normally posted to the appropriate center's internet website. You should also determine if there are any "import for export" follow-up assignments and be prepared to cover them as needed during your inspection. (See IOM 6.1.4.6 for more guidance.)

5.2.1 – Scope of Inspection

An establishment inspection is a careful, critical, and official examination of a facility to determine its compliance with the laws and regulations administered by the FDA. Inspections may be used to collect evidence to document violations and to support regulatory action, when appropriate; or they may be directed to obtain specific information on new technologies, commercial practices, or data for establishing food standards or other regulations.

With regards to facilitating on-the-job training or gathering multiple points of view or perspectives of firms being inspected, whenever practical, personnel with assignment authority should consider designating different investigator/s, or different lead investigators, at different times. This is recommended particularly when there have been multiple sequential NAI inspections or when the firm's management has been uncooperative.

The approach and scope (for example, full scope, limited scope; Level I, II or III; and full or abbreviated) you will use to conduct an inspection is defined by the compliance program, assignment, and/or your supervisor. Inspections may require that you conduct a general review of the firm’s operations and records for compliance, or, alternatively, that you direct your focus to certain operations or products. The degree and depth of attention given to various operations in a firm depends upon the information needed, or upon the violations suspected, or likely, to be encountered. The amount of time and attention required for a specific case will depend, at the least, on the following:

- Current compliance program
- Nature of the assignment
- General knowledge of the industry and its problems
- Firm history
- Conditions found as the inspection progresses.

As always, be sure to contact your supervisor should you encounter, or observe, any objectionable conditions that may be of public health significance, or that implicate establishments in other division(s). (See IOM Chapter 10 for more

information on safety, the use of protective gear, dealing with potential hazards and other safety issues, and trash disposal.)

5.2.2 – Domestic Follow-up of Import for Export Entries

In preparation for a domestic inspection of the initial owner or consignee, the domestic division should:

1. Review entry/line data and entry using the "*Import for Export - IFE*" section in OSAR Firm 360 and ORADSS report "*IMP046 Import for Export Entry Lines and Documents"* to determine if the firm has records of IFE entry/lines. The entry/line data can be found in the *"Shipment Lines"* worksheets. Links to the entry/line documents can be found in the *"Links"* worksheets which will contain the entry/line number, consignee/importer information and the document links. Additionally, the link to the report can also be found on the Office of Import Operations (OIO) Import for Export (IFE) intranet site.
2. If IFE entry/lines are noted in the report, follow-up of IFE entry/lines should be done during the initial owner or consignee domestic inspection. IFE entry/lines for the firm should be investigated during the inspection as outlined in section 5.5.7.5.

5.2.3 - Consumer Complaint Review

This section covers general information related to consumer and other complaints. Additional details can be found in program-specific sections, IOM 8.1.5.7, and other sections in Chapter 8 that cover complaint investigations.

Prior to conducting any inspection, you should review CMS, Complaint Dashboard, Firm 360, and the firm history to become familiar with all FDA complaint/injury records. Note that you may need to request from the Consumer Safety Reporting Team additional information about particular complaints not found, or seemingly missing, in FDA systems. Be especially alert to any complaints marked "Surveillance Information for Next EI," as these will need to be addressed during your inspection. When using OSAR and Firm 360 to review complaints, note that the "more detail" link needs to be opened to determine if the complaint was previously followed up on, or if it still requires follow-up.

5.2.4 – Technical Assistance

If you determine that specialized technical assistance is necessary in conducting inspections of new technologies, products, or manufacturing procedures, it may be available through Regulatory Technical Assistance Network (rTAN), Produce Safety Network, programmatic or national experts, other OII components, or center scientists and engineers. Check Compliance Programs for a list of contacts for technical experts as well.

If additional technical assistance is needed, contact your supervisor.

5.2.5 – Review of Compliance Actions and Recalls

During your pre-inspectional activities, you should note any compliance actions, recalls, and/or import alerts for products related to the firm you are inspecting. These may be found in the inspection assignment, OSAR and/or Firm 360. The Compliance Management System (CMS) can also provide detailed information. Focus on any potential problems that might have led to these actions and how they relate to the firm's operations. This review can help guide your inspection activities as you will want to determine if any referenced issues are still relevant for products you will cover.

(Each program has more details in its own section of this chapter of the IOM, starting with 5.8 – Foods, 5.9 – Cosmetics, etc.)

If your inspection finds issues with current products that may result in a recall, market withdrawal, or import alert, please notify your supervisor, and reference IOM chapters 6 and 7.

5.2.6 - Coordination with Centers/Compliance Branch/Laboratories/SLTT

Coordination with internal and external partners (for example, center(s); state liaisons; and state, local, tribal, and territorial agencies) may be a necessary component of your pre-inspectional activities. You should refer to the inspection assignment and any relevant Compliance Program(s) to determine the appropriate contacts in the center(s) for your inspection. The assignment may also request a pre-inspectional meeting with the compliance officer in the center(s) (as in the case of a recall follow-up, in which you may need to discuss the assignment with the division recall coordinator).

Additionally, there will be inspections/investigations where coordination with the state liaisons will be important to ensure collaboration with our state and local partners. Be aware of assignment-specific directions that may require the pre-notification of state partners (like, for example, the State Board of Pharmacy for compound pharmacy inspections). (Refer to IOM Chapter 9.1 for more information on cooperative efforts regarding federal, state, local, tribal, and territorial agencies, and international cooperation. See IOM Chapter 10 regarding coordination with local police for personal safety preparations as necessary.)

5.2.7– Pre-Announcement

Pre-announcements are mandatory for all medical device surveillance inspections—and some Bioresearch Monitoring (BIMO) inspections—in accordance with the criteria and instructions below. Routine produce farm inspections should be pre-announced, unless otherwise directed. (See Exhibit 5-17 for additional information about produce farm inspections). In some other program areas, pre-announcements may be made at the discretion of the program division. In general, though, it may be inappropriate to pre-announce inspections of food establishments, blood banks, source plasma establishments, and some BIMO inspections, but this is subject to program division discretion. If you are going to visit facilities where livestock (including poultry) or wild animals are housed or processed, review Exhibit 5-19 (Biosecurity). It is appropriate to discuss biosecurity procedures when you are inspecting these facilities.

ORA's primary purpose for pre-announcing is to ensure that the appropriate records and personnel will be available so that we may execute an effective inspection. It is *not* to make an appointment for the inspection. When contacting the firm, do not refer to it as an "appointment to inspect." When planning for a pre-announcement, it is important you communicate to the establishment the purpose of the inspection and a general idea of the records you may want to review. If you find, even after making your pre-inspection request known to the firm, that neither the appropriate personnel nor records are available to you during the inspection, note this in your EIR.

In general, the Agency usually announces foreign inspections in advance, partly due to logistics such as arranging travel and access to facilities, securing visas, and partly because of the high costs of conducting foreign inspections.

Unless you are directed to pre-announce an inspection in the compliance program or assignment, discuss pre-announcing with your supervisor and assure that you have management concurrence before contacting the firm. Explain the reason for the pre-announcement in the narrative report. (Subchapters 5.8 through 5.15 of the IOM contain additional, program specific pre-inspectional activities you should follow.)

5.2.7.1 – Criteria for Consideration

The pre-announcement of domestic inspections should generally be no less than five calendar days in advance of the inspection. Should a postponement be necessary, the decision to reschedule rests with the investigator/team, but the new inspection date should not be later than five calendar days from the original date. For changes to foreign inspections work with you trip coordinator. Inspections may be conducted sooner than five calendar days, if requested by or acceptable to the establishment, and if this date is acceptable to the investigator/team.

As noted above, for pre-announcement to be effective, establishments are expected to meet the commitment to have appropriate records and personnel available during the inspection.

Pre-announced inspections must not limit an investigator's authority to conduct the inspection.

5.2.7.2 - eNSpect Reporting

In the eNSpect "Pre-Announced / Unannounced to Firm" field select "Unannounced" when no notification was provided to the firm in advance of arrival at the firm for inspection. Select "Pre-announced" when the firm was notified of the inspection prior to the CSO arrival at the firm for the inspection. (See IOM 5.7 - Reporting)

5.2.8 – Travel Coordination and Planning

Travel is an integral part of inspections. As such, it needs to be planned and well-coordinated to go smoothly. (See IOM 1.2 OII Travel for information regarding travel authorizations using ConcurGOV (CGE).)

See IOM 1.4 - Division of Travel Operations for travel aides to assist you in domestic travel (see IOM 1.4.1) and foreign travel (specifically IOM 1.4.2). Additional sections in this chapter address Per Diem Rates, Actual Expense Reimbursement, Lodging, Miscellaneous Expenses, and Transportation Allowances/Expenses.

See IOM 10.17 - Employee and Traveler Health and Safety provides information on any occupationally related medical services you may need. For instance, immunizations needed prior to foreign travel, may be necessary. You will contact FDA Occupational Health Services (OHS) for such requests. (For more, refer to IOM 10.17.4.2 for details on Foreign Travel and IOM 10.17.5 for Employee and Traveler Safety.)

5.2.8.1 – Domestic

When preparing for a domestic inspection, consider the following questions and consult with your supervisor to help address them as needed:

- Do I need a travel authorization (TA)?
  - Is there enough time for the TA to be completed through the normal process?
- Is a government vehicle available?
  - Do I need to make a request for a specific government vehicle, such as a larger vehicle to transport a larger team for the inspection?
  - Will I have access to the government vehicle on the weekend, or before/after routine office hours, if needed?
- Do I need any special equipment?
  - Will that equipment fit in any government vehicle, or do I need to request a specific type or size of vehicle as noted above?
- Do I need to visit a resident post or laboratory while in travel status?
  - Do I have that associated contact information readily available?
- If I am pre-announcing the inspection, do I complete the TA in CGE before, or after, pre-announcement?
  - If I complete the TA after pre-announcement, will the TA be approved before I start to travel?
- If I am not pre-announcing the inspection, have I confirmed the likely operational status of firm before traveling, by reviewing a firm or establishment's current registration, updated website presence, posted operational hours, etc.?

For more on domestic travel, see IOM Chapter 1.4.1 Domestic Travel.

5.2.8.2 – Foreign

Foreign travel can be stressful, but careful planning and consideration can make travel abroad easier. IOM Chapter 1.4.2 provides you with links to the Foreign Travel SharePoint site, a timeline of the coordination process, and foreign travel contacts.

Before you start your foreign travel, also consider the following:

- Do I need special equipment?
  - How will I most appropriately travel with it? In my unsecured suitcase? Or in my carry-on bag?
- Does my supervisor...
  - Have my trip itinerary in case I need to be reached?
  - Have my government cell phone number in case I need to be reached?
- If I am on a team inspection...
  - Have I or we coordinated where we will meet?
  - Has everyone exchanged government cell phone numbers and is familiar with how to dial out once inside the destination country?
- Other general considerations:
  - Have I included my emergency contact information in my "Traveler's Profile," to be used by the agency in case of any emergency?
  - Have I received my Electronic Country Clearance, or eCC, via email? (Travelers are not supposed to start travel without this document.)
  - Have I secured and saved the local U.S. Embassy number, plus any other emergency numbers for the destination country, in case of emergency?
  - Have I registered my trip details at The Smart Traveler Enrollment Program (STEP)?
    - The Smart Traveler Enrollment Program (STEP) is a free service to allow U.S. citizens and nationals traveling and living abroad to enroll their trip with the nearest U.S. Embassy or consulate.
    - Receive important information from the embassy about safety conditions in your destination country, helping you make informed decisions about your travel plans.
    - Help the U.S. Embassy contact you in an emergency, whether natural disaster, civil unrest, or family emergency.
    - Help family and friends get in touch with you in an emergency.
  - Have I made copies of important documents (including my credentials, passport, driver's license, credit cards, vaccination cards, etc.) so that I'm able to securely keep copies with me while in travel status and at home?
  - Have I reviewed my destination country's corresponding Department of State International Travel page for the very latest health and safety information?
  - Have I packed in my carry-on bag, all necessary work items, like my regulatory notebook and credentials?

5.2.9 – Team Inspections

The use of teams to conduct inspections may be beneficial. Note that a team may consist of multiple investigators, as well as laboratory personnel, other FDA employees, and your supervisor, who may participate as part of the OII Quality Assurance program. Individuals well versed in a particular analytical or inspectional technique or technology are often asked, or selected, to support a team, given their potentially valuable assistance and advice. Combination product inspections also often entail the use of teams so that adequate and appropriate program expertise is brought to bear on these more complex inspections. (See IOM 5.12.1)

When inspection teams are involved in an inspection, the inspecting division will designate one investigator as the team leader. If the assignment is multi-commodity, the assignment will identify the lead program, which will, in turn, identify who the lead investigator will be. The team leader serves a critical role as this person oversees the inspection and bears overall responsibility for the inspection and the EIR. See IOM 5.2.8.1 – Team Member Responsibilities.

Each team member is responsible for preparing those portions of the report pertaining to their activities. Team members shall identify their portion of the narrative report, so they can later identify that portion as the part they performed and reported. Since reports should be written in the first-person point of view, one suggested approach for ensuring clarity surrounding each portion (or investigator contribution) is to head each portion with the statement: "The following operation(s) was/were observed and reported by Investigator _____", who can then continue their respective report in the first person.

As for signatures, all team members must sign the EIR, while only those team members present at issuance are to sign the FDA 483 or FDA 4056. Also, the issuance of the FDA 483 should not be delayed, in the absence of a team member's signature. (See IOM 5.5.10.5 for instructions for signing an FDA 4056 and a multi-page FDA 483.)

5.2.9.1 – Team Leader Responsibilities

The team leader is responsible for the following:

- Directing the overall inspection to accomplish the objectives of the assignment including all of the following most effectively:
  - Planning the inspection, including determining an orderly, efficient, and effective approach and sequence to be used, and discussing this inspection plan with the team.
  - Scheduling and coordinating team members' pre-inspection preparations.
  - Determining, to the extent possible, the firm will be open and operating.
  - Calling to pre-announce an inspection, if required.
  - Planning for needs of visiting scientists, if applicable.
  - When not familiar with all the processes or technology involved in the inspection, providing for primary coverage of those areas by other team members.
  - Modifying the inspection plan as necessary during the EI, to permit the following of leads, documenting evidence, etc.
  - Setting team policy on how communications with the firm are to be handled.
  - Discussing personal conduct in dealing with headquarters personnel as necessary.
  - Ensuring all team members understand their roles, early on, including who will take notes and who will report, etc.
  - Providing for an open and connected communications structure among team members, especially if members are working separately.
  - Reviewing inspection progress at least daily and discussing remaining objectives with team members, including setting concrete objectives for the following day.
  - Continually assessing the overall progress of the inspection to evaluate how the inspectional approach is working and to keep the division supervisor advised of the inspection's progress.
  - Providing individual guidance and direction to team members as necessary.
  - Advising each team member of reporting responsibilities and dates when drafts are to be provided.
  - Following up promptly on any delays or failures of team members to report as required.
  - Assisting the supervisor with further follow up, as needed.
- Making sure any person who joins the team after the inspection has started presents credentials and issues an FDA 482, Notice of Inspection to the firm prior to taking part in the EI (see IOM 5.3.1 Notice of Inspection (Form FDA 482) for more details).
- Issuing new notebooks for taking regulatory notes during the establishment inspection (EI) to any non-OII personnel on the team. Team leader is also responsible for instructions on notebook use, if necessary, and when the report is finished, for obtaining the non-OII personnel individual's signature on the original EIR

and their completed and properly identified regulatory notes. The team leader should then submit them to the leader's supervisor for filing.
- Drafting endorsement text in eNSpect.
- Preparing the Summary of Findings in eNSpect.
- Ensuring all headings of an administrative nature are complete in the establishment inspection report (EIR).
- Compiling and submitting the complete EIR.
- Resolving any disputes or differences of opinion among the team members, including items which may be listed on the FDA 483, FDA 483a, or FDA 4056.

5.3 – Safety during Inspections

5.3.1 – Safety (What You Should Do to Prepare for Potential Dangers/Risks)

Refer to IOM Chapter 10 for general safety information.

5.3.1.1 – Personal Safety

Physical and verbal resistance to FDA inspections and threats to, or assaults on, FDA employees engaged in their work are extremely rare. However, there will be times when you are confronted by unfriendly or hostile persons. OII offers various conflict resolution training courses to assist and prepare you for how to diffuse a situation (See IOM 10.3.3). Talk to you supervisor if you need assistance finding a course.

In most instances, conducting your activities with tact, honesty, diplomacy, and persuasiveness will be enough to defuse the situation. And while at times, you may have to adopt a firm posture, you should not resort to threats, intimidation, or strong-arm tactics. (Refer to IOM 5.3.13 for Hostile and Uncooperative Interviewees.)

5.3.1.1.1 – Safety Preparation

You should be familiar with the content in IOM Chapter 10 - Safety, as it relates to your assignments.

Additionally, the following are suggested items the program division may consider when preparing for your next assignment to assess if there are potential personal safety issues. This list is not meant to be all inclusive.

- Does the assignment involve working with other federal agencies, such as U.S. Marshals Service, Federal Bureau of Investigations, and U.S. Customs and Border Protection, in executing search warrants, seizures, etc.?
- Does the assignment involve working with or contacting FDA's Office of Criminal Investigations (OCI)?
- Does the assignment involve a firm where there is a suspicion and/or knowledge of questionable or illegal activities?
- Does the assignment involve a suspected tampering?
- Are you visiting an individual's residence?
- What have interactions with the firm's representatives been like previously and historically? What does the firm's establishment file indicate about personal safety over past inspections? Have any FDA state counterparts or other SLTT agencies indicated a concern for personal safety?
- What is the location of the firm or the operation? Is it in an area which may be unsafe?
- Is the firm known to the agency? Has the agency any additional information which would assist in your evaluation?

If these questions or others result in a concern for your personal safety, then a Personal Safety Plan should be developed and approved by program division management before conducting the assignment. (See IOM 5.3.1.1 – Personal Safety Plan for more.)

Your program division management is most familiar with the specific firm in question, the regulated industry, as well as other local federal, state, and local officials who may be able to provide you additional information and assistance. In addition, to leaning on the expertise of your program division management, consider also inquiring about or taking relevant training courses on conflict resolution. Note too that program divisions should notify the Medical Products Inspectorate (MPI) or the Food Products Inspectorate (FPI) to inform headquarters of any personal safety plan that is developed, so that personal safety issues may be tracked. The headquarter component will also maintain a library of Personal Safety Plans which may also be of use to your division. The headquarter component may be contacted at the following personal safety e-mail address: oiicsosafety@fda.hhs.gov .

5.3.1.1.2 – Dealing with Physical Resistance/Threats/ Assaults



If you receive physical resistance or threats, or if you sense the possibility of an assault, you should promptly disengage from the confrontation, get to safety, call 911 if necessary (for immediate police or medical assistance), and call your supervisor. Your safety is more important to the United States than the inspection, or the sample collection. See IOM 10.2 and 10.3. As soon as you are safely able to, you should make careful and exact notes about the encounter (for instance, who said what to whom, who did what, and whether someone tried, or succeeded, in threatening, assaulting, or taking information, equipment, or samples from you). Be careful and factual in any descriptions you give or write about such events, just as you do when recording other evidence that may result in a court case. The FDA will work with law enforcement government officials (for example, the Federal Protective Service (FPS), FDA's OCI, local police, and/ or United States Marshals to assist an inspection team if there is a reasonable fear or risk of ongoing danger to the investigator).

If you have been assaulted or threatened and you are unable to reach your supervisor or other division management, you should contact the local police in the area where the assault or threat occurred. After your safety and well-being is secured, proceed with the following:

- Use care in any descriptions you give or write about such events, just as you do when recording evidence that may result in a court case.
- Be sure that any inspected facility, where weapons have been observed, or where threats or assaults have occurred, is identified on that facility's “Endorsement” page of the inspection report for that facility.
- Be sure your supervisor is fully apprised of all incident details so that any subsequent investigators or agents to that facility will be alert to the safety concerns and risks.
- Your supervisor is responsible for checking the “Personal Safety Alert” box in eNSpect and for initiating the notification process to alert other federal or state agencies that also inspect the facility of the possible danger.

(For more information see IOM 10.3.1, Personal Safety Alert. For specific safety guidance related to inspections and interviews, see IOM 5.3.1.3 Hostile and Uncooperative Interviewees.)

Any perceived threat to your personal safety is of the utmost importance. Plan to exit the situation immediately and report it to your supervisor. Potential and perceived threats may include, but are not limited to, certain geographic locations (high-crime or war-impacted, for instance), concerns about entering a personal residence to conduct official business, or animals that are not caged or contained.

5.3.1.2 – Personal Safety Plan

A Personal Safety Plan is a tool developed to assist in managing and preparing for a potentially dangerous situation. Program divisions should develop a Personal Safety Plan when the conditions surrounding a specific

inspection, investigation, or sample collection indicate a plan is needed. The plan allows all those involved to carefully evaluate the specific inspection, and factors surrounding it, and to prepare for a safe and successful conclusion. Utilizing personal safety concepts prior to a potentially dangerous situation is common practice and part of the training programs of many other federal agencies.

The Personal Safety Plan should be developed by the investigator, supervisor, other investigators familiar with the facility, a compliance officer, if needed, and any other individuals (program, division, or headquarters (HQ) experts, etc.) who may be able to assist in the depth, scope, and specifics of the firm in question. Meetings held between these individuals, to ensure a well-developed and clearly understood plan, are suggested. The decision of who should help develop and/or approve the plan is made at the program division level.

The plan should document what specific roles and responsibilities are needed to conduct the inspection/investigation and/or sample collection in a risk-minimizing manner. The plan should also answer the questions: who, what, when, where, and why, concerning the potential danger(s).

Here are the seven principles of a Personal Safety Plan:

1. **Summary of potential hazards:** This section of the plan includes all the potential hazards, in detailed description, that prompted the need for a personal safety plan. Be sure to answer the questions: who, what, where, when, and why? Also describe any specific hazards that require personal protective equipment, or conditions/situations at the facility that may cause allergic reactions for some investigators or analysts. Also, summarize and include here any relevant information from past inspection reports, discussions with previous FDA, state, or local investigators, as well as information about any environmental or plant/facility-specific conditions or factors that could negatively impact or limit even a well-intended safety plan.
2. **Sources of information:** This section of the plan includes a listing of all the sources from which you gathered potential hazards, and information/data. For instance, if you gleaned information about hazards from a colleague or a state inspector, you would want to document their names, in this section, along with their respective statements. If your information came from another source; for instance, if it's database or document, make sure to include the name or title/description too. This section is important, as it documents factual evidence (sources), in the same way you notate all other evidence you gather.
3. **Response alternatives:** This section will be the *most important* part of your plan because it details what you propose to do, alternatively, to mitigate the hazards. Here, you will provide a list of practical responses to the existing risks or dangers, and options or solutions to consider. This section allows your supervisor to evaluate possible ways to handle the situation. Your explanation should also outline all the skills and tools you possess to assist you in handling the situation carefully, including trainings, experiences, and other procedures you have at your disposal. Roles and responsibilities of all involved in the plan should also be identified in this section, including those who will be based on-site and off-site.
4. **Communication:** Here you will provide all information about how communication will occur between participants on-site, between those on-site and off-site, and in collaboration with any emergency, law enforcement, or medical responders. You will also want to establish as part of your plan a predetermined frequency of check-ins with your supervisor, so that they may stay regularly apprised of your safety. Also, consider here the use of any special types of communication, for instance, code words for emergencies.
5. **Transportation:** Provide information here on how you and/or others will travel to the facility in question.
    a. Will there be a coordination point?
    b. Do you intend to use government-marked, or unmarked, cars?
    c. Who will ride in each car?
    d. What route will be taken going to and leaving the facility?

Consider where you will park the car when you arrive at the facility. Consider what modes of communication will be used to communicate if multiple vehicles are used.

6. **Equipment:** Here, name all equipment needed to initiate this plan. Is personal protective equipment needed? Is any special sampling equipment, or other equipment, needed? Also, include any other needed equipment, such as communication tools, FDA forms, etc. You should also be sure that anything listed here is in fully functioning mode.
7. **Emergency exit strategy:** Describe in this section what your exit strategy will be in the event of an emergency. Consider emergency strategies for safety issues, as well as those needed in the event of medical emergency. (Your goal here is to have a very clear plan for ensuring that no one is left behind.) It should also include the action step to contact your supervisor when you return to safety.
    a. How will the emergency be communicated to on-site and off-site colleagues?
    b. How will you exit the facility and return to your vehicle?
    c. Will there be a scheduled meeting point to account for everyone who is involved?

Special note for foreign inspections: When a Personal Safety Plan is warranted, a headquarters point-of-contact (POC) will assist the inspection team. The inspection team's management may also wish to participate so that there is clear understanding of what actions will be taken for the foreign inspection.

5.3.1.3 – Interacting with Hostile and Uncooperative Interviewees

Investigations and inspections are typically conducted in a reasonable manner. Nonetheless, there will be times when you are confronted by unfriendly or even hostile persons.

Your activities must always be conducted with calm, tact, honesty, diplomacy, and, as needed, persuasiveness. Do not resort to threats, intimidation, or strong-arm tactics.

Many times, a hostile or uncooperative attitude on the part of individuals being interviewed results from fear, timidity, or previous negative encounters with law enforcement personnel. In most cases, a calm, patient, understanding, and persuasive attitude on your part will overcome the person's reluctance or hostility. Oftentimes, the mere fact that you patiently listen while individuals share their views can encourage them to be more receptive to your requests.

While we cannot predict the behavior of the individuals we meet, especially in the absence of warnings issued from previous operations, we can consult various sources and consider other indicators to alert us to potential risks. These include:

1. Establishment inspection reports, endorsements, or memorandums that may show situations where investigators encountered belligerent or hostile individuals. These reports may be FDA reports and/or state contract reports, if available.
2. Discussions and conversations with FDA, federal, state, and local inspectors and investigators that may reveal instances where uncooperative individuals and problem situations were encountered.
3. The nature of the assignment, program, or information requested, which may indicate some degree of caution is needed.
4. A firm's geography, including a city or town's reputation among local law enforcement, which may alert you that some employees of the firm may be less than cooperative during the investigation.

As always, if you find yourself in a situation which, in your judgment, indicates violence or harm is imminent, stop the inspection and make an exit as soon as possible. Once safe, contact your supervisor and document the information in your regulatory notes.

5.3.1.3.1 - Safety Precautions

The FDA recognizes that there are situations where it is advisable to take precautions for your personal safety. When this occurs, or suspect this is the case, consult your supervisor. Some procedures that may be used to alert you to danger and risks, as well as minimize them include:

1. Conducting the inspection with a team of two or more persons.
2. Requesting additional information from state and/or local agencies who also regulate and inspect the facilities in question. In many instances, your state counterparts may have more information than you currently have regarding a facility. Conducting outreach to them is especially helpful in instances where firms have not yet been inspected by the FDA but have been by state counterparts.
3. Using an unmarked government car in lieu of a marked government car that will draw more explicit attention to you and your activities, and possibly provoke feelings of fear, distrust, or ire among local residents or firm personnel.
4. Assigning and using a non-personal FDA cell phone, or alternate communication device, for the inspection team. While some investigators carry personal cell phones, the FDA strongly advises that your personal cell phone *not* be utilized to contact the firm or any of its management. Such uses in the past have resulted in inappropriate contacts from the firm to the individual FDA investigator.
5. Requesting assistance from local law enforcement agencies prior to, or during, investigations. This assistance may include requesting information about the facility you are to inspect, assistance with communication devices, and/or police protection itself, if the police jurisdiction allows for such an action.
6. Using at least two investigators in potentially or likely hazardous investigations, such as those involving methadone or Schedule II Class Drugs. Additionally, personnel from the U.S. Drug Enforcement Administration, and/or state or local law enforcement agencies may also be requested to accompany you and your teammate(s).

5.3.1.3.2 – Procedures When Threatened or Assaulted



In instances when you are physically assaulted or threatened, you should get to safety immediately then notify your supervisor as soon as you are able to. If emergency response is required, always call 911 first before contacting your supervisor. Your supervisor can also summon local police, the U.S. Marshals Service, or contact OCI headquarters for assistance (301-294-4030). OCI often has contacts with local police and federal agencies based upon previous liaisons. Also, the program division should notify headquarters at oiicsosafety@fda.hhs.gov so that senior management may be made aware.

If you are physically attacked, you have the same recourse as any other U.S. citizen, in addition to the benefit of federal laws that protect government employees while in performance of their official duties. Your report of the incident, plus any medical attention sought and received may be used as documentation for the agency in support of any legal action taken against the firm or the individual.

5.3.1.3.3 - Notification of FBI And U.S. Attorney

It is a federal crime for anyone to kill, assault, resist, oppose, impede, intimidate, or interfere with a federal official in the performance of their official duties. (See sources of legal protection below.)

In case of an assault or threat against you, notify your supervisor immediately, so facts regarding the incident can be submitted to the FBI and the U.S. Attorney's office for immediate action.

Federal protections found in Title 18 of the U.S. Code include:

- Someone cannot forcibly assault, resist, oppose, impede, intimidate, or interfere with a federal official who is performing their official duties (18 U.S.C. 111)
- Someone cannot kill or attempt to kill a federal official who is performing their official duties (18 U.S.C. 1114)

See Title 18 of the US Code Sections 111 and 1114 for the complete text.

5.4 - Confidential Sources

5.4.1 – Interviewing Confidential Sources

An individual providing useful and credible non-public information is often referred to as a confidential source. (Such a source, while providing useful assistance to the agency, may not necessarily become a party to the actual FDA investigation.)

Refrain from providing your personal information to the confidential source (for example, your personal cell phone and/or e-mail); just use professional/official contact information.

These individuals usually have access to pertinent information or possess a distinct vantage point allowing them to obtain useful information. These sources typically do not want to be identified or take an active part in the investigation, as such, it's important not to divulge the identity of a confidential source of information.

Note, too, that the source individual may, or may not, be reliable for purposes of using information in court. In all situations, the information obtained must be vetted and reliable.

If you believe or suspect the information provided by the source may involve criminal activity, notify your supervisor. In all cases of criminal activity, including fraud, OCI is the primary investigative office for the FDA. If OCI does open a case, OCI will want to be involved or at least notified of any interviews you conducted and documented that may be useful to further the case. (See IOM 8.1.5.3 Criminal Investigations).

When faced with a situation involving human sources of information who want to remain anonymous, contact your supervisor and follow the procedures in this subchapter. You should also maintain awareness regarding your safety (see IOM 10.3 and IOM 5.3). If your management concurs with the decision to utilize a confidential source who wishes to remain anonymous, it is particularly important that you take the necessary steps to protect the identity of the source and protect any information that could lead to someone determining the identity of the source.

5.4.1.1 - How to Handle the First Contact

When you interview a potential confidential source, you should use the following procedures (See Section 8.1.6.1 Interviews for more):

1. Attempt to schedule an in-person interview with the individual, rather than a telephone interview. A face-to-face interview gives you the opportunity to assess their demeanor, body language, overall presentation, and truthfulness.
2. Allow the individual to choose the place and time of the interview, unless there is a concern for your personal safety. If you are unsure of the safety or privacy of the location the source provides, then you should suggest an alternate location. When you conduct the interview on non-FDA premises, be sure to notify your supervisor of your destination, purpose, and estimated time of return. When the off-site interview has been completed, check-in with your supervisor and alert them to the meeting's conclusion.

5.4.1.2 - Interviewing Methods/Techniques

It is strongly recommended that you have *two* investigators conduct interviews of a confidential source. This allows the lead investigator to conduct the interview, while the second investigator takes notes and acts as a witness to the interview. Some suggestions for a successful interview:

1. Prepare carefully and adequately. The investigators should develop the questions beforehand that they intend to ask the person during the interview, (for example, specific questions that will help "establish motivation"). You should record and number the questions to be asked in your diaries prior to the interview. This preparation assists in documenting the interview process and reduces the amount of note taking needed during the interview. The investigators should also discuss their interviewing strategy, before the meeting, including determining the method by which they will consult with each other during the interview, and, in the case of extensive interviews, how best to share interviewing and note-taking responsibilities.
2. Direct the interview in a way that will encourage the person to tell the story chronologically. This will help place complex situations or events into logical order.
3. If the person makes allegations, ask him or her how he or she knows the allegations are true. For instance:
    a. How were they able to know?
    b. Did they personally see, hear, or write about the information/incident?
    c. Can they provide proof of the allegations?

5.4.1.3 - Establish Motivation

At the end of the interview ask the person why he or she is divulging this information. This may reveal their motive(s) and help you shed light on the following possibilities:

1. Is the person a disgruntled current or former employee who harbors a grudge?
2. Is the person looking for some type of whistle-blower reward or notoriety?
3. Does the person just want to do the right thing?
4. Is the person involved in actual or prospective litigation about or related to the information?

5.4.1.4 - Anonymity

If the individual is requesting anonymity, inform them that the FDA:

1. Will not divulge their identity, the occurrence of the interview, or the sensitive information provided to the agency if the information could lead to the identity of the person, unless the FDA is required to disclose the information by law. For example, if the investigation leads to a hearing or trial and the individual is required to testify.
2. Will try to corroborate all information provided by the person, to minimize the chances they must later testify. However, testifying remains a possibility.

Ask the person for names of any other persons who might be willing to speak with you about the allegations and corroborate the individual’s story.

5.4.1.5 - Protect the Identity of the Source

Obtain sufficient personal information necessary to enable you to contact the person for follow up if needed. However, to maintain the confidentiality of the person, do not include the person's identifier information, such as sex, name, address, and phone number in the memorandum of interview. You should assign the confidential source a code name, or number, and use that identifier in memoranda and other communications relating to the confidential source (see IOM 5.4.1.7 item 2).

5.4.1.6 - Access

Know who is authorized by program division procedure to access the information and restrict access by and to any others accordingly. Share the minimum amount of information necessary to meet the purpose of the disclosure.

5.4.1.7 - Storage Requirements

1. Each program should establish procedures, in addition to those listed below, to properly store confidential information. Use security measures necessary to protect the confidentiality of personal information, whether it is in hard copy or electronic form, held on FDA premises, in an FDA home-based computer, or in any other form. Use whatever means necessary and appropriate to physically safeguard the information, such as storing in a safe, or locked file cabinets, or password-coded computers, etc.
2. When referring to the source in any manner (orally, in writing, electronically, etc.), consider using code to identify the source. For example, use a number rather than the individual's name, to identify the source. Use discreet subject headers in the file labels as appropriate. Personal privacy information should be safeguarded to the extent allowed by law.
3. Remove personal information from a file only after you have noted in the file your name, date, etc. Promptly return that information to the file.

5.4.1.8 - Disclosure

Do not disclose information from or about the source unless the disclosure complies with the law and FDA's procedures. Do not share non-public information outside of the Freedom of Information Act (FOIA) process unless the sharing is done according to our regulations and procedures. Refer any FOIA requests to FDA's Division of Freedom of Information (see item 3 below). See also IOM 2.3.

Use the following guidance with regards to disclosures of information from or about a confidential source:

1. Make duplicates of the personal information only to the extent necessary for authorized disclosure (inside or outside of FDA). Do not leave the copy machine unattended.
2. Make only authorized disclosures of the information, regardless of the manner of disclosing (oral, written, etc.). Do not use mobile telephones or leave voicemails containing the information. Avoid transmitting the non-public information by facsimile or e-mail.
3. If you receive a FOIA request for information from or about a source, consult with your supervisor immediately. Disclosure to a non-FDA government official of information from or about a source may be disclosed *only* if permitted by law and FDA procedures, and after consulting your supervisor, Office of Field Regulatory Operations and, if needed, OCI.
4. Immediately retrieve information from or about a source if inadvertently disclosed. Follow the Inadvertent Disclosure SOP.

According to FDA Records Management procedures, you should destroy personal information by shredding physical paper or degaussing electronic media. (Contact the Employee Resource and Information Center (ERIC) support to degauss electronic media.)

If a matter is referred to Office of Chief Counsel (OCC), consult with OCC prior to contacting the source again.

5.5 – Inspectional Activities

The previous subchapter described activities you should consider and do when preparing for an inspection. This subchapter is focused on activities *during* the inspection. It is general in nature and applies to all inspections. Programmatic sections describe specific activities to be done during inspections related to specific programs.

5.5.1 - Notice of Inspection (Form FDA 482)

Upon arrival at the firm, you should first locate the owner, operator, or agent-in-charge of the establishment. This should be the top management official on site, and you should be certain of this individual's status. Introduce yourself by name, title, and organization. Show your credentials to the official and present a properly signed and completed original of the FDA 482, Notice of Inspection or FDA 482d, Request for FSVP Records. The FDA 482 or FDA 482d should reflect the address of the home district of the firm.[2] For FSVP Inspections see IOM 6.8.1.4

The FDA-482, Notice of Inspection, is issued on site prior to the initiation of the inspection. The FDA-482 can be issued in the following ways:

- Physical paper copy with signature. (Be sure the printed version of the signed FDA-482 is legible)
- Electronically with your electronic signature certificate by email as a PDF attachment. If issued electronically, confirmation of receipt should be verified and documented.

Document your method of issuance in your regulatory notes.

If additional agency personnel accompany you during the inspection, they must also show their credentials to the top management official upon arrival at the site. A new FDA 482 or FDA 482d must be issued. Submit a copy with your EIR.

Next, explain the purpose of your visit. Readily accept any management offer to have a representative accompany you on the inspection.

If non-FDA officials accompany you during your inspection and do not have authority to enter and inspect, you should obtain permission (preferably in advance) from the most responsible individual at the firm. Note, however, that non-FDA officials, and those who do not hold FDA credentials, do not sign the FDA 482 or FDA 482d. (See IOM 5.1.4.2.1)

For multiple occupancy inspections in drug establishments, refer to IOM 5.1.4.3.3. Inspections of multiple firms, which are separate legal entities, should be reported under separate EIRs.

If you are faced with a refusal, or partial refusal of inspection, proceed as outlined in IOM 5.5.2.

Any time an FDA 482 is issued, you should also issue an FDA 484, Receipt for Samples, (at the conclusion of the inspection) if you collect any physical samples at the firm. (See IOM 5.1.4.2.3, and IOM 4.2.1, 4.2.3 and 4.2.4 for instructions for issuance of the FDA 482 in certain sampling situations.)

If you have any questions or concerns regarding when, or when not, to issue the FDA 482, discuss them with your supervisor.

5.5.1.1 – Multiple Date Inspections

If your inspection covers more than one day, advise management at the close of each day you have not finished the inspection and when you will return. Do this each day until you finish the inspection. An FDA 482 or FDA 482d is not required for each day of an inspection, or when different individuals are interviewed. If there will be an extended period of time (say, a week or longer) before you can return to the firm to complete the inspection, be sure to advise management of the delay and discuss with your supervisor whether or not you need to issue another FDA 482 or FDA 482d.

5.5.1.2 – Inspection of Vehicles

If you need to inspect any vehicles on site, owned or leased by the firm being inspected, the inspection of these is covered by the FDA 482, Notice of Inspection, you issued to the firm.

[2] For all firms within the state of Arizona, the home district is Denver District. Home district boundaries are identified in Appendix E.

If any vehicles (including trucks, trailers, railroad cars, etc.) which are not owned or leased by the firm are present and inspection is necessary, a separate FDA 482, Notice of Inspection, is required, along with the following steps:

1. Issue the FDA 482 to the driver of the vehicle.
2. If the driver is not present and if, after a diligent search, they cannot be located, issue a separate FDA 482 jointly to the firm being inspected and to the firm whose name appears on the cab. Enter the license number of the vehicle on the FDA 482. Give the original FDA 482 to the firm and leave a copy in the cab of the vehicle.
3. If there is no cab present, prepare a separate FDA 482 modified to read "*** to inspect unattended vehicle ***" and issue it to the firm being inspected as the "agent in charge" of the vehicle. Enter the license number of the vehicle, trailer, or railroad car number, etc., on the FDA 482. Should the firm being inspected refuse to accept the notice, leave it in a conspicuous place in the vehicle. Describe the circumstances in your EIR.

5.5.1.3 – Follow-Up Inspections by Court Order

At times you may be instructed to conduct inspections of firms by authority of an injunction or other court order. This situation provides separate and distinct inspectional authorities involving both the authority of the court order and the authority of Section 704 of the FD&C Act [21 U.S.C. 374], each providing independent courses of action.

When assigned to conduct such inspections, you should first obtain a copy of the injunction or other court order bearing the filing stamp and all relevant signatures. Prior to starting the inspection study, read the order thoroughly for any and all special instructions of the court. Your supervisor will assist you in determining the depth of the inspection necessary to cover these court requirements.

On the day of the pertinent inspection, take a clearly legible copy of the court decree (not necessarily a certified copy) with you to the firm to be inspected. Present your credentials in the same manner as for any other EI. Issue the FDA 482, Notice of Inspection, but modified to read:

> "*Notice of Inspection is hereby given under authority of injunction* (add the injunction number and/or other identification) a*gainst the firm and pursuant to Section 704…*".

Show the person to whom the FDA 482 was issued a copy of the Order, and, read the following statement to them:

> "*This inspection is being conducted under the authority of injunction [add the injunction number and/or other identification] [or other court order] granted by the United States District Court against this firm on [date]. The inspection will cover all items specified in the decree. In addition to the inspection authority granted in the court decree, I am issuing you a Notice of Inspection under the authority of Section 704 of the Federal Food, Drug and Cosmetic Act which authorizes inspections of firms subject to that Act.*"

If the firm refuses access to records, facilities, or information for which the decree provides inspectional authority, read out loud the pertinent section(s) or portion of the order to the person refusing so there is no misunderstanding as to the requirements of the decree. If the person still refuses, report the facts to your supervisor as soon as possible so the court can be promptly advised of the situation. (See IOM 5.5.2 for more information on handling refusals.)

When you prepare your EIR, describe the sequence of events in detail, including exactly what happened and how you handled the situation. This documentation will help support any charge of violating the court order and/or Section 704 of the FD&C Act [21 U.S.C. 374].

The court order may require a report to the court. Discuss this with your supervisor since the division will normally handle this part of the requirement.

5.5.1.4 – Conducting Regulatory Inspections When the Agency is Contemplating Taking, or is Taking, Criminal Action

If the agency is contemplating taking, or is taking, criminal action against a firm, you should *not* issue a Notice of Inspection to that firm without first discussing the matter with your supervisor. You should also review IOM 8.1.4 before proceeding.

Program division management will obtain guidance from the OCC and will allow, or not allow the inspection to proceed based on considerations related to the criminal investigation. Decisions to inspect under such circumstances should be based on considerations of whether the request is consistent with FDA's responsibility to ensure products are not produced or distributed in violation of the Federal Food, Drug, and Cosmetic Act or other federal law within FDA's jurisdiction. The program division should ensure that these considerations are documented. In no circumstance should an inspection be conducted solely to obtain evidence to support a possible criminal case. However, inspections conducted in accord with our overarching responsibility to protect the public, and limited in scope to the authorizing statute, are lawful, even when criminal action is being considered or pursued.

The Fourth Amendment to the U.S. Constitution prohibits searches without a warrant supported by probable cause. An exception to the warrant requirement is inspection of industries long subject to close supervision and inspection, which are conducted under a statute with no warrant necessary.

Three criteria must be met under this exception from the warrant requirement.

- First, the regulatory scheme authorizing the regulatory inspection must be supported by a substantial government interest.
- Second, regulatory inspections must be necessary to further the regulatory scheme.
- Third, the statute's inspection program, in terms of the certainty and regularity of its application, must provide a constitutionally adequate substitute for a warrant.

Section 704 of the FD&C Act [21 U.S.C. 374] is appropriately designed to allow regulatory inspections within appropriate limits. This provides the authority 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, or cosmetics. (See IOM 3.2..) FDA’s normal inspection procedures provide guidance on what should be considered “reasonable” under Section 704.

Should the evidence obtained during an inspection become material to a criminal case, it is possible a defendant will claim the use of statutory authority to conduct the inspection was a pretext to conduct an unlawful warrantless search. But if the limits of Section 704, and normal establishment inspection procedures are followed, the possibility a court will find the inspection to be pretextual should be minimal. Deviations from these limits will make it more likely a court would find the use of statutory authority to be pretextual and render the evidence obtained to be inadmissible.

Any concerns you may have related to the conduct of an inspection while a criminal investigation is being considered or pursued should be discussed with the OCC.

It is the responsibility of the office generating the inspection assignment to inform the program division if a criminal action is ongoing or contemplated. There may be occasions when neither the office generating the inspection assignment nor the program division conducting the inspection is aware that OCI is conducting a criminal investigation of a firm subject to regulatory inspection. That’s because OCI may determine it is not in the interest of the agency to disclose to other components of FDA the existence of its investigation, if OCI is not involved in the agency decision to conduct a regulatory inspection. However, OCI and other components of FDA

may also share information. (See also IOM 5.6.2 – When Evidence of Criminal Violation is Discovered in the Course of a Regulatory Inspection)

5.5.2 – Inspection Refusal

A refusal of inspection is refusal to permit entry or other action that prohibits you from obtaining records and information to which the FDA is entitled under the law. Discuss all refusals with the most responsible individual present at the establishment at the time the refusal was made. (See IOM 4.2.3 for information regarding refusal to permit sampling.)

5.5.2.1 – Refusal to Permit Entry

When you are faced with a refusal of entry, call the most responsible individual's attention to the applicable sections of the FD&C Act (that is, sections 301(f) and 704 of the Act [21 U.S.C. 331 (f) and 374] and section 351(c), 360A(a), (b) and (f); 360B(a); and 361(a) of the Public Health Service Act). Applicable sections of these laws are listed on the front and back of the Form FDA 482 for your convenience. If entry is still refused, leave the completed Form FDA 482 with the most responsible individual, exit the premises, and contact your supervisor immediately for further instructions. Document the refusal in your regulatory notes.

Note that in the case of drug and device inspections, refusal to permit entry may cause the product to be adulterated (see IOM 5.5.2.2).

For international inspections, a refusal to permit inspection may result in a recommendation for regulatory action (for example, an import alert, cancellation of Food Facility Registration, etc.). Refusal to permit an international inspection should be reported in a memo uploaded into an *Operation 15 – Foreign Investigation* and should not be reported as a "Washout" in eNSpect.

For international food inspections, section 807(b) of the FD&C Act (21 U.S.C. 384c(b)), authorizes the FDA to refuse admission of a food "into the United States if it is from a foreign factory, warehouse, or other establishment of which the owner, operator, or agent in charge, or the government of the foreign country, refuses to permit entry of United States inspectors or other individuals duly designated by the secretary, upon request, to inspect such factory, warehouse, or other establishment."

5.5.2.2 – Refusals during Inspection

Inspection refusals may take several forms. All refusals to permit inspection must be documented in your regulatory notes and eNSpect and reported in your narrative report under the "Refusals" heading.

For a refusal experienced during an inspection conducted under section 704 of the FD&C Act, the FDA must demonstrate that the inspection was attempted to be conducted at a reasonable time, in a reasonable manner, and within reasonable limits to show you exercised prudence to avoid refusal. You must have also presented your credentials and given the most responsible individual a properly prepared and signed FDA 482, Notice of Inspection, for domestic inspections. (See CPG Sec. 130.100 Inspectional Authority; Refusal to Permit Inspection.).

In the case of drug or device inspections, inspection refusals, as well as delaying, denying, or limiting your ability to conduct the inspection, may cause a drug or device to be deemed adulterated under Section 501(j) of the FD&C Act [21 U.S.C. 351(j)]. (See subsection 5.10.7.9 for drug and device refusals.) The FDA issued a Guidance for Industry entitled: *Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug or Device Inspection*.

5.5.2.3 – Refusals to Permit Access or Copying of Records

If management objects to the manner of the inspection, or the coverage of specific areas or processes, do not argue the matter but proceed with the inspection. However, if management refuses to permit access to or the

copying of any record(s) to which you are entitled under law, call attention to Section 301(e) of the FD&C Act [21 U.S.C. 331] or applicable sections of the Public Health Service (PHS) Act.

If management still refuses, document the refusal, and proceed with the inspection until finished.

In the case of drug or device inspections, if management refuses access to or copying of any record to which you are entitled under law, in addition to Section 301(e) noted above, call attention to Section 501(j) of the FD&C Act [21 U.S.C. 351(j)] (an adulterated drug or device could lead to prohibited acts under 301(a), (b), (c) [21 U.S.C. 331(a), (b), (c)]). (See IOM 5.3.2.2)

Furthermore, if during a drug or device inspection, management delays producing records you request to which you are entitled under law, without giving a reasonable explanation (such as requiring sufficient time to compile a large volume of records or translate the records into English), you may call their attention to 501(j) of the FD&C Act. Similarly, if management limits your access to or ability to copy any record to which you are entitled under law, you may call their attention to Section 501(j) of the FD&C Act. (See subsections 5.10.2 Drug Inspections and 5.12.1.1 Inspection Authority for Medical Devices for further guidance on responding to these situations.)

It is not an inspection "refusal" when management refuses to provide information (for example, formulations, lists of shipments and manufacturing codes, etc.) not specifically required by law or regulation. If the refusal is such that you cannot conduct a satisfactory inspection, discuss with your supervisor if a Warrant for Inspection should be requested. Inspection Warrants are further discussed in the Regulatory Procedures Manual Chapter 6 and IOM 5.5.3.

5.5.3 – Inspection Warrant

A refusal to permit inspection or a refusal to permit access to or copying of records may invoke criminal provisions of sections 301(e) and 301(f) of the FD&C Act [21 U.S.C. 331(e), (f)]. Furthermore, in the case of drug or device inspections, delaying, denying, limiting, or refusing an inspection may invoke criminal provisions of sections 301(e) and 301(f) [21 U.S.C. 331(e), (f)]. Depending on the individual situation, instances of refusal may be met by judicious use of inspection warrants.

Instructions for obtaining warrants are contained in the Regulatory Procedures Manual, Chapter 6-3. See your supervisor for additional information and instructions.

When you serve an inspection warrant, you are operating as an agent of the court, and so the warrant must be executed expeditiously once served. (See IOM 5.5.2.3 for guidance on how to handle any refusal after obtaining a warrant.)

In situations where a potential problem is anticipated with the service of a warrant, the program division should consider sending a supervisory consumer safety officer and a U.S. Marshal with the investigator to assist and supervise the serving of the warrant.

After successfully obtaining an Inspection Warrant, you should return to the firm and:

1. Show your credentials to the owner, operator, or agent in charge.
2. Issue the person a written Notice of Inspection (FDA 482).
3. Show that individual the original, signed Inspection Warrant.
4. Give them a copy (not the original) of the warrant.

The copy you provide need not be signed by the issuing judge, but the judge's name should be typed on the copy.

Follow the procedures of the court, or U.S. attorney involved, if their methods differ from the above.

When an inspection is made pursuant to a warrant, a Return, showing the inspection was completed must be made to the judge (or U.S. commissioner or magistrate) who issued the warrant. The Return, executed on the original warrant, should be made promptly and usually no later than 10 days following its execution.

5.5.3.1 – Refusals after Serving a Warrant

If you have been refused entry, obtained a warrant, tried to serve or execute it, and are still refused entry under the warrant, inform the person that the warrant is a court order, and such refusal may constitute contempt of court. If the warrant is not then immediately honored (entry and inspection permitted), you should leave the premises, and promptly contact your supervisor. Document the facts regarding the refusal in your regulatory notes.

If you have served the warrant, yet during the inspection you encounter partial refusal or resistance in obtaining access to anything the FDA is authorized to inspect by the warrant, you should inform the firm that that aspect of the inspection is part of a court order and refusal may constitute contempt of court. If the warrant is not then immediately honored, you should, again, leave the premises, and promptly contact your supervisor. Document the facts regarding the partial refusal or resistance in your regulatory notes.

5.5.4 – Consumer Complaints

Prior to conducting any inspection, you should review CMS, Firm 360, Complaint Dashboard, and the firm history to become familiar with all FDA complaint/injury records associated with the firm (See IOM 5.2.3).

Be sure to cover areas of the facility or production associated with these complaints with management, without revealing the complainant's name(s). Also handle whistleblower complaints with care to protect the identity of the complainant. Determine if the firm has had similar complaints on the same product.

Determine what action the firm has taken to identify the root cause of the problem and to prevent a recurrence in the future. (See IOM 5.7.1.4.10 for reporting instructions.)

Also, check the Programmatic section in this chapter and QMiS for any specific instructions for follow-up to consumer complaints during inspections.

5.5.5 - Recalls Identified or Initiated during an Inspection

Due to the potential public health impact of recalls, when you identify a situation that may be a potential or actual recall during your inspection, it is imperative to contact and submit any information, including documentation obtained, to your division recall coordinator (DRC) as soon as possible. The division should not have to wait for writing and submission of the EIR or memorandum when sharing recall documents with the DRC. (See IOM 7.2 for more information related to recalls.)

5.5.6 – Signing Non-FDA Documents

Occasionally a firm will request you sign various documents, including:

- A waiver which will exempt the firm from any responsibility or liability should an accident occur, and you are injured on the firm's premises
- Form letters concerning access to confidential information the firm does not want released
- A training form acknowledging that you were briefed on the personnel gowning procedures
- A written version of the information/data you are requesting during the inspection

If you receive any such requests to sign non-FDA documents, inform the firm that you are not authorized to sign such documents, letters, requests, waivers, etc., but will report their request in your EIR. One exception is that all FDA employees are authorized to sign in and sign out at a firm and to comply with security measures employed by the firm, including documenting the removal/replacement of seals to inspect vehicles and containers. (See IOM 4.3.3.3 and

4.7.4.6.) The key issue to remember here is you are not authorized to waive, without supervisory approval, *any* of the FDA's rights to inspect, sample, photograph, copy, etc., or to sign any interstate shipping record document which could suggest the firm could not be prosecuted under the Act.

5.5.6 – Inspection Walk-Through

A walk-through inspection of the premises should be conducted as early as possible to become familiar with the operation and to plan the inspection strategy. A walk-through visual inspection of the manufacturing site is helpful in establishing the depth of the inspection, learning about products and processes, identifying sources of manufacturing records and identifying potential areas of concern. The size of the facility, the number of employees, employee practices, environmental conditions inside and outside the facility, raw materials, manual and automated processes, potential sources of contamination, manufacturing flow, method of data collection are some of the factors to be taken into consideration in establishing the depth of the inspection. A visual inspection of a manufacturing site should also be used to check readily apparent potential problem areas such as, general housekeeping, state of operation for processes and processing equipment, and employee practices. Visual inspections of areas used for failure investigation, product sampling and testing, product reworks, returned goods, and product quarantine areas should also be inspected for obvious potential product problems.

Depending on the product being inspected, some of the general inspectional equipment you should have available may include a digital camera, eye and ear protection, and boots and protective clothing. If you are unsure what inspectional equipment is needed, consult with your supervisor. Some specialized equipment may include radiation or ethylene oxide (EO) monitoring devices, magnifiers, and timing devices. For some domestic and foreign sites, investigators may be required to be inoculated prior to the inspection for protection from potential environmental concerns, such as hepatitis, yellow fever, malaria, and live biological products which may be encountered in vaccine products. (See Chapter 10 for more.)

5.5.7 – General Inspection Procedures and Techniques

The procedures and techniques applicable to specific inspections for foods, drugs, devices, tobacco products, cosmetics, radiological health, or other FDA operations are found in part in the IOM (inspectional policy/procedure), and the compliance programs (program specific instructions). Some procedures and techniques which may be applicable to overlapping areas or operations are described below.

5.5.7.1 – Candling

Candling is defined as: "to examine by holding between the eye and a light, especially to test eggs in this way for staleness, blood clots, fertility and growth." Like most techniques learned through the food inspection programs, there are uses for this technique in other program areas, such as looking for mold in bottled liquids which could be drugs, devices, or biologics. Candling can also be useful in the examination of original documents to see underneath white-out or to look for over-writing.

Many types of products lend themselves to inspection by some type of candling. For these products, firms may have candling equipment which may be built into the production lines or may be a separate operation. Where checking products by candling, it may be possible to use the firm's candling equipment. All candling is best accomplished when light outside the item being candled is masked, so that the light passes through the object rather than being diffused around it. A heavy paper or cardboard template can be quickly prepared at the time candling is done.

5.5.7.2 – Label Review

Do not undertake a critical review of labels unless instructed by the assignment, program, or your supervisor. Limit your comments to the mandatory label requirements required by the acts. However, if after review of the formula,

it is obvious an active ingredient or an otherwise mandatory ingredient statement does not appear on the label, such discrepancy may be called to the management's attention.

If you are asked for other label comments, refer the firm to the appropriate center to obtain a label review.

When the labeling is suspect or when you are requested to collect labels/labeling, collect a copy of all labels and accompanying literature for further review. For medical devices, if there is a question regarding the need for a new 510(k) or Pre-Market Approval (PMA) supplement, it is essential the label and labeling be collected.

See IOM 5.5.11.2 regarding labeling for blood and blood products.

5.5.7.3 – Field Examinations (Field Exams)

A field examination is an on-site examination of a domestic product (or a foreign product in domestic channels of trade) sufficient to determine if the product complies with the acts enforced by FDA. A field exam can be conducted of any commodity in any location. It is important to conduct field examinations during food inspections to detect violations (for example, any undeclared sulfiting agents, certified color additives, and allergens). If the examination does not reveal a violation or the appearance of a violation, a sample of the lot is usually not collected. If your exam reveals a violation or potential violation, you should collect an official sample. Instructions on how to conduct a field exam are contained in FDA's "Inspection Guides" and "Compliance Programs" webpages. The Sample Schedules in Chapter 4 also provide guidance on lot examinations for special situations.

5.5.7.4 – Imported Products

Be alert to imported products whenever you conduct an inspection. During inspections of domestic firms, if you encounter imported products that appear adulterated, misbranded, counterfeit, tampered with or otherwise suspect, attempt to fully identify the product and the source of the imported products. Contact your supervisor and Division of Import Operations (DIO) if necessary.

5.5.7.5 – Import for Export

During the domestic inspection, follow-up on the IFE entry/lines as described below:

1. IFE entry/line information and documentation can be obtained through the "*Import for Export - IFE*" section in OSAR Firm 360 and ORADSS report "*IMP046 Import for Export Entry Lines and Documents".*
2. During the inspection, verify if the IFE articles:
   a. were used to produce an exported product,
   b. were destroyed, or
   c. are still under the firm's control pending disposition. If the articles are pending disposition, verify whether they are the same articles that were offered for entry (per supporting documentation).
3. If the articles were exported or destroyed, request the firm's import, export, and/or destruction records to verify that the imported articles were further processed or incorporated into another product and were exported in accordance with sections 801 (e) or 802 of the FD&C Act [21 U.S.C. 381 (e) or 382] or section 351(h) of the PHSA; or were destroyed. For drug products, an initial owner or consignee may be allowed to retain a sample of the imported article to comply with good manufacturing practices (GMP) regulations concerning sample retention.

Upon completion of the inspection, ensure the following actions are taken:

1. Document the status of the IFE product and if further follow-up is required in the EIR or a memo.
2. If further follow-up actions are needed, schedule a follow-up inspection or discuss with the Office of Import Operations (OIO), Division of Import Operations (DIO), to determine appropriate actions at the import level. If further follow-up is NOT required, document the completed follow-up in the EIR memo.

Any inspections identifying a prohibited act under section 301(w) of the FD&C Act [21 U.S.C. 331 (w)] should be forwarded immediately to the applicable program director (director of investigations branch or director of compliance branch) for regulatory action. (See RPM Chapter 9.) In addition, a copy of the violative inspection findings should be forwarded to fdaimportsinquiry@fda.hhs.gov.

5.5.8 – Inspection of Foreign Firms

Inspectional requirements generally apply to all inspections, including foreign inspections. However, there are some exceptions. For instance, the FDA 482 is not issued during inspections outside the country, unless the firm is a U.S. military facility. Be guided by relevant compliance programs, assignments, and the Guide to International Inspections and HHS Travel Manual for other differences.

5.5.8.1 – Review of Foreign-Language Documents

When reviewing documents in a foreign language, do not use any web and mobile applications' translation tools that have not been authorized by the FDA for this particular purpose. Use of these tools may result in unauthorized disclosure of non-public information. There are two Translation Web Tools available behind the FDA firewall. Details can be found at OII OIO SharePoint site. A video tutorial using these tools is available here.

If you are confident that manually entering a single word or short phrase into an electronic tool for translation could not possibly jeopardize trade secrets or confidential information, based on the information you are reviewing, you may do so. Be sure that, if all your searches were read together, the combination of searches would not result in any unauthorized disclosure.

5.5.9 – Inspectional Precautions (Dos and Don'ts During Inspections)

You should be alert to criticism or allegations that you may have contributed to, or caused, contamination at a firm. This is especially important in drug firms and high-risk food firms, among others. You must adhere to good sanitary practices to refute any such criticisms. You could also unknowingly introduce or spread disease during inspections of, or visits to, animal production or sale facilities; while conducting environmental investigations at poultry layer facilities or conducting dairy farm inspections; during audits of state activities; while investigating drug residue reports or working in a veterinary bioresearch area; or conducting produce safety inspections, among other situations. See IOM 5.3 and the IOM Safety Chapter for information outlining precautions you should follow.

Exercise caution with all your activities in the firm. Follow the firm's sanitation program for employees; wash and sanitize hands, shoes, vehicles, and equipment as indicated. Restrict unnecessary movement between various areas in facilities, and when possible, complete your activities in one area before moving to the next.

When inspecting areas where sterility is maintained, or sterile rooms are located (especially in infant critical food, pharmaceutical or device firms), follow the firm's guidance. In general, it is unnecessary to enter sterile rooms except in the most extraordinary circumstances. These areas are usually constructed to provide visual monitoring. Also, do not take any nonsterile items with you into sterile areas (including regulatory diary, pens, laptop, iPad, etc.). In this situation, you can record your observations in your regulatory notes immediately after leaving the sterile area.

Always use aseptic techniques, including hand sanitizing, when collecting in-line and raw material samples, as well as finished product samples subject to microbiological examination. (See IOM 4.3.5.)

Do not use or consume a firm's products at any of a firm's facilities. This could be interpreted as accepting a product as being satisfactory and could possibly embarrass you and the agency, both during the inspection and in the future. In general, consuming food products in a manufacturing area is considered an objectionable practice.

When conducting inspections of firms using chemicals, pesticides, etc., ask to review the Safety Data Sheet (SDS) (formerly known as Material Safety Data Sheets (MSDS)) for the products present or involved, to determine what, if

any, safety precautions you must take. This could include the use of respirators or other safety equipment. (See IOM 10.14 and 10.14.4 for more).

5.5.9.1 – Clothing

Practice these clothing precautions, for safety and sterility purposes:

- Wear clean coveralls or other protective clothing as needed by the inspection type and if circumstances dictate, use a clean pair when returning from lunch, or upon entering certain machinery or critical areas.
- Remove all jewelry and secure any items on your person, such as pens, pen caps, etc., so they cannot fall into the product or machinery. Do not depend on clips on pens, etc., to hold these items in your outer pockets.
- Individually wrap, or place into clean plastic bags and tape, any clean protective clothing to protect from contamination. If the package has been sterilized, you should also protect the package from possible contamination or puncture. The package should not be opened until you are ready to use the clothing. After use, clothing should be turned inside out as it is removed, and immediately placed in clean paper or plastic bags to prevent spread of contamination until washed and/or sterilized.
- Use disposable hair and head coverings throughout the inspection and disposable hand and foot coverings in areas where floor tracking or cross contamination may be a factor. Use hard hats and other protective devices where the situation dictates.
- If reusable protective boots are used, wash, and sanitize before each use. Always use sterile disposable boot covers when entering machinery, such as dryers, or where unavoidable contact with product is a factor.
- When discarding contaminated disposable head and boot coverings, it is suggested they be placed with used clothing for proper disposal after leaving the plant area.

(See Exhibit 19 – Biosecurity for protective clothing and equipment necessary when visiting livestock or poultry production areas.)

5.5.9.2 – Basic sanitary practices

You are not required to have a health certificate, take a physical exam, or submit to other external requirements to ensure compliance with sanitary procedures in the performance of your official duties. However, it is critical that you adhere to basic sanitation practices. (See IOM 10.8.1 – General Preventive and Protective Measures and Employee Safety & Occupational Health (sharepoint.com), 10.17.2– Immunizations, and 10.17.3 – Physical Examinations.

Employee health guidance as it pertains to any and all personnel working, inspecting, etc., in foods facilities, is addressed in the FDA Food Code. This general guidance related to employee sanitary practices and can be applied to any FDA-regulated product.

5.5.9.3 – Representatives Invited by the Firm to View the Inspection

While conducting an inspection, you may find that the firm's management has invited individuals who are not directly employed by the firm to view the inspectional process (for example, representatives from the press, trade associations, consumer groups, congressional staff, or other company officials).

Regardless of who the firm invites to observe the progress of an inspection, the presence of outside representatives should not disrupt the inspection. You should continue to conduct the inspection in a reasonable fashion. The presence of these individuals should have no impact on the way the inspection progresses, except you should take precautions to preserve the confidentiality of any information you may have obtained as a result of the agency's statutory authority. This is especially true when the firm or their representatives are either video- or audio- recording, or photographing, the inspection. Where applicable, refer to IOM 5.6.8 for procedures on how to prepare your own recording, in parallel with the firm's recording.

It is the agency's position that while the investigator must protect non-public (for instance, confidential) information provided to them during the inspection, it is the firm's responsibility to protect non-public information that may be observed or recorded by those individuals invited by the firm.

5.5.10 – Reports of Observations

The FDA 483, Inspectional Observations (see Exhibit 5-5), FDA 483a, FSVP Observations (see Exhibit 5-18), and the FDA 4056 Produce Farm Inspection Observations (See Exhibit 5-17) are intended to notify the inspected establishment's top management in writing of significant objectionable conditions, relating to products and/or processes, or other violations of the FD&C Act and related acts (see IOM 5.5.11) which were observed during the inspection. However, do not quote regulations or incorporate standards (e.g.ISO 13485:2016) when reporting your observations.

These observations are made when in the investigator's *judgement,* conditions or practices observed indicate that any food, drug, device, or cosmetic has been adulterated, or is being prepared, packed, or held under conditions whereby it may become adulterated or rendered injurious to health.

It is your responsibility to maintain the ability to attest in a legal forum that the observations were personally observed in conjunction with the supporting evidence. Inspectional observations should not be influenced, or appear to be influenced, by parties external to the inspection team, which could call into question the validity of the observations. *This should not prevent you from consulting with your supervisor or others, including the Centers, concerning your observations.*

The issuance of written inspectional observations is mandated by law and OII policy.

Be alert for specific guidance in assignments or compliance programs which may supplement the following general instructions.

5.5.10.1 – General Guidance

All FDA 483s, FDA 483a's, or FDA 4056s should adhere to the following general principles:

- Observations that are listed should be significant and correlate to regulated products or processes being inspected.
- Observations of questionable significance should not be listed but will be discussed with the firm's management so that they understand how uncorrected problems could become a violation. This discussion should be detailed in the narrative report.
- All copies should be legible.

Observations should have the following characteristics to be useful and credible:

- Each observation should be clear and specific.
- Each observation should be significant. (Length is not necessarily synonymous with significance.)
- Observations should not be repetitious.
- Observations should be ranked in order of significance.

If an observation made during a prior inspection has *not* been corrected, or is a recurring observation, it is appropriate to note this on the FDA 483, FDA 483a, or FDA 4056.

You should make every reasonable effort to discuss all observations with the management of the establishment as they are observed, or daily, to minimize surprises, errors, and misunderstandings when the FDA 483, FDA 483a or FDA 4056 is issued. This discussion should include those observations, which may be written on the FDA 483, FDA 483a, or FDA 4056, and those that will only be discussed with management during the closeout meeting. Industry may use this opportunity to ask questions about the observations, request clarification, and inform the inspection team what corrections have been or will be made during the inspection process.

The FDA 483 or FDA 483a should not include specific corrective actions taken by the firm in response to observations noted on the FDA 483, FDA 483a, or during the inspection, except as described in IOM 5.7.1.4.17. These actions should be reported in the narrative report.

Corrective actions not related to a significant observation are noted in the inspection notes and in the narrative report. (For annotations of the FDA 4056, refer to Section 5.5.11.4 - Annotation of the FDA 483 and the FDA 4056.)

Include the results of confirmed positive environmental samples on the FDA 483 or the FDA 4056 if results are known prior to closeout. The investigator should not prolong the inspection if the results are not known prior to close-out of the inspection.

There may be instances where same-day discussion of observations may not be possible due to the volume of documents collected and/or document review reveals observations on a different day than the documents were collected or other circumstances. When this occurs, the lack of a daily discussion of observations, or of any discussion, does not preclude the listing of significant observations on the FDA 483, FDA 483a, or the FDA 4056.

NOTE (for produce safety inspections): Corrective actions observed during a produce safety inspection are noted on the FDA 4056. Corrective actions not related to a significant observation are noted in the inspection notes and in the EIR. (For annotations of the FDA 4056, refer to Section 5.5.11.4- Annotation of the FDA 483 and the FDA 4056.)

5.5.10.2 – eNSpect Electronic Forms

eNSpect is an electronic FDA 483, FDA 483a, or FDA 4056 and EIR reporting system. Use eNSpect to generate the FDA 483, FDA 483a, or FDA 4056 where applicable citations exist. You should be able to write the entire FDA 483, FDA 483a, or FDA 4056 using eNSpect. However, when citations do not exist for *ALL* the commodity areas for which observations need to be included, eNSpect should not be used. In these instances, create the FDA 483, FDA 483a, or FDA 4056 outside of eNSpect and record this activity in eNSpect.

Use eNSpect for all EIRs, whether your FDA 483, FDA 483a, or FDA 4056 was generated using eNSpect, and when no FDA 483 was issued. (See IOM 5.7.1.)

5.5.10.3 - Preparation of Form FDA 483

It is not necessary to complete all headings of the FDA 483, when multiple page 483s are issued. Complete all headings on the first page and, on subsequent pages, only those necessary to identify the firm and dates inspected. FDA 483s should be issued at the conclusion of the inspection and prior to leaving the premises. However, in preparing some complex FDA 483s, it may be necessary to leave the premises and return later to issue and discuss your inspectional observations. In these cases, you should advise the firm's management that your inspection has not been completed and you will return to issue the FDA 483 and discuss inspectional findings. However, there should be no unreasonable or unwarranted delays in issuing and discussing the FDA 483.

Also note that during the inspection, you should not show the firm's management a draft, unsigned copy of the FDA 483, or an electronic copy of the FDA 483 on your computer screen. You should issue only a signed FDA 483 at the closeout discussion with management.

As noted above, FDA 483s, FDA 483a, and FDA 4056s should be issued in eNSpect unless there are no commodity specific sites in eNSpect, or you encounter technical difficulties, or are addressing certain multiple commodity situations (See IOM 5.5.10).

In these instances, your other options are:

- An electronic (non-eNSpect) version of the FDA 483, FDA 483a, or FDA 4056
- A handwritten FDA 483, FDA 483a, or FDA 4056.

Note that when using a handwritten or electronic (non-eNSpect) version of the FDA 483, FDA 483a, or FDA 4056, the current version must be used.

It is preferred not to identify individuals or firms by name i.e., suppliers and consignees within the FDA 483, FDA 483a, and FDA 4056. Where appropriate to support the FDA 483, FDA 483a, or FDA 4056 observation, identify the individual(s) or firm(s) by substituting other non-specific identifying information as below. Document your evidence in your EIR, fully explaining the relationship(s).

- The lot number for a component received from or shipped to firm "A".
- The invoice number for a shipment from or to firm "A".
- A patient #, record #, etc.
- The study number for a particular Clinical Investigator site.
- Other necessary but non-specific identifying information to show the observation's relationship to a particular firm and/or individual.

5.5.10.4 – Individual Headings, Form FDA 483

District office address and phone number - Legibly print the home district address where the **firm** is physically located, regardless of program area or investigator duty station. Include the district office telephone number and area code. If using eNSpect for the FDA 483, select the home district of the firm. For example, if a firm is located in Little Rock, Arkansas, then the district office would be the OHFI Central Division 4. (See Appendix E for boundary maps to assist you with this.)

For foreign inspections, the district office address will be provided by your trip planner.

Name and title of individual to whom report is issued - Enter the legal first name, middle initial, last name, and full title, of the person to whom the form is issued.

Firm or farm name - Enter the full, legal name of the firm, including any abbreviations, quotation marks, dashes, commas, etc.

Street address, city, state, and ZIP Code - Enter the street address, city, state, and ZIP Code. (Not a P.O. Box, unless P.O. Box is part of the address, such as on a rural route).

Date(s) of inspection - Enter the actual or inclusive date(s) of inspection.

FDA Establishment Identifier (FEI) number - If the FEI is on the assignment, enter it here. If not readily available, leave blank.

Type of establishment inspected - Enter the types of the establishment, such as bakery, clinical investigator, drug repacker, blood bank, cigarette retailer, or medical device manufacturer.

Employee(s) signature and employee(s) name and title - The names of everyone who participated in the inspection with the issuance of an FDA 482 should be listed on the FDA 483, FDA 483a, or FDA 4056, even if they are not available to sign the document. Each member of an inspection team should sign the FDA 483, FDA 483a, or FDA 4056. However, absence of a team member at the conclusion of an inspection need not prevent issuance of the form. (See IOM 5.2.8.1.) If you use an electronically generated FDA 483, FDA 483a, or FDA 4056, be sure you reserve a copy for the program division files – and note that an unsigned photocopy or printed duplicate is not acceptable. (See IOM 5.5.10.2.)

Additional headings on the FDA 4056:

Name of state and department (*if acting under the commission with FDA*) – If the FDA 4056 is used by a state acting under FDA commission, the name of the agency is listed here. (For an FDA-led inspection, place "N/A" in this box.)

Farm mailing address – Address, city, state, and ZIP code at which the farm receives mail

Farm physical location, if different from mailing address – Location identifiers such as GPS coordinates

Type of inspection –

- Initial – a first inspection of the farm
- Routine – a normal surveillance inspection
- Follow-up – a follow-up to a violative inspection
- For-cause – an inspection to follow-up on a specific issue, such as an outbreak or positive microbiological sample
- Other (please specify) – an inspection that doesn't meet one of the other categories (this category used very rarely)

For an initial inspection, you will check both the initial box and select an additional box (routine, for-cause, or other box) as appropriate for the type of inspection conducted.

Crops observed - List the crops for which some element or aspect of growing, harvesting, packing, and/or holding was observed during the inspection. If the farm grows or handles other crops, but those crops were not observed during the inspection, do not list them.

5.5.10.5 - Signature Policy

Everyone present under FDA inspectional authority at issuance must digitally sign--or if not able to do so, sign the first and last pages of the FDA 483 with initials on each intervening page in the designated signature block.

NOTE: if you are not using the official multi-part FDA 483 form, and a copier is not available, insert carbon paper to reproduce a signed copy of the FDA 483.

NOTE: If issuing the FDA 483 using eNSpect, the lead CSO's signature should appear on all pages of the FDA 483, while the remaining team members' signatures should appear on the last page.

NOTE: For FDA-4056. See Exhibit 5-17 - Produce Inspection Details.

5.5.10.6 - Date Issued

Enter the date the form will be issued to the firm's management.

5.5.10.7 - Observations

Where applicable, when formulating each FDA 483, FDA 483a, or FDA 4056 observation, you should attempt to answer the *Who* (using titles or initials when necessary), *What*, *When*, *Where*, *Why*, *How Much,* and *How Often* questions. You should also challenge each observation by asking "So What?" as a way to vet and affirm, the observation's significance.

Enter your reportable observations succinctly and clearly. Conditions listed should be significant and relate to an observed or potential problem with the facility, or its equipment, processes, controls, products, employee practices, or records. "Potential problems" should have a reasonable likelihood of occurring based upon observed conditions or events. Do not cite deviations from policy or guidance documents on the FDA 483, FDA 483a, or FDA 4056.

As appropriate, FDA 483, FDA 483a, and FDA 4056 observations should include relationship of observations to a given population. For example, "Two out of 50 records examined were ***" or "4 out of 12 bags examined were ***." When appropriate, an FDA 483, FDA 483a, or FDA 4056 observation may refer to "inadequate" conditions or qualities, as long as you provide supporting facts (examples) or explanations as to why the condition, practice, or procedure you have observed is inadequate.

It is preferred that you not identify individuals or firms by name, like suppliers and consignees, within the FDA 483, FDA 483a, or FDA 4056. Where appropriate to support the FDA 483, FDA 483a, or FDA 4056 observation, identify the individual(s) or firm(s) by substituting other non-specific identifying information, as suggested below. But be sure to document your evidence in your EIR, to fully explain the relationship(s).

Non-identifying information may include:

- The lot number for a component received from or shipped to firm "A"
- The invoice number for a shipment from or to firm "A"
- A patient number, or record number. (See IOM 5.5.11.3 item 7)
- The study number for a particular clinical investigator site.
- Other necessary, but non-specific, identifying information to show the observation's relationship to a particular firm and/or individual (for example, a supplier number from the inspected firm's internal supplier database consisting of a five-digit number).

Presently there are three ways to generate an FDA 483, FDA 483a, or FDA 4056:

- eNSpect
- Electronic (non-eNSpect) version
- Traditional hard copy (including handwritten)

When using a traditional hard copy or electronic (non-eNSpect) version of the FDA 483, FDA 483a, or FDA 4056, the current version must be used.

5.5.10.8 - Medical Device Inspections

All FDA 483s state the following before the listed observations:

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

Medical device inspections, however, require specific additional language that you should insert on the FDA 483 after the above statement:

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

5.5.10.9 - Correction of FDA 483, FDA 483a, And FDA 4056 Errors

Special note: *The following procedures do not pertain to any adverse conditions noted and then corrected during an inspection. Observations of this type stand and should remain on the FDA 483, FDA 483a, and FDA 4056.*

Because the Inspectional Observations (FDA 483), Request for FSVP Observations (FDA 483a), and Produce Farm Inspection Observations (FDA 4056) forms are of critical importance to both the agency and regulated industry--and because individual forms, such as the FDA 483, FDA 483a, and FDA 4056 may become public through publishing in industry trade press, FOIA inquiries, headquarters postings, and other means--it is critical that complete and accurate documentation of any corrections made to these official documents occurs.

5.5.10.9.1 - Errors Discovered Prior to Leaving the Establishment (eNSpect)

For corrections to an FDA 483, FDA 483a, or FDA 4056 created in eNSpect:

All corrections/deletions should be made in eNSpect. If there are technical difficulties that prevent you from issuing an amended eNSpect 483, you may handwrite the corrections on the original (maintain a copy for the EIR) and inform the firm representative(s) that you will make corrections and provide them with the corrected eNSpect 483.

- Changes made to correct errors in the text of the observation will show on the face of the final printed FDA 483. Any changed text deletions should remain visible as a strikethrough along with the correction that was made. (For example, to change “lot 1234” to “lot 5678,” so that it correctly appears as, “lot ~~1234~~ **5678**” you would select the text to be altered, right click, then select font and select strike-through. Or to add to “lot 1234” so that it includes” lot 5678,” you would embolden the additional lot in this way: “lots 1234 **and 5678**”.
- If an entire observation is removed, or the underlying citation is changed, incidental text should be used to add the statement, "An observation concerning *** was removed, or the underlying citation was changed based on discussions with management."
- Addition of a new observation or changes to the observation.

5.5.10.9.2 - Errors Discovered Prior to Leaving the Establishment (Non-eNSpect)

For an FDA 483, FDA 483a, or FDA 4056 created outside eNSpect:

- Make handwritten changes to correct the error(s) on the original FDA 483, FDA 483a, or FDA 4056, and initial the changes. Correct errors by striking through the erroneous text and entering the correct information (if any). When possible, retrieve and destroy all uncorrected copies of the FDA 483, FDA 483a, or FDA 4056, either provided to or produced by the establishment.
- If the establishment has photocopying equipment available and will provide you with a copy of the corrected original FDA 483, FDA 483a, or FDA 4056, then obtain a copy of the corrected original document from the establishment.
- If you have an FDA-issued scanner, make a digital copy of the corrected original. If you do not, and the establishment has photocopying equipment available and will provide you with a copy of the corrected original FDA 483, FDA 483a, or FDA 4056, then obtain a copy of the corrected original document from the establishment to attach to the EIR.
- If the establishment has no such equipment or refuses to provide you with a photocopy of the original corrected FDA 483, FDA 483a, or FDA 4056, you should duplicate corrections you made on the original and initial the changes using a carbon copy or other copy of the original form. Retain the corrected copy of the FDA 483, FDA 483a, or FDA 4056 to attach to the EIR.

5.5.10.9.3 - Errors Discovered after Leaving the Establishment

Normally, you should not use the amendment process to issue additional FDA 483, FDA 483a, or FDA 4056 items after the inspection has been closed out and you have left the premises. However, if you think you must, consider the following guidance:

- Regarding eNSpect FDA 483, FDA 483a, or FDA 4056, discuss any errors with your supervisor. Make all corrections/deletions in eNSpect per 5.5.10.9.1.
- Regarding non-eNSpect FDA 483, FDA 483a, or FDA 4056, discuss any errors with your supervisor. If necessary, prepare a revised FDA 483, FDA 483a, or FDA 4056.
- When issuing the corrected FDA 483, FDA 483a, or FDA 4056, you should personally deliver the amended FDA 483, FDA 483a, or FDA 4056 to the firm for discussion. If personal delivery is not practical, then mail or electronically by email as a PDF attachment. The FDA 483, FDA 483a, and FDA 4056 must be sent in a manner that protects Trade Secret and Confidential Information. The

amendment to the firm with a full explanation provided in a cover letter. Include a copy of the original FDA 483, FDA 483a, or FDA 4056, and the amended FDA 483, FDA 483a, or FDA 4056, and cover letter, in the EIR. In addition, you should call the person to whom the original FDA 483, FDA 483a, or FDA 4056 was issued to discuss the change(s). Document this discussion in your EIR.

Special Note: The issuance of an amended FDA 483, FDA 483a, or FDA 4056 in person or via mail does not change the inspectional end date. The inspectional end date remains as the date that the original FDA 483, FDA 483a, or FDA 4056 was issued.

5.5.11 - Reportable Observations

You should cite factual observations of significant deviations from the FD&C Act, PHS Act, 21 CFR, and other acts where the FDA has enforcement authority, unless these citations require concurrence, or are specifically prohibited – see IOM 5.5.11.3 Non-Reportable Observations.

However, do not report opinions, conclusions, or characterize conditions as "violative." The determination of whether any condition is “violative” is an agency decision made after considering all circumstances, facts, and evidence.

Examples of reportable observations generally fall into one of two categories, either adulteration or other. See below.

5.5.11.1 – Adulteration Observations

For assistance, review Sections 402, 501, 505(k), 601, and 704 of the FD&C Act [21 U.S.C. 342, 351, 355(k), 361, and 374]. Adulteration observations include specific factual observations of:

- Foods, drugs, devices, or cosmetics consisting in whole, or in part, of filthy, putrid, or decomposed substances.
- Undesirable conditions or practices, bearing on filth or decomposition, which may reasonably result in the food, drug, device, or cosmetic becoming contaminated with filth.
- Insanitary conditions or practices that may reasonably render the food, drug, device, or cosmetic injurious to health.
- Careless handling of rodenticides or pesticides.
- Results of field tests (for example, organoleptic examination of fish, crack-out of nuts, etc.) that reveal adulteration.
- Observations of faulty manufacturing, processing, packaging, or holding, of food, drug, or device products as related to current good manufacturing practice regulations, including inadequate or faulty record keeping.
- Observations of faulty can closures and/or deviations from recommended processing times and temperatures.
- Deviations from the animal proteins prohibited in ruminant feeds requirements (21 CFR 589.2000).
- Results of analytical laboratory findings that reveal adulteration.

5.5.11.2 - Other Observations

You may include other factual observations of significant deviations from the FD&C Act [21 U.S.C. 301], 21 CFR, Government Wide Quality Assurance Program (GWQAP) requirements, and other acts as directed by compliance programs and other agency directives. In some cases, you may cite labeling deviations as directed below. (This list of potential “other observations” is not all- inclusive.)

- Observations indicating non-conformity with commitments made in a New Drug Application, New Animal Drug Application, or in an antibiotic certification or certification exemption form. (See Section 505 FD&C Act, [21 U.S.C. 355].)

- Observations indicating manufacturing of human cellular products that are unapproved new drugs in violation of section 505(a) of the Federal Food, Drug and cosmetics Act (FD&C Act), 21 U.S.C § 355(a), as well as unlicensed biological products in violation of section 351(a)(1) of the Public Health Service Act (PHS Act), 42 U.S.C. § 262(a)(1) should be included with the prior concurrence of CBER.
- Observations, forming the basis for product non-acceptance under the GWQAP. (See IOM 5.2.3.5.)
- Deviations from blood and blood products labeling requirements, as specified in 21 CFR 606.121 and 21 CFR 640.
- Animal protein products, and feeds containing such products, that are not in compliance with the labeling requirements of paragraphs (c) through (f) of 21 CFR 589.2000. (See Section 403(a)(1) or 403(f) of the FD&C Act [21 U.S.C. 343(a)(1) or 343(f)].)
- Deviations from the applicable labeling regulations for human cells, tissues, and cellular and tissue-based products (HCT/Ps), as specified in 21 CFR 1271 and CP 7341.002.
- Observations indicating drug misuse, failure to maintain proper drug use records, and/or poor animal husbandry practices during drug residue investigations. (See the applicable compliance program(s) for guidance.)
- Observations indicating non-conformity with the post marketing adverse drug experience reporting requirements, as specified in 21 CFR 310.305, 314.80, 314.98, 314.540, or 600.80 or other post marketing requirements, as specified in 21 CFR 314.81 or 600.14. (See Sections 505 and 760 of the FD&C Act [21 U.S.C. 355(k) and 379aa].)
- Observations indicating non-conformity with the Medical Device Reporting requirements as specified in 21 CFR 803 (See Section 519(a) of the FD&C Act [21 U.S.C. 360i]).
- Observations of non-conformity to the Medical Devices Reports of Corrections and Removals requirements as specified in 21 CFR 806 (See Section 519(f) of the FD&C Act [21 U.S.C. 360i(f)]) should be verified with the program's division recall coordinator.
- Observations of non-conformity to the Medical Device Tracking requirements, as specified in 21 CFR 821 (See Section 519(e) of the FD&C Act [21 U.S.C. 360i(e)]).
- Observations of non-conformity to the Unique Device Identification (UDI) requirements of 21 CFR 801 Subpart B and 21 CFR 830.
- In general, observations indicating noncompliance with medical device pre-market notification requirements and pre-market approval requirements under FD&C Act sections 510(k) and 515 [21 U.S.C. 360 (k) and 360e] respectively, should be included with the prior concurrence of CDRH and/or CBER.
- Reporting observations noted at a contract facility to the contracting facility is allowed under 21 CFR 200.10. But before doing so, consult with your supervisor to determine if appropriate.
- Observations indicating non-compliance with LACF/Acidified food registration and failure to file scheduled processes. Before doing this, verify lack of such, as covered in CP 7303.803A.
- Deviations from the applicable labeling requirements for outsourcing facilities, as specified in Section 503(B)(a)(10) of the FD&C Act [21 U.S.C. 353b].
- Observations at animal food facilities that are not subject to animal food regulations (for example, not required to register as a food facility) indicating food safety noncompliance with the FD&C Act adulteration or misbranding provisions in FD&C Act section 402 and 403 [21 U.S.C. 342 and 21 U.S.C. 343]. (See Compliance Program 7371.000: Comprehensive Animal Food Inspection for more details.)

5.5.11.3 - Non-Reportable Observations

As implied, non-reportable observations should not be reported on the FDA 483. These objectionable conditions fall into three basic categories:

1. Observations of significant deviations from specific laws and/or regulations, as identified in items 1-9 below.
2. Observations of deviations from specific laws and/or regulations that in your judgment are of "questionable significance" and "deemed not to merit inclusion on the FDA 483, FDA 483a, or FDA 4056," but do warrant discussion with management.
3. Observations, based on your judgement, that deviate from official published guidance, but do not deviate from regulations, and warrant discussion with management.

(See IOM 5.5.12 regarding discussions with management at which time other verbal observations may be discussed.)

Do not report observations pertaining to:

1. Label and labeling content, except per IOM 5.5.11.2, items 2, 3, 4, 5, and 12 above.
2. Promotional materials.
3. The classification of a cosmetic, animal-grooming aid, or device as a drug.
4. The classification of a drug as a new drug, or new animal drug.
5. Non-conformance with the New Drug Regulations, 21 CFR 312.1 New Drugs for Investigational Use in Human Beings: Exemptions from Section 505(a)) unless instructed by the particular program or assignment.
6. The lack of registration required by Section 415 and 510 of the FD&C Act. The lack of registration per 21 CFR 1271 Subpart B Procedures for Registration and Listing, promulgated under Section 361 of the PHS Act.
7. Patient names, donor names, etc. If such identification is necessary, use initials, code numbers, record numbers, etc.
8. The use of an unsafe food additive or color additive in a food product.
9. The lack of approval, conditional approval, or indexing for an animal drug

Non-reportable observations and any corrections made related to them must be discussed with management and be described in the narrative report. See IOM 5.7.1.4.17.

5.5.11.3.1 – Reporting

Be sure to follow any program-specific instructions on how to report when using eNSpect.

You may record non-reportable observations on the FDA 483 or FDA 483a in the three categories in IOM 5.5.11.3 as follows:

- Category 1: You should select the appropriate eNSpect cite, verify or set the "Print type" to "Do Not Print," and save the observation in the eNSpect database. This should be done even if there are no other reportable observations (for example, Lack of Food Registration, as covered in IOM 5.8.1.5, is not reportable).
- Category 2: You should always report these observations under the "General Discussion with Management" heading in the EIR, as specified by IOM 5.5.12.4. Additionally, you may select the appropriate citation in eNSpect, enter the "specifically" text regarding the observation, set it to "Do Not Print," save, and it will be automatically entered into the EIR when it is generated.
- Category 3: There are no eNSpect cites for official guidance. These observations are discussed with management and should be entered directly into the EIR under the "General Discussion with Management."

5.5.11.4 - Annotation of the FDA 483 or FDA 4056

Offer to annotate the FDA 483 for all medical device inspections. The program division has discretion to annotate the FDA 483s in other program areas. BIMO inspections are generally excluded from annotations. Annotations of FDA 483s for inspections in other program areas may be done if both the establishment and the investigator/team believe annotation will facilitate the inspection process. When an FDA 483 is annotated it should be done in accordance with the guidance that follows.

Inform the establishment of the annotation process at some point prior to the final discussion with management. Determine from management whether they wish to have their FDA 483 observations annotated. This is voluntary on the part of the establishment. If the establishment does not want one or more observations annotated, you must honor the request.

The actual annotation of the FDA 483 should occur during the final discussion with management. They should appear as succinct comments about the status of the FDA 483 item. The annotations can be made after each observation, at the end of each page of the FDA 483, or at the bottom of the last page of the FDA 483 prior to the investigator's signature. (See IOM 5.5.12 for discussions of FDA 483 observations with management.)

If the establishment chooses to annotate the FDA 483 observations, the FDA 483 should be annotated with one of the following comments, as appropriate:

1. Reported corrected, not verified.
2. Corrected and verified.
3. Promised to correct.
4. Promised to correct by [insert date].
5. Promised to correct within [time interval].
6. Under consideration.
7. Annotation Intentionally Left Blank.

On the FDA 4056, if the produce farm has corrected the item or has committed to correct it, the description section should include one of the following annotations:

1. Reported corrected, not verified.
2. Corrected and verified.
3. Promised to correct.

The term "verified," as used in the above phrases, means "to confirm; to establish the truth or accuracy." In these instances, you are responsible for the verification. In some situations, you will not be able to verify the corrective action unless there is further program division or center review, or until there is another inspection of the establishment.

The establishment's stated objections to any given observation, or to the FDA 483 or FDA 4056, should *not* be annotated on the FDA 483 or FDA 4056. If firm does not wish to annotate the FDA 483, select “No annotation” in eNSpect, or if issued outside eNSpect, do not annotate. The EIR should include the establishment's objections to the observation and the fact that the establishment declined to have the observation annotated.

When an establishment has promised corrections and furnishes a date or timeframe (without a specific date) for completion, then you may add "by x date" or "within x days or months" in the annotation. Where the investigator and the establishment have "agreed to disagree" about the validity of an observation on the FDA 483, you may annotate this observation with "Under consideration," or with no annotation based on the establishment's desire.

All corrective actions taken by the establishment and verified by FDA should be discussed in detail in the EIR.

5.5.11.5 - Government Wide Quality Assurance Program (GWQAP)

A Memorandum of Understanding (MOU) between the FDA and the Department of Defense (DoD) Defense Logistics Agency (DLA) requires the FDA to determine if medical products offered for delivery to the DLA were produced in accordance with the contract requirements. GWQAP staff request these source inspections and provide OII staff copies of the DLA contract (Form DD1155, Order for Supplies or Services) with the requirements and specifications agreed by the manufacturer.

When performing product acceptance examinations under the GWQAP, you must discuss all deficiencies with management and report these deficiencies in writing on the FDA 483. This includes all deficiencies related to the FD&C Act, as well as deficiencies in complying with contract requirements that result in non-acceptance. There must be a clear differentiation on the FDA 483 between these two types of deficiencies.

Consult these steps:

1. Enter the FD&C type deficiencies (for example, good manufacturing practice (GMP) deviations) first on the FDA 483.
2. In eNSpect, you may use incidental text to describe deficiencies in contract provisions.
3. Alternatively, if you are issuing the 483 outside eNSpect, after the FD&C type deficiencies, draw a line across the printed or electronic page and add a heading "The Following Additional Contract Non-Conformances Were Observed."
4. Enter each deficiency, which forms a basis for non-acceptance, followed by the reference to the applicable contract requirement or specification.
5. Describe the GQWAP observations in the EIR under the *Objectionable Conditions and Management's Response* section.

5.5.11.6 – Issuance of the FDA 483, FDA 483a, or FDA 4056

The FDA 483, FDA 483a, and FDA 4056 should be issued to the most responsible individual physically available on site at the closeout, per 5.5.10.3. If the 483a is issued remotely, it is to be issued to the most responsible individual at the virtual closeout.

A copy should be sent to the top management of the firm, including foreign management, unless the individual to whom you issued the original is the top official of the firm.

The signed FDA 483, FDA 483a, or FDA 4056 can be issued in the following ways:

- Physical paper copy. Be sure printed versions of the signed FDA 483s, FDA 483a, or FDA 4056s are legible.
- Electronically by email as a PDF attachment (onsite, prior to leaving the premises). The FDA 483, FDA 483a, and FDA 4056 must be sent in a manner that protects Trade Secret and Confidential Information.
- Electronic media transfer to the firm (for example, USB or CD/DVD). Follow all IT security policies and procedures when using electronic media, including FDA policy with regards to portable media devices in IOM 5.6.6 and in the FDA Information Systems Security and Privacy Guide).

If the FDA 483, FDA 483a, or FDA 4056 is issued electronically, document your method of issuance and discussions with management in your regulatory notes, per IOM 5.5.12– Discussing Issues with Management.

Upload into eNSpect one copy of any signed, modified, and/or amended FDA 483, FDA 483a, or FDA 4056 issued to the firm.

5.5.12 – Discussing Issues with Firm Management

5.5.12.1 – Communication During the Inspection

During the inspection, it is important to discuss findings you may have with firm management in a timely fashion, where possible, so they can be aware of and have an opportunity to respond to your concerns. At minimum, a meeting should be held once each inspection day with firm management to discuss any findings you believe will lead to an observation on a form FDA 483, or a discussion item, as well as any outstanding items that need to be revisited. During the meeting, you should be prepared to discuss the findings using evidence obtained during your inspection and relate those findings to the applicable laws and regulations. Investigators should refrain from providing advice or consultation during their discussions and should note any firm management feedback related to inspectional findings during the meeting.

5.5.12.2 – Closing Meeting Report of Observations (FDA 483)

Prior to meeting with firm management to conclude the inspection, ensure you have obtained all necessary information to satisfy your assignment, including both a clear understanding of the authority and responsibility of management and evidence to support any objectionable conditions you observed during your inspection.

At the conclusion of the inspection, meet with the most responsible individual (see IOM 5.6.3.1) available to summarize the purpose and scope of your inspection and to discuss the objectionable conditions that you observed. Objectionable conditions may be identified as reportable (See IOM 5.5.12.3) or non-reportable (See IOM 5.5.12.4).

During the discussion, be direct, courteous, and responsive. Explain the significance of each item and relate both reportable and non-reportable objectionable conditions to the applicable sections of the laws and regulations administered by the FDA. Use care to not appear overbearing or arbitrary in your attitude or actions.

Investigators should also refrain from providing advice or consultation during their discussions. Do not volunteer information about other firms or their practices. Ignore casual exploratory questions or remarks from management about competitors or their processes. Your casual and seemingly innocuous remarks may reveal privileged information. Therefore, remain alert and diligent throughout your conversation and avoid voluntarily, or unknowingly, divulging information, which may be privileged or confidential and possibly compromise the FDA's and your own integrity.

Describe in your narrative report all significant conversations with management or management representatives. In most instances it is not necessary to quote management's response verbatim; paraphrasing the replies is sufficient. However, if the situation is such that quoting their reply, or replies, is necessary, enclose them in quotation marks.

5.5.12.3 – Reportable Observations

Issue the Form FDA 483, 483a, or FDA 4056 in accordance with IOM 5.5.12.2 at the close of the inspection. Explain the significance of each observation and relate it to the applicable sections of the laws and regulations administered by the FDA.

During the discussion, be direct, courteous, and responsive with management. Do not be overbearing or arbitrary in your attitude or actions. Do not argue if management voices a different view of the observations. Explain, to the best of your judgment, the conditions you observed that may be determined by the FDA, after review of all the facts, to be violations. Make clear that the prime purpose of the discussion is to call attention to objectionable practices or conditions, which should be corrected.

Determine management’s intentions regarding correcting objectionable conditions, including time frames. Where applicable, request from the firm whether they intend to annotate the observations (see IOM 5.5.11.4). Advise

firm management if the FDA receives an adequate response to the form FDA 483, 483a, or FDA 4056, or other objectionable conditions, within 15 business days of the end date of the inspection, as it may impact FDA's determination of the need for subsequent action. Additional instructions on this response may be provided based on program procedure.

The firm may propose corrections or procedural changes and ask you if this is satisfactory. If this involves areas where your knowledge, skill, and experience are such that you know proposed responses will be satisfactory, you can so advise management. However, do not assume the role of an authoritative consultant. Do not recommend products or services of a particular establishment. If asked to suggest a product or consulting laboratory, refer the inquirer to a classified directory, or trade publications or organizations.

If significant deviations are observed during a domestic inspection, you should inform management during the closeout discussion the conditions you observed that may, after further review by the agency, be considered violations of the FD&C Act or other statutes. Legal sanctions available to the FDA for domestic firms may include seizure, injunction, civil money penalties, and prosecution.

If significant deviations are observed during a foreign inspection, you should inform management during the closeout meeting that significant deviations observed during a foreign inspection could result in a facility's product(s) being detained and potentially refused entry into the United States.

5.5.12.4 – Discussion Items ("Do Not Print" Observations, Other items)

Non-reportable observations are not listed on a form FDA 483, FDA 483a, or FDA 4056, and are provided verbally to the firm at the close of the inspection. (See IOM 5.5.11.3 for a discussion of the different categories of non-reportable observations.)

Regardless of the nature of the non-reportable observation, you should explain the concern(s) clearly and succinctly to firm management. Where the issue may represent a deviation from a regulation, you should refer the firm to that regulation. You may explain to the firm that although the Discussion Items will not be listed on the form FDA 483, FDA 483a, or FDA 4056, they will be documented in the EIR and may be followed up on at the next inspection. For non-reportable observations which potentially represent significant deviations from specific laws/regulations, or as directed by your program division, you may encourage the firm to respond to the matter to the FDA in writing as you would for reportable observations.

As with reportable observations, determine management's intentions regarding correcting observed conditions, including time frames. The firm may propose corrections or procedural changes and ask you if this is satisfactory. If this involves areas where your knowledge, skill, and experience are such that you know the proposed response(s) will be satisfactory, you can advise management. Do not assume the role of an authoritative consultant, and do not recommend products or services of a particular establishment.

5.5.12.5 – Receipt for Samples

You must issue a Form 484, Receipt for Samples, if you collect any physical sample during an inspection. In general, do not issue the Form 484 prior to concluding the inspection, even if the sample is collected at the start of the inspection, as issuance of the form closes the inspection (See IOM 4.2.5). If a Form 484 is issued before the inspection is completed, issue another Form 482, Notice of Inspection, before resuming the inspection. Also, if the person to whom the Form 482 was issued is not available, give it to someone else who meets the definition of "owner, operator, or agent-in-charge." Submit an exact copy with the EIR. Also, do not comment on the type of examination expected, or promise a report of analysis.

5.5.12.5.1 – Items Requiring a Receipt

Issue an FDA 484 for any food, drug, device, or cosmetic, or portion thereof, physically removed from the establishment.

NOTE: A receipt must always be issued to anyone from whom you obtain Rx drugs. This includes individuals, as well as firms. (See IOM 4.2.5.4 and IOM 4.6.2.40.)

The following are examples of materials also requiring a Receipt for Samples:

- Air filter pads.
- Rodent pellets, nesting material, package cuttings, insects, and insect frass.
- Any other physical evidence physically removed from the plant, including in-line and environmental swabs.

5.5.12.5.2 – Items Not Requiring a Receipt

Do not issue an FDA 484 for:

- Items or materials examined during the inspection but not removed from the establishment (report adverse results of analysis of materials on FDA 483 and FDA 4056 as indicated in IOM 5.5.11.1).
- Labels and labeling, including promotional materials.
- Photographs taken during the inspection.
- Record(s), including production, quality control, shipping, and interstate records.

Firm management may request copies of documents or records you obtain from their firm. There is no objection to supplying them. See IOM 5.6.11.3 for procedures when a firm requests a receipt for records copied during an inspection or investigation.

5.5.13 – Post-Inspectional Contacts

If the firm contacts you after the inspection regarding the inspection or follow-up, you should refer the request to your supervisor. You should not respond directly to the firm regarding the adequacy of the firm's response to inspectional observations or any follow-up being planned.

After the inspection is concluded, if you find that a document or other required information is missing, you should discuss the needed information and how to proceed with your supervisor.

5.6 - Evidence Development (Types of Evidence)

5.6.1 – Definition of Evidence

Evidence is defined as information in the form of documentation or verbal statements and the material objects admissible as testimony in a court of law used to obtain a ruling on a controversy. The recognition, collection, and effective presentation of admissible evidence is essential to successful litigation. (See IOM 3.3.)

Evidence is required to support your observations and reports of violative conditions, even if not facing potential litigation. Evidence may take several forms during your inspection, with common ones listed below. See the referenced sections for further information about the collection and maintenance of those evidence types.

- Samples (See IOM 5.6.4).
- Exhibits, including both physical material (also referred to as filth exhibits) obtained from the firm (see IOM 5.6.5) and copies of records obtained from the firm, usually via electronic means (see IOM 5.6.6).
- Photographs or video recordings taken by the investigator (see IOM 5.6.7).
- Observations made by the investigator and captured in Regulatory Notes, including statements made by firm personnel (See IOM 2.1.4.2).

- Written statements of knowledgeable persons, such as those captured in the form FDA 463a, Affidavit (See IOM 4.4.5).

Although inspectional procedures to detect adulteration and contamination, etc., are described under specific headings in the IOM related to one type of inspection, the same procedures and/or techniques may also apply to other areas. For instance, the procedures to detect contamination from filth, insects, rodents, birds, etc., described in IOM section 5.8.7.2, may also apply to drugs or other products. Your experience and training will help you identify techniques that you can use to detect possible violations during your inspections.

5.6.2 - When Evidence of a Criminal Violation is Discovered During a Regulatory Inspection

There may be occasions where you are conducting a regulatory inspection at a facility and, during the inspection, you discover evidence of a criminal violation. If this occurs, you should continue the regulatory inspection as you would under normal circumstances. (See IOM 5.2.2.4.) Document the observation and notify your supervisor as soon as possible. The program division should refer your observations to OCI for their consideration. Evidence of the observation could be used in a criminal investigation, and the evidence could legally be disclosed to criminal investigators.

If you become aware of an ongoing criminal investigation, notify your supervisor. The program division should follow the Regulatory Procedures Manual (RPM) and notify the appropriate center of any OCI involvement in a center-directed inspection.

The discovery of evidence of a criminal violation may also be relevant to FDA's responsibility to ensure articles are being produced in conformity with the FD&C Act. Additional inspections may be warranted. Such inspections should be planned and documented in accordance with IOM 5.5.1.4 - Conducting Regulatory Inspections When the Agency is Contemplating Taking, or is Taking, Criminal Action.

5.6.2.1 - Use of Evidence Gathered During a Criminal Investigation

The extent to which information gathered during a criminal investigation may be shared with FDA counterparts and partners will vary with each case. Investigators should determine the extent of information sharing in accordance with the following guidelines.

Information and evidence gathered during a criminal investigation may be shared with regulatory personnel, subject to two reservations:

1. Information obtained pursuant to grand jury subpoena or testimony may not be shared. Disclosure of such information to anyone other than individuals identified by the Department of Justice attorney involved could subject the individual making the improper disclosure to sanctions for contempt by the court. Only the court can authorize disclosure beyond these parameters. Information obtained by other means (search warrant, cooperative witnesses, surveillance, etc.) may be shared, subject to the following paragraph.
2. There may be a need to protect the confidentiality of the criminal investigation. For example, disclosure to regulatory investigators might prematurely disclose the existence of the criminal investigation or the identity of confidential informants. However, whenever you are calculating the need to protect the confidentiality of information gathered during a criminal investigation through means other than the grand jury, you must consider whether it will be in the interest of public health to protect the confidentiality of that information.

Criminal investigators should consult their supervisors to determine whether disclosure should be made to regulatory investigators.

5.6.2.2 - Use of Evidence Voluntarily Provided to the Agency

Criminal and regulatory investigators may share information and evidence voluntarily provided to the FDA, without use of the regulatory inspection authority, search warrant, or subpoena. If criminal investigators decide not to share such information because of a need to protect the confidentiality of the criminal investigation, they should consider the potential impact on the public health of protecting the confidentiality of that information.

5.6.2.3 - Concurrent Administrative, Civil, and Criminal Actions

It may be appropriate to seek administrative and/or civil remedies against a firm or individual under investigation for criminal violations. There are many issues involved in determining whether such actions may proceed concurrently, or whether certain actions should proceed first. Each situation must be evaluated on an individual basis. If administrative and/or civil remedies are under consideration against a firm or individual also under investigation for criminal violations, representatives from the center responsible for evaluating the administrative and/or regulatory action should meet with the OCI headquarters staff to discuss issues related to the timing of administrative, civil, and criminal actions. The OCI and other components of FDA may share information subject to the reservations set out above.

5.6.2.4 - Working with a Grand Jury

Finally, if you are assigned to work with a grand jury, you should not participate in a regulatory inspection or other regulatory matter involving the same firm or individual(s). Such participation is contrary to long-standing agency policy, might be unlawful, and could result in sanctions against the investigator and the agency. You should not participate in any regulatory matters that could result in improper disclosure of grand jury information, even after the grand jury investigation is closed. Grand jury proceedings remain secret even after they are concluded. Under no circumstances should you undertake such participation without first obtaining clearance from the DOJ attorney or the OCC attorney assigned to the grand jury case. (See IOM 3.8.2 for additional information on grand jury proceedings.)

5.6.3 – Individual Responsibility

Always determine and report the full legal name, title, mailing address, and email address of the top management official(s) to whom FDA official correspondence, including FMD-145 correspondence, should be directed. If an email address does not exist, this should be noted.

Always determine and report the full legal name and title of persons interviewed, who supplied relevant facts and the name, title, mailing address, and email address of top management officials to whom FDA correspondence should be directed. If an email address does not exist, this should again be noted.

Always determine and report the full legal name, title, mailing address, and email address of the responsible individual to whom FMD-145 correspondence should be directed. If an email address does not exist, this should be noted.

Obtain correct names and titles of all corporate officers and/or company officials.

You should also identify and report responsibilities for the following firm representatives:

1. Top management official (TMO), synonymous with the owner, operator, or agent-in- charge of a facility. The TMO holds the ultimate duty, power, and responsibility for the inspected facility and is usually the individual at an inspected facility to whom credentials are displayed and any FDA forms 482, 483, and 484 are issued. The TMO of a facility may not be present during an inspection (for instance, they may be located at the corporate office).
2. In the absence of the TMO, the individual who is the most responsible person present at the time of the inspection, and to whom credentials are displayed and any FDA forms 482, 483, and 484 are issued.

3. Those present for the inspection and who were interviewed and supplied relevant facts. Determine and report the full legal name and title.

5.6.3.1 – Responsible Individuals

The identification of those responsible for violations is a critical part of the inspection, and as important as determining and documenting the violations themselves. Responsibility must be determined to identify those persons to hold accountable for violations, and with whom the agency must deal to seek lasting corrections. (See IOM 3.3.1.4)

Document and fully report individual responsibility whenever:

- It is required by the assignment,
- Inspectional findings suggest the possibility of regulatory action, or
- Background information suggests the possibility of regulatory action.

5.6.3.2 – Duty, Power, Responsibility

Duty – An obligation required by one's position. A moral or legal obligation.

Power – Possession of the right or ability to wield force or influence to produce an effect.

Responsibility – An individual who has the duty and power to act is a responsible person.

Three key questions to consider:

- Who had the duty and power to detect the violation?
- Who had the duty and power to prevent the violation?
- Who had the duty and power to correct the violation?

5.6.3.3 – Inspection Techniques: How to Document Responsibility

Obtain pertinent educational and experience backgrounds, and the duties and powers of the officers and employees in key managerial, production, control, and sanitation positions. Ascertain the experience and training of supervisory personnel, in terms that will describe their qualifications to carry out their responsibilities.

There are numerous ways to establish and document responsibility. Evidence may be obtained during interviews as well as record reviews specifically intended to determine responsibility. Cover and report items such as:

- Organizational charts.
- Statements by individuals admitting their responsibility or attributing responsibility to others.
- Company publications, letters, memos, and instructions to employees.
- The presence or absence of individuals in specific areas at specific, significant times, and their observed activities directing, approving, etc.

The following questions may be useful, to help you establish relationships between violative conditions and those responsible:

- Who had knowledge of the conditions?
- Who should have known of the conditions because of their specific and/or overall duties and positions?
- Who had the duty and power to prevent or detect the conditions, or to ensure that they were prevented or detected?
- Who had the duty and power to correct the conditions, or to ensure that they were corrected? What was done after the person(s) learned of the conditions? Upon whose authority and instructions?
- What orders were issued (When? By whom? To whom? On whose authority and instructions?)?

- What follow-up was done to ensure orders were carried out (When? By whom? On whose authority and instructions?)?
- Who decided corrections were, or were not, complete, and satisfactory?
- What funding, new equipment, new procedures were requested, authorized, or denied in relation to the conditions? Who made the requests, authorizations, or denials?

You should also establish the various duties and powers related to a firm's general operations to help further clarify specific relationships to violations. The following questions may help you ascertain such key details:

- Who decides what processing equipment to buy?
- Who decides what raw materials to purchase?
- Who decides what products to produce and what procedures to follow in production?
- Who authorizes production schedules, including how much to produce, what to make, and when to stop or alter production?
- Who decides what production controls are used?
- Who decides what standards are set for products, raw materials, and processes?
- Who decides how to correct or prevent adverse conditions? How much is spent and who is hired to correct or prevent adverse conditions, including, when to clean up?
- Who decides how products will be labeled e approved, and what products to ship?
- Who decides when to reject raw materials or products? When to initiate a recall? And what acceptable quality levels should exist for products?
- Who decides when to hire or fire personnel?
- Who will accept the FDA 482, Notice of Inspection and FDA 483 Inspectional Observations, FDA 483?; Who refuses an inspection?
- Who designed and implemented the quality assurance plan, and receives reports of Q.A.? Who acts, or should act, upon those reports?
- Who is responsible for auditing other facilities, contractors, vendors, Good Laboratory Practices (GLP) sites, etc.?
- In the firm's business relationships, who signs major contracts, purchase orders, etc.?

In some circumstances, documenting individual responsibility requires investigative techniques that lead to sources outside the firm. These sources may include contractors, consultants, pest control or sanitation services, local health officials, and others. Obtaining copies of documents exchanged between the firm and outside parties may help establish responsibilities. Additionally, do not overlook state officials as another possible source of helpful information.

During the inspection, you may observe persons who hold responsible positions and/or influence in the firm whose abilities or judgment may be affected by an obvious infirmity, or disability. If it is obvious the infirmity adversely affects the person's responsibilities or duties that are under FDA oversight, describe in your EIR the extent of the infirmity and how it relates to the purported problem or adverse condition.

5.6.4 - Samples

Samples, including Factory Food Samples and packaged finished products collected during inspections, provide the necessary links to establish routes of contamination and/or actual product adulteration (for more on in-lines, see IOM 4.3.6.6.3). Samples also clearly establish the jurisdiction of the FDA over the products and/or operations and form the basis for judicial actions. However, in many cases, collection of the physical product is unnecessary or impractical, in which case a documentary sample, consisting of copies of relevant documents and labeling, may be collected instead (see IOM 4.6.1.3). The type and nature of the sample collected will depend on a variety of factors, including

instructions in the applicable Compliance Program for the inspection you are conducting. (Refer to IOM Chapter 4 for more information regarding the collection of samples, including 702(b) portion requirements, which apply to many physical sample types.)

Collect physical samples for laboratory examination only when they contribute to confirming the suspected violation, or when directed by the assignment or your supervisor. Lack of a violative physical sample is not a bar to pursuing regulatory and/or administrative action providing the cGMP deficiencies have been well documented. Likewise, physical samples found in compliance are not a bar to pursuing action under cGMP charges.

If a physical sample is collected during an inspection, ensure that you are familiar with the requirements for issuing the form FDA 484, Receipt for Samples, as outlined in IOM 4.2.5. Remember that the form FDA 484 must be issued at the close of the inspection and prior to departing the firm (see IOM 5.5.12.5).

There will be times when one program division will request that another program division collect surveillance or compliance samples on its behalf. The requesting program division should create an assignment for the sample collection using the Assignment Management Service (AMS), providing as much specificity as possible to assist the investigator in collecting the appropriate material(s).

5.6.5 – Exhibits

Exhibits can be extremely effective and important forms of evidence to establish existence of violative conditions or products. Exhibits may refer to either records or physical material(s) (other than an official sample) which are collected from the firm to demonstrate insanitary conditions contributing, or likely to contribute to, filth in the finished product, or to practices likely to render the product injurious or otherwise violative. Photographs and video recordings taken by the investigator are also considered exhibits and are addressed in IOM 5.6.7.

5.6.5.1 – Records Collected as Exhibits

The type and nature of records obtained to document objectionable conditions will vary greatly depending on the matter being documented. Regardless of the record, you should heed the following guidance:

- Do not remove the firm's only copy of records. If duplicates are not available, whenever possible, scan, photograph, or photocopy.
- Review all reproductions or copies to ensure all relevant information is readable.
- Obtain all records using appropriate methods, including handling them in a manner to preserve the chain of evidence, such that the content may be attested to later. (Methods for properly obtaining and handling electronic records are provided in IOM 5.6.6.)
- Identify exhibits according to IOM 5.6.10.2.
- During inspections, do not accept any records that would be used as Exhibits by email from outside the FDA.

Note: This is not applicable to remote FSVP inspections.

5.6.5.2 – Physical Material Collected as Exhibits

Certain physical materials (other than official samples) may be collected to support objectionable conditions. These materials should relate to insanitary conditions contributing, or likely to contribute, to filth in the finished product, or to practices likely to render the product injurious or otherwise violative.

Submit as an investigational or INV sample physical exhibits collected during an inspection (see IOM 4.1.5). Describe each subsample and assign a unique subsample number to each exhibit. Group similar subsamples on one collection report.

When collected during an inspection, describe, and refer to the INV sample(s) in your EIR, relating them to objectionable conditions. Diagrams of the establishment, floor plans, flow charts, and schematics are useful in preparing a clear concise report and in later presentation of testimony. A small compass is useful in describing exact locations of objectionable conditions in the plant, in your diagrams, and locations from which samples were taken, etc.

Examples of physical exhibits include:

- Live and dead insects, insect frass (droppings), webbing, and insect-chewed materials; nesting material of rodents and/or other animals; and other behavioral evidence of the presence of insects, rodents, and other animals.
- Components and finished dosage forms.
- Samples of in-process ingredients, in-process materials, and unpackaged finished products, including Factory Food Samples or "in-lines." Note: Samples of packaged finished products and ingredients are official samples. For details about official samples, see IOM 4.1.1 and 4.1.4.
- Manufacturing and control devices or aids.
- Evidence showing the presence of prohibited pesticide residues. (A method you can consult for swabbing for prohibited pesticide residues can be found in Laboratory Information Bulletin # 1622.

5.6.6 – Electronic Records

Electronic records are defined in 21 CFR 11.3(b)(6) as any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by an electronic system. This term applies specifically to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted, under any records requirements set forth in agency regulations. This also applies to electronic records submitted to the agency under requirements of the FD&C Act and the PHS Act, even if such records are not specifically identified in agency regulations. In both instances, these records should be maintained and handled as identified in IOM 5.6.6.2.3. Electronic data obtained from a firm provides an investigator with a wealth of information that can be used to assess industry's compliance with the FD&C Act and promulgated regulations.

5.6.6.1 - Electronic Databases, Queries, and Records Requests

Firms may use proprietary programs developed in-house, or off-the-shelf programs, to generate and/or store records used to show regulatory compliance. This includes blood bank databases, drug production records, medical device complaints, and/or service records. In addition to accessing individual electronic records (for example, in PDF file format), these programs can often be queried to generate copies of the databases or summary data in alternative commonly used file formats, such as Microsoft Excel. During an establishment inspection you may request and receive copies of data from, or summary data generated by the firm about, their electronic databases. Any methods used must maintain the integrity of the electronic data and prevent unauthorized changes.

Of note: Do not personally access a firm's system to review electronic records, databases, or source data during the course of an inspection, unless it is:

- a bioresearch monitoring inspection which meets the criteria outlined in section 5.14.2.1 or
- a biologics inspection where it is not practical to oversee the firm's personnel while they access their system, (see section 5.13.2.5.1).

When it is necessary to access a firm's data during an inspection, you should:

- Oversee the firm's personnel accessing their system and have them answer your questions.

- Request the firm run queries specific to the information of interest.
- Request the firm provide the parameters used to generate the data.
- Request the firm to transmit the electronic data securely to the FDA or provide it on electronic storage media.

Firm electronic data can be dynamic with real-time updating. Your request may require the firm to develop one or more custom queries to provide the requested information. A custom report query is the method of using the reporting software to pull the specific data requested during the inspection (for example, all complaints from the last 12 months with specific data fields). You must assume the query logic is not validated and take appropriate action to ensure the data is accurate and no data has been omitted due to a programming logic error occurring at the firm.

Do not use the firm's equipment or personnel to perform computerized data manipulation for the purpose of real-time review and analysis. If you perform analysis on the working copy of the data from an electronic database (including sorts, pivot tables, or other reviews) to develop or support observations, you should request the firm conduct the same analysis and provide a copy of this analysis (the firm is under no obligation to do so). This can be done by requesting an electronic file that includes only the information of interest (for example, an Excel spreadsheet of failures of a certain type for a specific time period) or requesting a paper copy of the information of interest.

Before requesting a copy of computerized data or electronic records, you should ascertain the following:

1. Determine the program used by the firm to maintain the data of interest. Programs may be capable of outputting data in one of several file types; it is best to obtain data files in a format compatible with programs currently used by the agency such as PDF or XLSX. Check the program you plan to use to ensure it can handle the file type you will be requesting. If necessary, some file types may have standard, built-in conversion programs to facilitate review, such as converting a Microsoft Word document to an Adobe PDF. Other types of file conversion may be difficult and should not be attempted without the necessary knowledge and availability of conversion-type programs where applicable. If help is needed for file conversion, assistance may be available within the program division.
2. Determine what fields of information are routinely captured by the firm. This can be accomplished by requesting a printout of the data structure of the data file or observing firm personnel inputting data at a computer terminal or workstation. It is common for databases to contain numbers or other coded information requiring translations from look up tables to generate meaningful text. You should determine if information fields contain coded data, and if so, a code breakdown should be obtained. Information about code breakdowns should be in the SOPs for that computerized system. Be aware, in relational databases, there may be linking data fields that exist in other tables that should also be considered in the overall data request.
3. If the files are too large to be securely transmitted or to fit on electronic storage media, file compression can be used. If possible, ask that the firm prepare the data in a compression format that is self-extracting. Self-extracting files are executable files and should be virus-scanned before and after executing. All electronic storage media should be scanned prior to being used on any FDA computer. Whatever compression utility is used, make sure you have the software necessary to obtain the uncompressed files for review.

5.6.6.2 – Receiving and Handling Electronic Records

Refer to your program for approved methods of secure transmittal of electronic records, as well as instructions that can be provided to regulated industry. Secure means of transmittal may include approved cloud file-sharing, or use of FDA Electronic Submissions Gateway. If there are no mechanisms available for a firm to securely transmit

the data electronically to the investigator, the data may be provided to the FDA by receiving electronic media from the firm or you can provide the firm with new electronic media or an encrypted portable media (e.g, data locker) that has been wiped. OII procedures for the use of electronic media will be identical for both domestic and foreign inspections/investigations. Those foreign locations that may present a security challenge will be handled on a case-by-case basis through the foreign trip-planning process and will be discussed with the investigator prior to departing the United States.

Data received on electronic media presents a challenge to both IT security and physical security of the media. The information obtained from the firm may be commercial confidential information (CCI), and as such, must be protected to the greatest extent possible. It is your responsibility to make sure the physical data source remains secure. Likewise, data obtained from extra-governmental sources may contain viruses or malware that may be included with the information provided to the investigator, either on purpose or accidentally. The transfer of electronic data must be evaluated to facilitate safeguarding the security of both FDA and firm information. You should be cognizant of issues that may arise with the use of electronic media and be vigilant while using it.

The Device Control Data Loss Prevention (DLP) tool at the FDA blocks most FDA users from using unauthorized USBs, as this is against FDA security policy (as described in FDA Staff Manual Guide 3251.12, Appendix Z). Certain OII Investigators have been granted an exception and are permitted "read access" to firm-provided USBs to transfer firm provided data onto their computers. However, they are not permitted "write access," as FDA data should not be written to a device that is not Federal Information Processing Standard (FIPS) 140-3 compliant and/or approved on the FDA Master Approved Technologies (MAT) list. If you are an investigator and are having problems accessing content on a firm-provided USB, please contact your information system security officer (ISSO).

If you provide the electronic storage media to the firm, use only clean and preformatted media. An additional safeguard is to request the firm reformat the media on their own computer to assure it is usable and "clean."

There are no guarantees the files provided via secure transmission on electronic storage media will be usable data. It is your responsibility to make a working copy to view the copied files and verify the files both contain the information requested, and that the information is useable to you, prior to closing the inspection.

5.6.6.2.1 - Original Copy

An original copy is an unaltered copy of a source electronic record collected to support observations of potential violations or used as evidence in administrative or judiciary proceedings. Any original copy included in an EIR, memorandum, or C/R, must be stored as to maintain the chain of custody and ensure the records may be verified any time after collection.

When records are received via a secure transmission method, the resulting file made available to the CSO must be treated as the original copy. A working copy of the file should be created, and the original transferred to a secure directory for preservation in accordance with program records management procedures, as it may be used to support observations of potential violations or used as evidence in administrative or judicial procedures.

Any electronic storage media containing electronic records received during an inspection should be considered and handled as the original copy. The original copy (USB, CD, DVD, etc.) of electronic records should be secured to ensure the integrity of the data when used to support observations of potential violations or used as evidence in administrative or judicial proceedings. Handle and prepare the media in accordance with IOM 5.6.6.2.3 below.

5.6.6.2.2 - Working Copy

A copy of an electronic record that is created from the original copy and is used to review and analyze the records, to not alter the original copy. This is an exact copy of the original copy electronic records.

5.6.6.2.3 - Identifying and Securing Electronic Storage Media

When electronic storage media are used to obtain electronic records, you should follow these steps to ensure their proper identification and security:

1. If you provide the disk(s)/USB drives to be used, use only new electronic media or an encrypted portable media (e.g. data locker) that has been wiped.
2. Label each original copy of electronic storage media, accordingly, with:
   a. Firm name.
   b. Date and your initials.
   c. The name of the appropriate software and version to ensure readability of the information.
3. Make a working copy of the electronic storage media.
   a. First virus-scan the original storage media by taking the following steps:
      i. Disconnect your machine from the FDA network, the VPN, and the internet.
      ii. Insert the media into your computer (USB drive into USB port or CD/DVD into drive).
      iii. Do NOT click ok on or accept any Windows prompts for driver installations.
      iv. Right Click on the drive of interest.
      v. Select "Scan for threats"
      vi. If any threat (for example, a virus or malware) is detected, do not select “Clean” or “Delete”, as the data may be used as evidence. Instead, keep the computer disconnected from the network and report the incident to ERIC at 866-807-3742 and the FDA Cybersecurity and Infrastructure Coordination Center (CIOCC) at CIOCC@fda.hhs.gov or 855-533-2762. Maintain chain of custody on the electronic media. Alert your supervisor of the issue and the steps taken.
      vii. If the scan detects zero (0) threats, proceed forward.
   b. Copy the original information from the electronic storage media onto a working copy.
   c. Verify the data is useable.
4. Seal any original copy(s) with an FDA-415a in an FDA-525 or similar envelope. Complete blocks 2, 3, 5, 7, and 12 of the FDA-525 and seal with an Official Seal, FDA-415a. If you use a larger envelope, identify the envelope with your name, title, home District and program Division, date, firm name, firm address (include zip code), and description of the contents of the envelope. Mark the FDA-525 or similar envelope as containing electronic storage media, or other media, and document the software type and version(s) required to open the included software (for example, Microsoft Word 2016, Microsoft Excel 2016, or Windows Photo Viewer). The electronic storage media or other media should be stored as part of the hardcopy exhibits in the designated file room. See IOM 5.7.3.1.
5. Prepare electronic record(s) for inclusion in the EIR, Memorandum, or C/R.

5.6.7 – Photographs or Video Recordings

Photos taken during inspections are not investigational samples. They are exhibits. Only use FDA-issued equipment, such as a government-issued camera, to take photographs; use of personal equipment may subject that equipment to preservation and discovery in future litigation.

Since photographs are one of the most effective and useful forms of evidence, every photo should be taken with a purpose. Photographs should only be taken for evidentiary purposes (for instance, to document violations and

environmental surface subsample sites). Photographs should be related to insanitary conditions or depict violative conditions.

Safety note: Evaluate the area where you intend to use, or are contemplating using, electronics for any personal or other safety concerns (see IOM 10.12.2). Potentially explosive conditions may be present that may **limit or prohibit the use of photography** equipment, including flash photography. These conditions may include dusty areas or other areas where explosive or flammable vapors may be present.

Additionally, the high risk for cross-contamination of manufacturing processes may also warrant the use of alternate equipment or procedures (for example, in certain active pharmaceutical ingredient (API) facilities, in the vicinity of potent compounds, and in penicillin-manufacturing operations). Alternative approaches may include the use of dedicated equipment or requesting firm personnel to take photographs on your behalf. If firm personnel are amenable to the request and take photos on your behalf, those photos should be handled as other electronic records obtained from the firm, per IOM 5.6.6.2. If you should encounter any refusals to permit photography, see IOM 5.6.7.1 below.

Examples of conditions or practices effectively documented by photographs include:

- Evidence of rodent- or insect-infestation and faulty construction or maintenance that contributes to these conditions.
- Routes of potential, as well as actual, contamination of raw materials or finished products.
- Condition of raw materials or finished products.
- Employee practices contributing to contamination or violative conditions.
- Manufacturing processes that may lead to the product being violative.
- Manufacturing and various other records showing errors, substitutions, penciled changes in procedure, faulty practices, deviations from GMPs, NDAs, or other protocols, altered or inadequate assays or other control procedures, and any variation from stated procedure. (See IOM 5.3.8.2 for identification of records.)
- Effluent contamination of water systems. (See IOM 5.6.3.2 for techniques for photographing this type of contamination.)

When photographing labels, make sure your picture will result in a legible label with any text or characters large enough to be read by an unaided eye. With regards to labels or documents that have been whited-out, a suggested technique is to photograph them by holding a flashlight against the whited-out side, and taking a close-up photo of the reverse. This will produce a photo with a mirror image of the whited-out side.

Guidance on maintaining and preserving digital photos/video are provided in IOM 5.6.7.3 and 5.6.7.5. If you use a non-digital (film) photography method, see guidance in Exhibit 21 (Film Photography) and consult your supervisor. Ensure your actions to process and obtain the resulting photographs or video is documented in your notes.

5.6.7.1 - In-Firm Photographs

Take your camera or other FDA equipment for taking photographs into the firm and use it as necessary, just as you use other inspectional equipment. Only FDA equipment is to be used to take photos while conducting official business. Do not request permission from firm management to take photographs during an inspection because taking photographs is part of our agency's authority to conduct inspections, as part of Section 704(a)(1) of the FD&C Act [21 USC 374(a)(1)].

If management objects to taking photographs, explain that photos are an integral part of an inspection and present an accurate picture of firm conditions. You can also advise management that the U. S. Courts have held that photographs may lawfully be taken as part of an inspection. If management continues to refuse, provide them with the following references:

- Dow Chemical v. United States, 476 U.S. 227 (1986): This Supreme Court Decision dealt with aerial photographs by EPA, but the Court's language seems to address the right to take photographs by any regulatory agency. The decision reads in part, "… When Congress invests an agency with enforcement and investigatory authority, it is not necessary to identify explicitly each and every technique that may be used in the course of executing the statutory mission. …"
- United States of America v. Acri Wholesale Grocery Company, A Corporation, and JOSEPH D. ACRI and ANTHONY ACRI, Individuals, U.S. Division Court for Southern Division of Iowa. 409 F. Supp. 529. Decided February 24, 1976.

If management still refuses, obtain the name and contact information for the firm's legal counsel, and advise your program division management immediately. If the firm does not have legal counsel on retainer, collect the name and contact information for the most responsible individual. Program division management will advise their assigned Senior Enforcement Advisor (SEA) in the Office of Chief Counsel (OCC) of the situation, and OCC will then contact the firm's legal counsel or most responsible individual to discuss FDA's legal right to take pictures during inspections. OCC will relay the results of this conversation to program division management. If you have already taken some photos do not surrender any storage media or film to management, and do not agree to delete any photos. Advise the firm that it can also take photos and obtain copies of the photos taken by the FDA under the Freedom of Information Act. (See IOM 5.6.7.7.)

If management of a drug or device firm does, or will, not give a reasonable explanation for its objection, such as a showing that the chemical properties of products manufactured at the facility are such that taking photographs would adversely affect product quality, you may advise management that the refusal may constitute a limiting of the inspection under Section 501(j) [21 U.S.C. 351(j)] of the FD&C.

5.6.7.2 - Photo/Video Identification and Submission

One of the most critical aspects about photographs or videos is the ability for the agency to provide testimony clearly verifying the authenticity of the conditions depicted in the photograph or video. Regardless of the method used to create the recording, you must create a trail, starting with the taking of the photo or video, confirming its original accuracy and establishing a record describing the chain of custody.

The following action steps help protect authenticity:

- Make sure each photograph or video is described in your regulatory notes in sufficient detail to ensure positive correlation of the photo or video with your inspectional findings.
- Do not delete any photographs taken during an inspection, even if the photograph may be blurry or unusable for the final report, as it may raise questions about missing evidence. Such photographs should be described in your regulatory notes and stored with other photographs from the operation.
- To establish identification for a series of photos, photograph the card with your name, program division address and phone number, prior to beginning to take photographs. This will help identify files and assist in tracking, if any media becomes separated from its identification envelope during processing or storage.

Proper procedures will also allow the agency to provide evidence confirming the authenticity of the photographs or video recording in the event you are not able to testify personally.

Photographs and videos must be identified when included as part of an EIR or sample. If using another technology, consult your supervisor for guidance on identifying the photographs or video for submission.

5.6.7.3 – Digital Photographs or Video Recordings

Many digital cameras can record high resolution images and video with corresponding large file sizes stored initially on the device, often in the form of removable, non-volatile flash memory cards or non-removable flash

memory built into the device. This presents a challenge to investigators, since the original digital images, captured at the moment the images are recorded to the device's storage, must later be copied and eventually uploaded into eNSpect or another electronic system. Due to the cost of flash memory cards and the large file sizes we typically deal with, it is not usually feasible to purchase new memory cards for each inspection/investigation and preserve the storage media directly, as investigators did in the past when using photographic film. Instead, we must handle these files in a way that ensures the accuracy of any subsequent copies. As such, and regardless of the type of technology you use to create photos/videos, you are responsible for collecting, handling, documenting the chain of custody, storing, and submitting your evidence in a manner inconsistent with your ability to testify to its authenticity in a court of law. (See IOM 5.6.7.2)

When the electronic storage media (such as a removable flash media card) containing the "original" photos/videos is not able to be preserved, an "original copy" of the photos/videos must be created in the exact original format to preserve the chain of custody. To do so, you may transfer the "original" photos/videos first, onto either an FDA computer system (for example, the investigator's laptop) or FDA cloud storage system, and then transfer the photos/videos to the final method of preservation to create the "original copy" (for instance, burning to permanent storage media such as a CD-R), so long as the image/video data is not modified during this process.

5.6.7.4 – Glossary of Digital Terminology

Some basic terminology you should be familiar with when referring to digital devices.

5.6.7.4.1 - Original

The file recorded by a digital device on digital storage media at the moment in time when the user takes a picture or makes a recording. This concept is similar to a film camera where the photographic film records the image when exposed by light. The film image negatives produced when the film is developed would be considered the originals and prints would be considered copies.

5.6.7.4.2 – Original Copy

An exact copy of the original file recorded by the digital device (camera, video recorder, etc.). The original copy will retain all the characteristics of the original and the contents of the file are indistinguishable from the original. As this is a copy, some of the metadata (such as the date the file was created) may differ from the original.

5.6.7.4.3 - Permanent Storage Media

An electronic storage media format in which the digital files can be stored for the requisite time prescribed by records schedules, as opposed to temporary storage media which may be used to facilitate the transfer of the files. "Permanent" does not refer to the length of time the data can be stored safely on the media; storage media should be selected based on the length of time storage may be necessary. Examples are CD-Rs, DVD-Rs and other approved media.

5.6.7.4.4 - Time/Date Metadata

Data within the digital photo/video file(s) based on an internal clock within the digital device used to record, indicating when the photo/video was recorded. As the internal clock may or may not be accurate, you should, prior to use, ensure that the internal date/time clock is set for the location/time zone where the photographs or videos are being taken. This time/date may or may not be imprinted visually on the photo/video, as was common in the past for many cameras.

5.6.7.4.5 - Working Copy

Any copy of the original copy used for review, processing into exhibits, and as the basis for any enhancements. Creating a working copy decreases the chance the original copy is damaged during review and processing.

5.6.7.5 - Preparing and Maintaining Digital Photographs/Video as Regulatory Evidence

Protect a digital photo or video's chain of custody (and authenticity) using these procedures:

1. Prior to using the FDA equipment to take digital photos or video, verify that the date and time on the internal clock is correct. If removable storage media is used, reformat/clear it using the device's settings to delete any files not related to the current assignment. If non-removable storage media is used, ensure that the location the files will be saved does not contain any images unrelated to the current assignment. Depending on your inspection and the capacity of your storage, additional removable media may need to be obtained.
2. Handle your device and any storage media in a manner that protects your evidence and maintains the trail of the "chain of custody" for the evidence you have collected. For example, always keep the camera and removable storage media in your personal possession or hold under lock and key in a secure storage area. Also, keep any additional removable storage media containing images or video in your personal possession until transferred to permanent storage media. For devices which support it, ensure that the device or storage system is encrypted with a strong password. As necessary, document these facts in your regulatory notes or written report (EIR, CR etc.).
3. As soon as it is practical, create an original copy of the digital photos or video by copying all the images/videos from the device/removable storage to permanent storage media, such as an unused CD-R. You will want to verify that the computer you are using is set to the correct date and time, too, prior to creating an original copy. Depending on the permanent storage media used, more than one may be needed to store all photos/videos on hand. Also, each image or video should be transferred in the original file format maintaining the resolution at the time it was captured. If possible, avoid the use of compression when transferring the files to the permanent storage media. For very large files, consult your supervisor if you encounter issues transferring the files to permanent storage media. And prior to making the working copy from the original copy, identify the media containing the original copy. It is important to identify the original copy as soon as possible to prevent possible mix-up of the original copy with any working copies. To do so for EIRs, you should identify the relevant copy with the firm name, FEI, date taken or inclusive dates of inspection, and your initials. For sample collections, you should identify copies with sample number, collection date, and your initials.
   NOTE: If using optical media like a CD-R or DVD-R as the permanent storage media, use a permanent CD-safe marker to identify the original copy CD-R. Do not use ball point pens or similar tipped markers since the optical media may be damaged, and do not use adhesive labels on the media itself. (See National Institutes of Standards and Technology document, "A GUIDE FOR LIBRARIANS AND ARCHIVISTS Care and Handling of CDs and DVDs" for techniques to identify optical media.)
4. Where applicable, document in your regulatory notes the verification and identification of each photographic image comparing them to your regulatory notes, which were recorded at the time the photographs were taken.
5. Make only one working copy from each original copy. Make any additional working copies using the initial working copy, as copying from the original copy should be limited in order to best preserve it. Working copies should be used to print photos, for insertion into an EIR, for cropping and other editing needs, and/or for preparing for submission with the written report.
6. After making the initial working copy, seal the original copy of the permanent storage media in an FDA-525, or similar envelope, until submitted with the written report (for instance, the EIR or C/R). Complete blocks 2, 3, 5, 7, and 12 of the FDA-525 and seal with an Official Seal, FDA-415a. If you use a larger envelope, identify the envelope with your name, title, home program division, date, firm name, firm address (include zip code), description of the contents of the envelope and seal with an Official Seal, FDA-

415a. If possible, the investigator (who took the photos and will authenticate them at trial) should securely store the sealed permanent storage media until it is submitted with the written report. (If you should break the seal for any reason, see IOM 4.7.4.5 – Broken Official Seals and "Temporary Seals.")

7. Where applicable, document in your regulatory notes the verification and identification of each photographic image or video, comparing them to your regulatory notes, which were recorded at the time the photograph(s) or video(s) were taken.
8. Document in your report (for instance, the EIR or C/R) and regulatory notes any steps taken for any unusual editing of original photo images and/or video. For example: the need to superimpose over an important area of the image, enhance an image, create composite images, etc.
9. Do not scan the FDA 525, or envelopes containing the permanent storage media, and upload as exhibits. The actual photographs included and described in the EIR are the official exhibit and are maintained in the eNSpect system. The officially sealed permanent storage media should be included with the unlabeled hard copy exhibits and attachments filed in accordance with applicable procedures and accompanied by the following statement (as found in section 5.7.1.4.15 – Additional Information): *"The officially sealed original copy and unsealed working copy discs containing the photographs taken during the inspection are filed with the unlabeled exhibits and attachments."*
10. Using the working copy photographs and video, prepare for inclusion as an exhibit to the EIR following the instructions found in SOP ORA-OO.004, "Using eNSpect to Create, Store, and Preserve Electronic Records Associated with an Establishment Inspection Report."

5.6.7.6 – Inserting Photos into an eNSpect Establishment Inspection Report (EIR)

Digital photos taken during an inspection can be inserted into the body of a report in eNSpect when it is helpful to explain issues observed during your inspection. However, inserting digital photos into the body of the EIR can dramatically increase the file size of the eNSpect document, so should be used judiciously. For each photo inserted in the EIR body, include the following information in close proximity to it: the photo number, the date the photo was taken and by whom, and a brief narrative description of what the photo depicts. If several photos are to be inserted, try the following steps, in Microsoft Word, to minimize file size:

1. After inserting the photo into the EIR and placing it where desired, click to select the photo, then select the "Picture Format" ribbon at the top.
2. Select "Compress Pictures" on the ribbon.
3. Select a resolution appropriate to your needs; generally recommended: "Print (220ppi)."

For any photographs inserted in the body of the EIR, attach an additional copy as an exhibit to the EIR. A narrative description should be placed below the digital photograph. Include the photo number, the date photo was taken and by whom, and a brief description of what the photo depicts.

NOTE: When any digital photos are used in an EIR, either by inserting in the body of the EIR or attaching as an exhibit, follow the steps in IOM 5.6.7.5 – Preparing and Maintaining Digital Photographs as Regulatory Evidence to preserve the original copy.

5.6.7.7 - Photograph Requests

Do not routinely advise firms that they may have copies of photos. However, if management of the firm initiates the request, advise them it is possible to obtain copies of photographs taken in their plant under FOIA. Their request should made online. Direct them to the FDA website and How to Make a FOIA Request. The firm must bear the cost of duplicating the photographs, and since photographs are records in an investigative file, they will not be available under FOIA until the file is closed.

Do not discourage firms from taking their own photographs at the same time and of the same scenes as you are.

5.6.8 – Recordings

Normally, you would not use a recording device during an inspection. However, some firms may record an inspection or close-out meeting using audio or video with or without your knowledge. Because of this, you should always assume that you are being recorded during an inspection. If you are aware an individual is recording you during the closeout meeting, you should advise them that, while we do not object to this procedure, we will also record the discussion using our own tools to ensure the accuracy of our records. Contact your supervisor if you are at all unsure about recording a portion of the inspection.

Occasionally a firm's management may record the serving of an inspection warrant or, in a hostile situation, may want to record everything. In such cases, depending on the circumstances, you may prepare your own recording in parallel with the firm's recording. Do not depend on the firm to provide a duplicate of their recordings.

There are multiple devices that can be used to make recordings. The easiest is to use your government-issued cellular phone or tablet device. Your laptop also has recording capabilities. If you need to make a recording during the inspection, use your best judgment and whatever technology you have available to you--but do not use personal devices, like your personal cellular phone.

It's important that each recording be identified at the beginning of the record, with a statement such as:

"This is Investigator (your name) of the U.S. Food and Drug Administration speaking in the (state location) of (firm name), (address), (city), (state), and (zip code). It is now (time) a.m./p.m. on (date). Present are (list individuals present with title). This discussion is being recorded by both the representative of (firm name) and by me. We are going to discuss the inspectional findings of an inspection conducted at this firm on (inclusive dates)."

At the close of the discussion and prior to leaving the firm, the recording should be verbally identified as follows:

"This is (your name) speaking. It is now (time) a.m./p.m. on (date). This was a recording of the discussion with management at the conclusion of an inspection of (firm name and address) conducted on (dates)."

You should name the file in a way so that you can easily identify what the recording covers, for example "Close-out Meeting on xx-xx-xxxx (date) with (firm)." The file must be transferred to a permanent media device (for example, USB drive or CD).

If the recording covers a different situation, not a conclusionary meeting, for instance, you should modify your descriptive identification accordingly. If the representative of the firm refuses permission to record the discussion, continue with your discussion and report the facts in your EIR.

5.6.9 - Guaranties and Labeling Agreements

Review 21 CFR 7.12, 7.13, 101.100(d), 201.150, and 701.9, for information concerning guaranties and labeling agreements.

5.6.9.1 - Guaranty[3]

Certain exemptions from the criminal provisions of the FD&C Act are provided wherein a valid guaranty exists as specified in Section 303(c) of the FD&C Act [21 U.S.C. 333 (c)]. Obtain a copy of any Food and Drug guaranty that the firm claims to use relating to a violation noted during your inspection. **Note:** No person may rely upon any guaranty unless they have acted merely as a conduit through which the merchandise reached the consumer.

5.6.9.2 - Labeling Agreement

Products regulated by the FDA are normally expected to be completely labeled when introduced into, or while in, interstate commerce. Under certain conditions exemptions are allowed when such articles are, in accordance with

[3] The term *Guaranty* as used in the FD&C Act is now commonly written *Guarantee*.

trade practices, to be processed, labeled, or repacked in substantial quantity at an establishment other than where they were originally processed or packed. (Sections 405, 503(a) and 603 of the FD&C Act [21 U.S.C. 345, 353(a), and 363] also provide exemptions from complete labeling for products.)

5.6.9.3 - Exemption Requirements

To qualify for this exemption, the shipment must meet one of the following:

1. The shipper must operate the establishment where the article is to be processed, labeled, or repacked; or
2. If not the operator of the establishment, the shipper must first obtain from the owner a written agreement signed by and containing the post office addresses of such persons and such operator and containing such specifications for the processing, labeling, or repacking of such articles as will ensure that such article will not be adulterated or misbranded within the meaning of the Act, upon completion of the processing, labeling or repacking.

Submit copies and dates of written agreements where unlabeled articles are shipped in interstate commerce.

5.6.10 - Records Obtained

Many types of inspections and investigations require collection of copies of records to document evidence of deviations. In some cases, this may involve voluminous copies of GMP records, commitments made in the pre-approval process, adherence to the requirements of the Low-Acid Canned Food regulations or other areas. Copies of records are also obtained to document interstate commerce, product labeling and promotion, and to identify the party or parties responsible for a variety of actions. Copies of records can be obtained in paper or electronic format. All records become part of the government's case should it go to litigation.

Normally, during litigation proceedings, the best evidence rule prevails in court, whereby the copy of the record in the custody of the government can be authenticated, if the original record is not produced by the custodian of the record.

It is imperative that the government witness (usually the collector of the record(s)) be able to testify where, when, and from whom the copies were obtained, and that the copy is a true copy of the source record, based on their review of the source record.

5.6.10.1 - Verification of Source Records

You must verify the copy of the record(s) you received is an accurate representation of the original or source record(s) so you are able to testify that your copy is an exact duplicate of the original or source record. You should document in your regulatory notes that you have authenticated copies of records and when, where, and from whom copies were obtained.

Other than for identification purposes, do not write on, highlight, or otherwise alter copies of original records obtained from the firm as they will no longer be an accurate representation of the source record. You may write on a second copy of records, provided they include both a copy of the original or source record and their altered copy as exhibits to the EIR.

5.6.10.2 - Identification of Records Collected

Articles used as evidence in court cases must be identified appropriately and adequately so you can later testify the records entered as evidence are, in fact, the very ones you obtained. This includes all records as noted in IOM 5.6.11, and any others for evidence in administrative or judiciary proceedings. When identifying and filing records, you must ensure the record is complete and no identification method or filing mechanism covers, defaces, or obliterates any data on the record.

You must identify records submitted in support of an inspection or investigation, including records provided in an Establishment Inspection Report (EIR) or narrative memorandum. The identification must positively identify the

specific copies you received during your inspection or investigation, which will also help you avoid any filing mix-up. If labels are used to identify records, they must be permanently applied so any removal will be obvious.

Electronic labeling should be used to identify records collected. Identification should include at least the firm name, FEI Number, date(s) of the inspection, the lead CSO's initials, exhibit number, and page number(s). (Refer to JA-000102 eNSpect Labeler, "Using eNSpect to Create, Store, and Preserve Electronic Records Associated with an Establishment Inspection Report.") When you collect a sample during an inspection, each page of the copied records will become part of the collection report and should be identified (as noted in IOM 4.4.2- Identifying Sample Records). Identification of records attached to memoranda is described in 8.1.9.2.

5.6.10.3 – Listing of Records

If management requests a list of the copies of records you obtain, prepare it in duplicate, and leave the original with the firm. Many firms prepare duplicate copies of documents requested during our inspections. In the interests of conserving inspectional time, you may ask the firm to prepare the list of copies concurrently with the photocopying, and you then verify the accuracy. Do not use form FDA-484, Receipt for Samples. Describe the circumstances in your report including the name and title of the individual to whom you gave the list. Submit the duplicate list with your report as an exhibit.

5.6.10.4 – Patient and/or Consumer Identification on Records

During many types of inspections and investigations you will review and collect records that specifically identify (by name) patients or consumers. Under most state privacy laws, this information is confidential. Some firms may mistakenly believe this information is not releasable to the federal government; however, federal laws preempt state laws. With few exceptions, we are entitled to review and copy the complete record, including the identifying patient/consumer names. The agency, for its part, however, is then required to maintain the confidentiality of the records/files, as with any confidential record you collect. Any disclosure of the information contained in the record(s) can only be initiated by law, for instance, via a judge's order, disclosure, Congressional order, etc. If you encounter resistance from the firm in providing patient records, you may refer them to 45 CFR 164.512(b), which explains the exemptions allowing the FDA access to the patient records. (See IOM 8.1.6.2- Medical Records.)

Some general, routine guidance:

1. For records copied related to an injury or complaint investigation, in which you obtain patient identification, the identification should remain intact and stored in the official FDA files. For any inspection/investigation involving a regulation-required Informed Consent, such as clinical investigations, IRBs, bioequivalence testing, etc., patient identification should remain intact and stored in the official FDA files.
2. For most other inspections/investigations--such as MQSA, plasmapheresis, blood donations, etc.--only the patient initials and unique identifier supplied by the firm (such as donor number, donation number, etc.) need be routinely retained in the FDA files.

It is not uncommon for a firm to voluntarily purge the documents of the pertinent identifiers as they are copied. You must verify (by direct comparison to the original document) that you received an accurate reproduction of the original--minus the agreed-to purging--prior to accepting the copy.

As with any inspection, there are times when the specific identifiers must be obtained, copied, and retained, such as if/when further interview of the patient/consumer could be necessary. If in doubt, err on the side of obtaining the data. It is always easier to delete later, than to have to return to obtain the information, especially in cases, while not frequent, where questionable practices may result in the loss of the information.

All documents obtained containing confidential identifiers will be maintained as all documents obtained by FDA containing confidential information, that is, in the official FDA files. Confidential identifiers may be flagged in the

official FDA files for reference by reviewers to assure no confidential data are released under FOIA. (See IOM 5.1.5.)

5.7 – Reporting

Following an inspection, you are required to prepare a report of your findings. As soon as possible after the close of the inspection, enter in the start and end date of the inspection in eNSpect. You must also select a suggested "Inspection Conclusion" in eNSpect for each process covered.

Write your EIR with the intended use in mind. Your reports may vary greatly--from a brief summary of an inspection of a firm in a state of compliance with applicable regulations, to documentation of a firm in which the agency must take regulatory action to correct deficiencies.

5.7.1 - Establishment Inspection Report (EIR)

The Establishment Inspection Report (EIR) consists of the data and summary you enter using eNSpect (eNSpect EIR Coversheet), your narrative report (5.7.1.1), and any attachments, and exhibits. Checklists completed during the inspection (such as the BSE Checklist) should be submitted as unlabeled attachments. The signed original narrative report is maintained electronically.

5.7.1.1– Narrative Report

The narrative report is the written portion of the EIR which describes the investigator's inspectional findings and may be prepared as a Summary of Findings (IOM 5.7.1.2) or a Comprehensive (IOM 5.7.1.3) report. The format that you choose will depend on the type of inspection, the inspection basis, anticipated inspection classification, and the specific assignment and/or compliance program.

For all reporting formats, additional reporting may be required by compliance programs, Inspection Protocol (IP)s, assignments, or division management. Report the required information as requested in the source document, or under the most appropriate report heading. As each program has specific requirements for the narrative portion of the EIR, please refer to your program's reporting section for guidance. (For FSVP reporting, see Chapter 6.)

Narrative reports must be prepared as soon as possible after you close the inspection and completed within time frames commensurate with the inspection classification, the anticipated regulatory action, and any other direction provided by the assignment or supervisor. Reports must be written in a manner to communicate the findings of your inspection accurately and concisely, ensuring it is appropriate for the intended use. It is critical to document the key elements of proof - Jurisdiction, Interstate Commerce, Violation, and Responsibility (IOM 3.3.1 JIVR) - to the extent necessary to support regulatory action, if anticipated.

Depending on the Program Accomplishment Codes (PACs) added to the inspection assignment, eNSpect may trigger the use of tabular EIR and/or inspection protocols (see the eNSpect User Guide for additional information).

Your EIR should adhere to the following:

1. Be written in English
2. Be factual, objective, and free of unsupportable conclusions.
3. Be concise and descriptive while covering the necessary aspects of the inspection.
4. Not include opinions about administrative or regulatory follow-up.
5. Not include information that could identify confidential or anonymous informants.
6. Generally, be written in the first-person using the active voice.
7. Be signed by all FDA and commissioned personnel participating in the inspection. (See IOM section 5.1.2.5.1 when more than one FDA or commissioned person participated in the

inspection and IOM section)

8. Include the firm name, inspection dates, and the FEI in the header, and the page number in the footer.
9. All reports should be prepared in or uploaded to eNSpect.

(If an amendment to an endorsed narrative report is required, refer to IOM 5.7.6.)

5.7.1.2– Summary of Findings Report

A Summary of Findings report is to be prepared for all NAI and VAI **domestic** inspections (anticipated classification), including any follow-up to a violative inspection for the PACs or conditions listed below unless one of the following exceptions apply:

- It is the initial inspection of the firm
- The inspection is anticipated to be classified OAI
- Foreign inspections (unless otherwise directed)
- As directed by assignment (including for-cause), compliance program, center agreement(s), or your supervisor
- Training for new investigators or those learning a new area

NEW** In efforts to clarify the reporting formats, the Abbreviated inspection report option has been removed and is now incorporated into this updated Summary of Findings report option. This merging also results in the expansion of the summary of findings report option to include use with follow-up to OAI inspection (anticipated NAI or VAI only), as allowed by program area. Updates include adding change reporting elements to the History, Interstate Commerce, Jurisdiction, Individual Responsibility and Persons Interviewed, the Firm's Training Program, Manufacturing/Design Operations, and Manufacturing Code sections. ***Change reporting*** means reporting significant changes in the firm's operations since the previous inspection, such as changes in management, products produced, manufacturing processes, and recall procedures. Section headers may be included where needed but are not required.

For those programs which allow a Summary of Findings report for a follow-up to a violative inspection, these are conducted directly following an OAI-classified inspection to determine whether corrective actions have been implemented, and/or whether significant violations continue. For violative follow-up inspections anticipated to be classified NAI and VAI, reports should focus on the corrective actions implemented by the firm to correct violative conditions observed during the previous OAI inspection.

The Summary of Findings report includes all applicable information required by the following elements; however, a separate section heading for each element is not required. If applicable information is covered elsewhere earlier in the report, it is not required to be reported redundantly under other sections covered.

5.7.1.4.1 – Summary

5.7.1.4.2– Administrative data

5.7.1.4.14 – General Discussion with Management

5.7.1.4.10 – Complaints (report coverage of complaints received by FDA; change reporting only for firm's complaint procedures)

5.7.1.4.13 – Refusals (as applicable)

5.7.1.4.16 – Samples Collected (as applicable)

5.7.1.4.17 – Voluntary Corrections (as applicable)

5.7.1.4.18 – Exhibits Collected (as applicable)

5.7.1.4.19 – Attachments

Observations (printable or non-printable) for applicable inspections anticipated to be classified as VAI, the EIR should include all applicable information in the following required elements:

5.7.1.4.12 – Objectional Conditions and Management Response

5.7.1.4.12.1 – Supporting Evidence and Relevance

5.7.1.4.12.2 – Discussion with Management

Change reporting only:

5.7.1.4.3 – History

5.7.1.4.4 – Interstate (I.S.) Commerce

5.7.1.4.5 – Jurisdiction (Products Manufactured and/or Distributed)

5.7.1.4.6 – Individual Responsibility and Persons Interviewed

5.7.1.4.7 – Firm's Training Program

5.7.1.4.8 – Manufacturing/Design Operations

5.7.1.4.9– Manufacturing Codes

5.7.1.4.10 – Recall Procedures

A Summary of Findings report is to be used for the following Program Assignment Codes (PACs) or types of inspections as listed below:

Human Foods

- 03040 (GMP)
- 03040L (Limited Scope Preventive Controls)
- *03040F (Full Scope Preventive Controls) *ONLY if the firm has had a prior FSPC inspection
- 03040Q (Qualified Facilities),
- 03040R (Modified Requirements)
- 03842(H) (Seafood/HACCP)
- 03844H (Import Seafood HACCP)
- 03847(H) (Juice/HACCP)
- All Interstate Travel Program (ITP) PACs: 18029A (air), 18029B (bus), 18029C (railroad), 18029D (vessels), 18029E (support facility construction), 18029F (conveyances under construction).

NOTE: 03040T (Sanitary Transport), 03R897 (Intentional Adulteration) is to be included in a Summary of Findings inspection in conjunction with one of the PACs above.

Animal Foods

- As directed by your supervisor.

Biologics

- 41002D - INSPECTION OF HCT/PS - ALL OTHER 361 HCT/PS PRODUCTS (tissue distributor, storage)
- 41002B - INSPECTION OF HCT/PS - 361 REPRODUCTIVE – if NAI
- 42001F - BLOOD BANK INSPECTION PROGRAM - LEVEL 1 (only applicable for Hospital Transfusion Service/Blood Bank)

- 42001G - BLOOD BANK INSPECTION PROGRAM - LEVEL 2 (only applicable for Hospital Transfusion Service/Blood Bank)
- 42002F - INSPECTION OF SOURCE PLASMA ESTABLISHMENTS - LEVEL 1
- 42002G - INSPECTION OF SOURCE PLASMA ESTABLISHMENTS - LEVEL 2
- 42001H - BLOOD BANK INSPECTION PROGRAM - DONOR CENTERS

For biologics, a Summary of Findings report is to be used for inspections that are NAI, or under an abbreviated assignment, or under other PACs as directed by your supervisor.

Human and Animal Drugs

- CGMP Surveillance inspections under the 56002 series and 71001 series program accomplishment codes anticipated to be NAI, or as directed by your supervisor. For firms that have not been inspected in the previous 5 years, please consult your supervisor.

Medical Devices and Radiological Health

- All medical device surveillance inspections or as directed by your supervisor.
- Radiological health laser, sunlamps and x-ray (86001, 86002, and 86003) or as directed by your supervisor.

Office of Bioresearch Monitoring Inspectorate

- See Section 5.14.6 for reporting requirements.
- Non-initial NAI inspections

Office of Import Operations

- HACCP inspections under PAC 03844H

All Programs

- Any other PAC determined to be applicable as directed by the Associate Commissioner for Inspections and Investigations (ACII).

5.7.1.3– Comprehensive Report

A comprehensive report should be prepared for:

- Initial inspections
- Inspections anticipated to be classified OAI
- As directed by assignment (including for-cause), compliance program, center agreement(s), or your supervisor
- Foreign inspections unless otherwise directed
- Where needed as part of training and development of an investigator

The comprehensive report format includes all report elements listed below. This represents the minimal information needed to produce an EIR that supports further agency regulatory action, as warranted. Additional report headings may be added, as needed, to communicate important information about the inspection, relevance of inspectional observations that may impact public health, and to address specific requests from directed assignments.

Required elements:

5.7.1.4.1 - Summary

5.7.1.4.2– Administrative data

5.7.1.4.3– History

5.7.1.4.4– Interstate (I.S.) Commerce

5.7.1.4.5– Jurisdiction (Products Manufactured and/or Distributed)

5.7.1.4.6– Individual Responsibility and Persons Interviewed

5.7.1.4.7– Firm's Training Program

5.7.1.4.8– Manufacturing/Design Operations

5.7.1.4.9– Manufacturing Codes

5.7.1.4.10– Complaints

5.7.1.4.11– Recall Procedures

5.7.1.4.12– Objectionable Conditions and Management's Response

5.7.1.4.12.1– Supporting Evidence and Relevance

5.7.1.4.12.2- Discussion with Management

5.7.1.4.13– Refusals (as applicable)

5.7.1.4.14– General Discussion with Management

5.7.1.4.15– Additional Information (as applicable)

5.7.1.4.16– Samples Collected (as applicable)

5.7.1.4.17– Voluntary Corrections (as applicable)

5.7.1.4.18 - Exhibits Collected (as applicable)

5.7.1.4.19 - Attachments

5.7.1.4– Individual Headings

5.7.1.4.1– Summary

Provide the following:

1. The reason for the inspection, including if it was announced or unannounced, and other details (for example, its associated compliance program(s), assignment number, trip number, etc.).
2. The inspectional approach (comprehensive or directed), the scope of the inspection (full scope PC or full) and the type of inspection (preventive controls, seafood HACCP, API, medical gas, etc.).
3. A brief description of the business, a description of processes used, and the products produced.
4. The date, classification, inspectional observations (written observations and discussion items), and other findings from the previous inspection, if applicable.
5. The status of voluntary corrective actions since the previous inspection.
6. A list of the products, systems, and processes covered during the current inspection, and the types of records and documents reviewed. For human drug reports, list all systems the firm has currently employed and additional information as specified and/or required in any assignment or compliance program guidance manual.
7. A summary of the written observations, discussed observations, and other findings, refusals, samples collected, warnings given to management, and a summary of management's response or voluntary corrections.

5.7.1.4.2- Administrative Data

1. The firm name, address, phone, website address, and general e-mail address of the firm.
2. Report the names and titles of the investigator(s), analyst(s), non-FDA officials, etc. present during the inspection. Report the name of the firm's responsible official who gave permission to non-FDA officials without inspection authority to accompany you during your inspection. (See IOM 5.1.3 and 5.2.2.)

3. The inclusive date(s) of the current inspection, i.e., list the actual dates in the firm.
4. If a team inspection and some individuals were not present during the entire inspection, indicate dates in firm for each team member.
5. For foreign inspections with Locally Employed Staff (LES)/Foreign Service National[4] (FSN) participation include this language:

   This inspection was supported by (name of LES/FSN) during the period of (fill in dates LES/FSN participated), who is a Locally Employed Staff (LES) hired by the United States Embassy and assigned to FDA to work in support of FDA activities. All information, including documents collected during this inspection and any translation from local language to English by (name of LES/FSN) that supports the Form FDA 483, Inspectional Observations, FDA 483a, Form FDA 4056, (if a form was issued) and the Establishment Inspection Report (EIR) was collected in collaboration with the FDA investigator(s).
6. Full names and titles to whom FDA Official Credentials were shown,
7. Full names and titles to whom any FDA forms were issued to or signed by during the inspection (FDA 482, 483, 484, 463, 4056, etc.); where appropriate, explain the reason a form(s) was not issued to or signed by the most responsible individual (this may be reported in the Individual Responsibility and Persons Interviewed heading below),
8. Full name, title, address (if different from the address of the inspected establishment), and email address of the top management official at the inspected firm to whom the FMD 145 letter should be addressed. If an email address does not exist for this person, then this should be noted. If the firm requests an alternate point of contact for FMD-145 correspondence provide their contact information as well.
9. Full names, titles, and addresses (if different from the address of the inspected establishment) of most responsible corporate official(s) to whom other correspondence, e.g., Warning Letter, should be addressed (for initial inspections and inspections anticipated to result in regulatory action).
10. If this was a team inspection, who wrote which section of the EIR.
11. Full names and titles of inspectors from other government agencies (to include federal, state, local or foreign) at the facility during the inspection.
12. Full names and titles of who provided translation of foreign language documents.
13. If an inspection is conducted at premises also used for living quarters document that you are inspecting a residence and if the owner was agreeable. (IOM 5.1.4.3.1)
14. Full name and title of the individual you provided with guidance documents and list the documents provided.

5.7.1.4.3- History

1. Report the legal status of the firm (corporation, partnership, limited liability company, sole proprietorship, etc.), and the state and year of incorporation, as applicable.
2. List the parent corporation, corporate address, and any relevant subsidiaries with respective FEIs.
3. Provide a summary of any previous agency actions (for example, issuance of an untitled letter, warning letter, injunction, seizure, and/or import alert) and significant inspection history pertinent to the current inspection.

[4] According to the State Department: *Foreign Service Nationals (FSNs) are employees of the U.S. State Department who provide administrative, technical, fiscal, and other support at posts abroad. They are usually citizens of the same country as the host country but can also be third-country citizens. FSNs are also known as Locally Employed Staff (LE Staff).*

4. Include any recalls, market withdrawal, etc., since the last inspection.
5. Report the core hours of operation and any seasonal variations.
6. Report all current registration(s) status or any changes to registration status, and describe any inaccuracies identified in the firm's registration(s). (for example, food facility registration, shell egg registration, AF/LACF registration, drug registration and listing, device registration and listing, tobacco registration and listing, radiation safety reports, tissue establishment registration, human cell and tissue establishment registration, blood establishment registration, etc.). For HFP commodities do not report the FURLS Food Facility Registration number (Per CPG section 110.300). Report if the firm is located on tribal land or is owned/operated by a federally recognized Native American tribe or tribal member.
7. Report all FDA-regulated activities located at the establishment, including those not associated with a registered activity and those not covered during the current inspection. (Note: All associated establishment types should be captured in Firm Management System (FMS)).

5.7.1.4.4-- Interstate (I.S.) Commerce

1. Report the estimate of the percentage of products shipped outside of the state (or exported to the United States) and the basis of the estimate.
2. Report the firm's general distribution patterns (for example, direct sales to consumers; states, regions, and/or countries shipping to) of the firm and how the products reach the firm customers (for example, firm truck, common carrier truck, rail, vessel, or air freight).
3. If there is an apparent violative product, provide examples of interstate shipments of violative product(s); or if no such shipments, provide examples of interstate shipments of major components of apparent violative products.
4. For foreign inspections, list significant U.S. consignees to whom the firm's products are shipped.
5. For domestic inspections regarding human drugs, list significant consignees to whom the firm's products are shipped.

5.7.1.4.5- Jurisdiction (Products Manufactured and/or Distributed)

1. Describe or include a list of a representative number of currently marketed products in all program areas subject to FD&C Act or other statute enforced by FDA or counterpart state agency, including any believed violative.
2. Collect appropriate labeling (product and case labels, inserts, brochures, manuals, promotional materials of any type) for those products believed violative or representing any significant new or unusual operation, industry or technology; or as directed by your supervisor.
3. Report the firm's general promotion patterns (for instance, via website, advertisements, trade shows, etc.).
4. Report and document any applicable labeling agreements (and obtain a copy) and statutory guaranty given or received per Sections 301(h) and 303(c)(2) of the FD&C Act [21 U.S.C. 321 (h) and 333 (c)(2)] (IOM 5.3.7.2)

In addition, a product's label, labeling, and promotional materials are a critical part of determining its intended use.

1. In instances where a regulatory action is being considered based on product labels, labeling, and/or other promotional materials (including any information found on websites), you should collect all available documentation. This includes all written, printed, or graphic matter on the immediate container of an article or accompanying the article (the product's label and labeling, see FD&C Act, 201(k) and (m) [21 U.S.C. 321(k) and (m)] and IOM 4.4.9.1). Accompanying

labeling could include brochures, pamphlets, circulars, and flyers, as well as copies of audio and video files.

2. A thorough review includes a review of the firms' internet presence. If you are concerned with information on the firm's website, ensure copies of webpages are collected in hard copy and included with the report.
3. In cases where there may be a dispute about whether a product is a drug or a dietary supplement, you should collect all materials which claim a product is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.

5.7.1.4.6- Individual Responsibility and Persons Interviewed

Report with whom you dealt, and in what regard (both during and prior to the start of the inspection):

1. Report the chain of command with names and titles of key operating personnel, to include the top management official. Include an organizational chart, if necessary, to clarify roles.
2. Describe roles and authorities of responsible individuals, including the full names (see IOM 2.5) and titles of individuals providing you with information.
3. Who accompanied you during the inspection,
4. If the regulatory action is anticipated, report full names and titles of owners, partners, and corporate officers who have the duty, power, responsibility, and authority to prevent, detect, and correct violation(s), and how this is demonstrated and/or documented. See IOM 5.6.3.2
5. For human drug inspection reports, also include the name, title, physical mailing address, phone, fax number and e-mail address for any U.S. agent or broker who represents the company when dealing with the FDA.

5.7.1.4.7- Firm's Training Program

A firm's training programs are of particular significance when making inspectional findings revealing that people may not be adequately trained. As such, explain the firm's training program(s) as stated in the applicable compliance program, and/or as it correlates to the deficiencies observed during the inspection. You should also consider providing an overview of the firm's new-hire and ongoing refresher training programs as they potentially bear upon any deficiencies observed.

You should also report if the firm is subject to any specific regulatory training requirements (for example, LACF Better Process Controls School, Seafood HACCP, Preventive Controls PCQI, qualified individual) and how the firm is meeting those requirements.

5.7.1.4.8- Manufacturing/Design Operations

1. Describe the firm's general overall operations, equipment, processes, and products. If necessary, to help illustrate the firm operations, include any relevant schematics, flow plans, photographs, formulations, and diagrams. If previously inspected, report any changes in the firm's general overall operations, including significant changes in equipment, processes, and/or products since the previous inspection.
2. List names and sources of any new or unusual components or raw materials.
3. Report equipment considered new or unusual, unless otherwise directed.
4. Submit pertinent formulas or batch manufacturing records (especially those being manufactured during your inspection) and processing instructions with labeling of suspect products.
5. Indicate which aspects of the firm's processes or systems you observed, versus those that the firm described to you.

6. Describe contractors used and for what purpose, if relevant to observations noted during the inspection.

For human and animal food inspection reports, as applicable, include the following:

1. Unless otherwise directed, choose a product that has not been covered during a previous inspection. Use a risk-based analysis to include consideration of ingredients, processing, and personnel.
2. Describe the product(s) covered and include basic food information, including finished product name, product description with packaging, pertinent ingredients, intended use, and conditions of storage and distribution.
3. Describe the process flow (receiving through distribution) and a description of the process at each step.
4. For full-scope preventive control or HACCP inspections, describe the results of the hazard analysis and the adequacy and implementation of written programs. Describe any deficiencies noted compared to your hazard analysis.
5. Describe the firm's general sanitation procedures.
6. Describe any coverage of additional food safety regulations that apply to the product(s) inspected (for instance, LACF, infant formula, bottled water, etc.).

For human drug inspection reports:

For inspections conducted using CP 7356.002, the EIR should be organized by systems covered during the EI. For pre-approval inspections (PAI) under CP 7346.832, the EIR should be organized by the objectives covered during the inspection. Provide additional details for the system elements found to be deficient, or the subject of an FDA-483 observation.

5.7.1.4.9- Manufacturing Codes

Describe the manufacturing coding system (lot, batch, product, etc.),and provide a key to interpretation of codes.

For medical device inspections reports: Where appropriate, include a description of the system used to identify and maintain control of components during the manufacturing process, as well as the codes used for traceability, including the unique device identifier (UDI). Ensure the Device Identifier (UDI-DI) is submitted to the Global Unique Device Identification Database (GUDID) (for applicable finished devices).

5.7.1.4.10- Complaints

Complaints include those reported to the FDA by consumers, health care professionals, industry, etc.; and all complaints received by the firm.

1. Describe the firm's complaint procedure. If the firm has no procedure, describe how complaints are handled by the firm.
2. Report your review of the firm's complaint file(s).
3. If returned goods and/or documents for returned goods are examined, describe findings. If not examined, so indicate.
4. Report your follow-up of FDA-received complaints and action taken by the firm in the complaint coverage box for each FDA complaint. Correlate any consumer/trade complaints, Adverse Event Reports, MDR's, MedWatch reports to specific objectionable conditions observed.
5. Enter the Suggested Follow-up Disposition for each FDA complaint covered during the inspection.

5.7.1.4.11- Recall Procedures

Describe plans and procedures for removing products from marketing channels if necessary. If these procedures are in written SOP-type format, you may reference any copies obtained to aid in your explanation.

5.7.1.4.12– Objectionable Conditions and Management's Response

If any observations were provided to management in writing (for instance, via a FDA 483, FDA 483a, or FDA 4056) at the conclusion of the inspection, list each observation. For each observation, provide information organized under the two headings, "Supporting Evidence and Relevance," and "Discussion with Management" below.

NOTE: Observations of a verbal nature (including non-reportable observations and discussion items) should be reported in sufficient detail under "General Discussion with Management." (Correlate any exhibits, samples, etc. to any "verbal" observations).

5.7.1.4.12.1- Supporting Evidence and Relevance

You should adequately describe the observations, evidence, and their relevance on the FDA 483, FDA 483a, or FDA 4056. And provide any additional information needed to support those observations. For example:

- Identify specific pages of exhibits and/or samples (e.g., procedure title, section, paragraph, sentence), labeling text, interstate shipping records which in your judgment document violations so supervisors, compliance officers, and other reviewers can readily evaluate your evidence.
- Describe verbal statements (verbatim if possible) by firm officials having knowledge, duty, power, and responsibility to detect, prevent, or correct the apparent violation.
- Identify the responsible party for each apparent violation (if known.)
- Identify which team member (if applicable) was responsible for the observation.
- When appropriate explain how this observation relates to the overall situation, for instance, its impact on the product, batches, or lots involved, and any relationships to other products, processes, or other FDA 483 or FDA 4056 observations.
- The duration of the problem.

5.7.1.4.12.2- Discussion with Management

Discussion with management:

- Report management's response to each specific observation.
- Report, time frames given for corrections and/or corrective action, if provided.
- Report any disagreements with, or refusals, to correct the observation

5.7.1.4.13- Refusals

Refusals are documented in eNSpect and should populate in your report. Provide additional details, as necessary, such as, who made the refusal and, if available, why the refusal was given.

In the case of drug and medical device inspections, provide full details of all instances of delaying, denying, limiting, or refusing an inspection.

5.7.1.4.14- General Discussion with Management

1. Report the names and titles of all individuals present at the close of the inspection, including those present via electronic media. If someone participates via electronic media describe type used.
2. Include the name and title to whom the FDA 483, FDA 483a, or FDA 4056 was issued.
3. Provide additional discussion items not provided in writing at the conclusion of the inspection, such

as: questionable labels, labeling and/or labeling practices; commercialization of products covered by IDE or IND; fraudulent health claims; registration/listing deviations; lack of approved PMA, 510(k), NDA, ANDA; etc. These include all verbal observations not included, or meriting inclusion, on the FDA 483, FDA 483a, or FDA 4056 (see IOM 5.2.3).

4. Report all significant conversations with management or management representatives to include descriptions of any warning, recommendation, or suggestion given to the firm, and to whom they were given.
5. Report management's general responses to the inspection and/or to groups of items listed on the report of observations or discussed at the conclusion of the inspection.
6. Report if management was informed that:
    - Significant observations that may, after further review by the agency, be considered violations of the FD&C Act or other statutes.
    - Legal sanctions available to the FDA may include seizure, injunction, civil money penalties, and prosecution.
    - Significant deviations observed during a foreign inspection could result in a facility's product(s) being refused, or detained upon entry, into the United States.
7. Report if management was advised that if FDA receives an adequate response to the FDA-483, or other objectionable conditions, within 15 business days of the end date of the inspection, it may impact FDA's determination of the need for subsequent action.

5.7.1.4.15- Additional Information

1. When issues with imported products are encountered during inspections, you should document the product and foreign manufacturer in the EIR. Such examples include rejected APIs due to non-conformance with the USP or applicable compendium, foods without appropriate labeling, etc. Email a copy of the EIR to fdaimportsinquiry@fda.gov and explain the reason for the referral.
2. Report any pertinent facts, which do not fit in another section of the EIR. For example, this might include firm biosecurity requirements, and the documentation of noteworthy travel logistics/issues, like detailed directions to firms that are otherwise difficult to locate, lodging limitations in proximity to the firm, and locations where extensive in-country foreign travel from the firm to the hotel is required.
3. If photographs are taken during the inspection, include the statement, "The officially sealed original copy and unsealed working copy discs containing the photographs taken during the inspection are filed with the unlabeled exhibits and attachments."
4. If electronic records were received on electronic storage media during the inspection include the statement, "The officially sealed original copy [USB, CD, DVD, etc.] [and unsealed working copy] containing the electronic records provided by the firm during the inspection are filed with the unlabeled exhibits and attachments."

If electronic records were received via secure transmissions to the FDA, include the statement, "Electronic records provided by the firm during the inspection were obtained via [insert description of secure transmission used] and true copies of these files were stored on FDA servers in accordance with record management procedures."

*The bracketed information should be edited based on the actual storage devices obtained and if working copies were created.

For human drug inspection reports - PDMA Coverage*:*

1. Describe what sample loss, theft, or diversion reports were covered during the inspection.
2. Describe the firm's sample audit and security systems, including a review of the firm's SOPs. Significant problems that may contribute to the firm's inability to adequately monitor sample distribution via sales representative, mail or common carrier should be addressed under “Objectionable Conditions.”

5.7.1.4.16- Samples Collected

List the sample number(s) and describe each sample collected during the inspection.

5.7.1.4.17- Voluntary Corrections

1. Provide a brief description of improvements initiated by the firm in response to a previous inspection, report of observations, and/or regulatory actions.
2. Report voluntary destructions, recalls, and similar actions since the prior inspection or during this inspection.
3. Report any follow-up to recalls identified during the inspection (may be by referencing Attachment B recall report).
4. Include recalls to specific objectionable conditions observed.
5. Provide the identity of person(s) responsible for the corrections.
6. Report any appropriate voluntary corrections in FACTS CARS. For human and animal food inspections, report any appropriate voluntary correction in eNSpect CAR.

5.7.1.4.18- Exhibits Collected

List all exhibits attached. (For assistance, see IOM 5.6.5 - Exhibits.)

Briefly describe or title each exhibit attached and include the number of pages for each exhibit listing in eNSpect.

NOTE: For complex inspections, a cross-reference from the FDA 483, FDA 483a, or FDA 4056 and verbal observations to applicable exhibits and samples can be useful during further review.

5.7.1.4.19– Attachments

List all attachments. (For assistance, see IOM 5.7.5 - Attachments.)

Briefly describe or title each attachment and include the number of pages for each attachment listing in eNSpect.

After issuance do not number, alter, or label FDA documents (for example, assignment memos) or forms (for example, FDA 463a, FDA 482, FDA 483, FDA 4056).

5.7.1.4.20- Signature

All participants will sign the final narrative portion of the EIR. (Refer to current eNSpect user guide for guidance on electronic signatures for multiple participants.) In rare situations (for instance, in situations of extended leave, retirement, or deployment) a participant may not be available to sign the EIR. These situations should be documented in the endorsement.

In some cases, electronic signature by all participants is not possible. An example as to how this can be accomplished is to forward an electronic "draft" copy of the EIR for all to review, then followed or accompanied by the original signature sheet. When signed, return to the lead investigator for uploading into eNSpect.

In rare situations (e.g., extended leave, retirement, deployment) a participant may not be available to review and sign the EIR. The supervisor should state in the endorsement "endorser acknowledges the inability of the participant to sign the EIR due to unavoidable circumstances".

5.7.2– eNSpect Reporting

5.7.2.1– eNSpect Reporting

During an inspection, you will collect and subsequently report information in eNSpect. Each tab within eNSpect should be completed as follows:

Assignment tab:

The assignment tab primarily gives general inspection assignment details, specific inspection guidance if needed.

Team information should be reviewed and updated as appropriate to include the FDA and non-FDA participants in the inspection.

Firm Information tab:

Overview and Additional Details should be reviewed and updated to support OEI Maintenance, per SOP-000051, OEI Development and Maintenance Procedure. OII is responsible for ensuring all investigators verify, correct, and enter changes to the OEI (including Profile data for profilable firms) on the "Firm Information" tabs in eNSpect during each inspection and investigation, prior to 483 issuance or endorsement (whichever comes first). Consult with your OEI point of contact if you are unable to make updates.

Firm Profiling should be reviewed during each inspection and the compliance status for each profile class code associated with the firm's operations and/or products should be updated. Consult with your supervisor to ensure data is accurately updated. (For additional information regarding firm profiling see your programmatic section of Chapter 5.)

Corrective Action Report (CAR) should be utilized to report the firm's corrective actions to written and discussed observations for food products. A corrective action report should be completed in eNSpect Firm Information tab, or CMS. (See the current version of the eNSpect User Guide for instructions on entering a CAR in eNSpect.)

NOTE: For Food and FSVP inspections, if you annotated an FDA 483 or FDA 4056 with corrections, then you must also document those corrections as discussed above.

Additional fields may be available in eNSpect in addition to those already discussed. These fields should be reviewed and updated as appropriate for the product covered.

Inspection tab:

Details shall be entered for each inspection to include, but not limited to, the inspection date(s), inspection basis, FDA responsible organization, announcement status, inspection refusals, recalls, samples, consumer complaints, and trip number for foreign inspections. As soon as practical after the close of an inspection, you must enter the start and end date in eNSpect.

Consumer Complaints tab must be completed in eNSpect for every inspection. Record your review of the firm's complaint files in the appropriate text box. If FDA complaints require coverage, record the complaint coverage and suggested Follow-up Disposition for each complaint number listed in the assignment.

Inspection Protocols (IP) are questionnaires associated with specific PACs. The inspection may have one or more IP depending on the scope of the inspection and associated PACs. IPs should be completed if applicable for the PACs covered during the inspection.

Observations shall be documented in eNSpect whenever possible and in accordance with IOM 5.5.10. When you are not able to document observations in eNSpect, then the most current version of the FDA 483, FDA 483a, or FDA 4056 must be used.

EIRs should be written in eNSpect. The EIR must be written in accordance with IOM 5.7.3. Exhibits and attachments shall be labeled and uploaded as appropriate.

Coverage and Conclusions shall be entered for each PAC and product covered during the inspection and include the PAC, establishment type, process code, inspection conclusion, and product covered. The "Suggested District Decision" may also be entered by the investigator at the discretion of division management. Enter time spent on each PAC (see IOM 5.7.2).

Endorsements include an "Inspection Summary" and "Endorsement Text." The Inspection Summary highlights key information from the inspection; often this is like the narrative report summary or the supervisory investigator's endorsement text. Endorsement Text will be entered in accordance with IOM 5.7.6.

5.7.2.2- eNSpect Establishment Inspection Report Coversheet

Per SOP-000051 - OEI Development and Maintenance Procedure, each OII Program Division and HQ Office is responsible for ensuring that all investigators verify, correct, and enter changes to the Official Establishment Inventory (OEI) (including Profile data for firms that require profiles) on the firm's maintenance screens in eNSpect during each inspection and investigation, prior to 483 issuance or endorsement (whichever comes first). Consult with your OEI point of contact if you are unable to make updates.

Inspectional accountable time reported into eNSpect consists of the hours devoted to file reviews (operational preparation), actual on-site inspectional time, document preparation (attachments and exhibits), and EIR (narrative) write-up. Do not report travel time in eNSpect.

You should report the actual amount of inspection accountable time. Additional time required to complete the assignment due to giving or receiving training should be reported separately from inspectional time.

5.7.2.3– Operation/Inspection Basis

The inspection basis is the underlying reason for conducting an inspection. If that basis changes, then the supervisor will update the operation basis in eNSpect to reflect the updated, suitable basis. Reference the Assignment Management System (AMS) and eNSpect User Guide for operation basis definitions and the various available options when creating an assignment.

5.7.3 – Exhibits

Exhibits are materials included with the EIR and collected from the firm after the inspection is initiated and before the inspection is closed out. Impressive exhibits are extremely effective and important forms of evidence to establish existence of violative conditions or products.

Collect only records and documents that are relevant to your inspectional findings or are required by the assignment or Compliance Program. Exhibits should contribute to the objective of the assignment, clarify the report, and clearly document any violations. Exhibits include flow plans, labels, schematics, layouts, batch records and procedures, etc. Reference and explain exhibits in your narrative report. Copies of procedures, patient records, etc., which do not serve as evidence of a violation should not be collected unless you are directed to do so. Both electronic or physical materials that are collected from the firm, and are not needed as exhibits, should be destroyed in accordance with FDA Records Management Procedures and program, division, or office policy.

Labeling exhibits should reveal the entire label and must be legible. Generally, one copy of the label is sufficient, but check with the Compliance Program and/or assignment. (See IOM 4.4.7 for exceptions.) In addition, the label, labeling, and promotional materials are a critical part of determining a product's intended use. As such, you should follow this guidance:

- In instances where a regulatory action is being considered based on product labels, labeling, and/or other promotional materials, including any Internet websites, you should collect all available documentation. This includes all written, printed, or graphic material on the immediate container of an article or accompanying the article (the product's label and labeling, see FD&C Act, 201(k) and (m) [21 U.S.C. 321(k) and (m)] and IOM 4.4.7). Accompanying labeling could include brochures, pamphlets, circulars, and flyers, as well as audio and video files. Use good judgement in collecting this evidence. If you are unsure, contact your supervisor or center compliance office.
- A thorough review includes a review of the firms' internet presence. If information found there relates to any violative conditions observed or other concerns you might have, collect from the firm (generally PDF or hard copy) of the relevant webpages and include them with your report. Refer to section 5.7.4 for information about when collecting website information would be considered an attachment.
- In cases where there may be a dispute about whether a product is a drug or a dietary supplement, you should collect all materials claiming a product can be used for the treatment of any disease.

Pertinent portions of exhibits in foreign languages should be translated, especially if they document violations, unless extenuating circumstances prevent such translation. A statement regarding who provided translation on the documents should be included in the "Administrative" section of the report.

For photographs included in the report see IOM 5.6.7.

Exhibits are identified and included with the final EIR. Electronic labeling should be used to identify exhibits submitted with an EIR. Identification should include at least the firm name, FEI Number, date(s) of the inspection, the initials of the lead investigator, exhibit number, and page number(s) (see IOM 5.6.5). (Also refer to JA-000102 eNSpect Labeler - *Using eNSpect to Create, Store, and Preserve Electronic Records Associated with an Establishment Inspection Report*.)

Exhibits do not include FDA forms, copies of assignments, or information obtained outside of the firm. For example, website downloads using a computer that is not traceable to the U.S. government, printed prior to the start of the inspection, are not exhibits.

Exhibits which include medical records obtained during an investigation or inspection should be handled in accordance with current personal privacy disclosure rules. Such patient records should remain intact and stored in the official files. All external requests should be handled by the Government Information Specialist who handles FOIA requests.

5.7.3.1 - Electronic Records as Exhibits and Attachments

Electronic records included as exhibits or attachments to the EIR should be stored to protect the integrity of the data. (Refer to IOM 5.6.10) Electronic records should be protected from degradation, including preventing exposure of the electronic storage media to extreme temperatures and magnetic fields if necessary. Additional precautions to preserve the electronic records may be required, and you should be guided by your program division procedures for handling electronic storage media. (See IOM 5.7.3 Exhibits and 5.7.4 Attachments)
If electronic records were obtained via electronic storage media, do not scan and upload the FDA 525 or envelopes containing the USB, CD, DVD, or other storage devices containing electronic records to eNSpect. The actual records included on the storage device and uploaded into eNSpect are the official exhibit. The original officially sealed storage device and unsealed working copies should be included with the unlabeled hard copy exhibits and attachments filed in accordance with applicable procedures. The following statement should be included in the Additional Information section of the report: "Electronic records provided by the firm during the inspection were

obtained via [insert description of secure transmission used] and true copies of these files were stored on FDA servers in accordance with record management procedures." (See IOM 5.7.1.4.15)

The bracketed information should be edited based on the actual storage devices obtained and if working copies were created.

For information on handling photographic or video storage media, see IOM 5.6.7.5 – Preparing and Maintaining Digital Photographs/Video as Regulatory Evidence.

5.7.4 – Attachments

Attachments are defined as any materials not provided by the firm during the inspection and referred to in the EIR, such as assignments, Center-provided protocols, website information printed during inspectional preparation, etc. Non-evidentiary materials attached to the narrative portion of the EIR should be identified as "Attachments," in the same way exhibits are (see IOM 5.6.10.2). Documents attached to the EIR may be referred to under the attachments heading, such as a copy of the FDA 463a, the FDA 482, FDA 483, FDA 4056, etc. (in form number order), but such documents/forms may not be numbered, altered from their issued state, bear adhesive identification labels, etc. List and attach copies of associated reports (Recall Attachment B Report, etc.).

5.7.5 – Endorsement

Supervisory investigators evaluate inspection findings, determine the classification of the inspection, and recommend an action, in accordance with applicable compliance programs, assignments, or policies. They also determine or approve final content of the endorsement of the EIR. However, investigators should prepare proposed endorsements for their supervisor. Endorsements should fit in the available space provided in eNSpect; however, if the endorsement exceeds the character space provided in eNSpect, a separate endorsement should be prepared, fully identifying the firm, with a summary of the endorsement included in eNSpect. The eNSpect endorsement field should indicate that a separate endorsement has been prepared and uploaded to eNSpect. The eNSpect Record will be used as the endorsement and routing document to accompany the EIR. (See also IOM 5.7.1.2.)

The endorsement generally contains the following information:

1. The reason for the inspection (for example, the workplan, or assignment from headquarters). State the subject of the assignment and reference the compliance program followed.
2. A brief history of previous findings (for example, relevant FDA 483, FDA 483a, and FDA 4056 observations, and/or discussion items), including classification of previous inspection, any action(s) taken by the program division, and/or corrective action(s) taken by the firm, in response to inspectional observations from the previous inspection.
3. A concise summary and evaluation of current findings and samples collected.
4. Refusals, voluntary corrections, or promises made by firm management.
5. Any FDA-received consumer complaints covered during inspections.
6. Classification and follow-up consistent with inspectional findings and in accordance with applicable compliance program, assignments, or policy. Action may include notification of other program divisions and headquarters as warranted.
7. Distribution consistent with program division policy and the requirements of the specific compliance programs.

When endorsing in eNSpect, include notification to the Division of Import Operations (DIO) at fdaimportsinquiry@fda.hhs.gov when any violative, imported products are identified.

In rare situations (for example, in instances of extended leave, retirement, or deployment) a participant may not be available to sign the EIR. The supervisor should state in the endorsement: "Endorser acknowledges the inability of the participant to sign the EIR due to unavoidable circumstances." (See section 5.7.1.4.20)

The existence of Personal Safety Alerts (see IOM 5.3.1.1) or Personal Safety Plans (see IOM 5.3.1.2) pertaining to the firm should be included in the endorsement section only, not in the EIR.

The endorsement should be updated to indicate if an amendment to the EIR (see IOM 5.7.7) or an amended FDA 483, FDA 483a, or FDA 4056 has occurred.

PROFILES: Updating eNSpect with the Compliance Status for each profile class code associated with the firm's operations and/or products is the responsibility of OII and Center investigators, supervisors, and compliance officers. (See Exhibit 5-14 for more information on profiling CGMP/QS Compliance Status.)

5.7.5.1 – Reporting Verified Corrective Actions

A compliance achievement, also known as a verified corrective action, is the observed repair, modification, or adjustment of a violative condition; or the repair, modification, adjustment, relabeling, or destruction of a violative product when either the product or condition does not comply with the acts enforced by the FDA.

eNSpect should be used to report any verified corrective actions that are not the result of legal actions. See Field Alert 63: Observation and Corrective Action Report and Corrective

Action Report New Expanded Functionality.

5.7.5.2 - Reporting Criteria

There are three criteria for reporting:

1. The detection or identification of the problem. A problem may be observed by the FDA, other federal officials, or by state, local, tribal, and territorial (SLTT) authorities referring them to the FDA; or as a result of an inspection, investigation, sample analysis, or detention accomplished by ORA, or states under contract to ORA.
2. The correction of the problem. The correction is directly attributable to the efforts of OII or state officials under contract to OII (involving contract products only) and is unrelated to the filing of a legal action, such as a seizure, prosecution, or injunction.
3. The verification of the correction of the problem. The correction is verified by the FDA, other SLTT authorities and reported in writing to the FDA; and is based on an inspection, investigation, sample analysis, or letter from a firm to FDA certifying the problem has been corrected.

5.7.5.3 - Data Elements

For instructions on entering corrective actions in eNSpect, refer to the user manual.

For instructions on entering corrective actions in FACTS, see Exhibit 5-15.

Only when the corrective action(s) has been verified should a FACTS CARS be reported. The data elements are those entered/coded in FACTS (See IOM Exhibit 5-15) and include the following:

1. PAC. Should there be insufficient space to code all corrections verified on an occasion, record the most significant corrections.
2. PROBLEM TYPE. The problem type is the problem(s) identified during the operation(s). Use the List of Values (LOV) found in this field on the Compliance Achievement Reporting Screen. If “Other” is chosen, you should include an explanation in the “Remarks” field.
3. CORRECTIVE ACTION. The action the establishment took to correct the identified problem. Use the LOVs found in this field on the CARS screen. If "Other" is selected, you should include an explanation in the "Remarks" field.

4. VERIFICATION DATE. Use the date the corrective action(s) is verified, either through an establishment inspection, an investigation, or a letter from the establishment certifying the corrections have been made. Include documentation to verify the action such as repair receipts/plans.
5. CORRECTING ORGANIZATION. The FDA, other federal agency, or state or local authority, which observed the verified correction. Use the LOVs found in this field on the CARS screen.
6. REPORTING ORGANIZATION. The FDA, other federal agency, or state or local authority, which is actually inputting the verified correction. Use the LOVs found in this field on the CARS screen.
7. REASON FOR CORRECTION. The action the FDA took to make the correction happen. Use the LOVs found in this field on the CARS screen. If "Other" is chosen, you should include an explanation in the "Remarks" field.

5.7.6 - Corrections to Endorsed Establishment Inspection Reports

If your EIR requires correcting or clarification after it has been endorsed, an amendment may be prepared at the request of your supervisor. Amendments should only be required for significant errors or omissions, regarding, for instance, dates, names, lot numbers, types of operations, or any grammatical errors that change the intended context of the report.

The amendment will be written using the original EIR as the starting document. The word "Amendment" should be placed after the words "Establishment Inspection Report" in the header. A sequence number should also accompany the word Amendment (example: "Amendment 1"). Ensure any changes you made to correct errors in the text of the EIR remain visible; additionally, embolden all additions made, and strike through all removals made. The amended narrative report should be processed through eNSpect.

The amended operation must be endorsed. At the beginning of the endorsement text, indicate that an amendment has been made to the report with a brief explanation as to why an amendment was necessary and if additional documents were added to the report.

5.8 – Human and Animal Foods

5.8.1 – Human and Animal Foods Inspections

Food inspections are conducted to ensure the safety of our nation's food supply through the evaluation of the firm's compliance with applicable statutory and regulatory requirements.

5.8.1.1 - Inspectional Authority and Records Access Authorities

See IOM subchapter 3.2 for general statutory inspectional authorities, including general inspectional authority and records access authorities in the FD&C Act and the PHS Act. Refer also to RPM Chapter 10-4 INSPECTION OF FOOD RECORDS – SECTIONS 414(a) and 704(a).

If, during an inspection, you believe the FDA has and needs to exercise its authority to access required records, and:

- the firm refuses to provide access to the records, or
- based on experience, the program division anticipates that the firm may refuse to provide access to records, or
- the firm requests that the FDA provide a separate written request for records,
- then, notify your supervisor and consult with the center compliance office.

In addition to the statutory authorities, the FDA has the regulatory authority to obtain records and information in low acid canned food (LACF) and acidified food (AF) facilities:

- 21 CFR 113 requires commercial processors of low-acid foods packaged in hermetically sealed containers to maintain complete records of processing, production, and initial distribution.
- 21 CFR 114 requires the same of commercial processors of acidified foods.
- 21 CFR 108.25(g) and 21 CFR 108.35(h) provide that a commercial processor shall permit the inspection and copying of the records required by 21 CFR 113 and 21 CFR 114 by duly authorized employees of the FDA.

Your demand for these records must be in writing on an FDA 482a, Demand for Records, signed by you, with identification of the records demanded as follows:

"As mandated by 21 CFR 108, 113 and 114 for all LACF and/or ACF products produced by this firm: all documents and records related to all thermal processes, production, and quality control as well as all analytical and maintenance documents and records which may have a bearing on any changes to equipment or thermal processes."

If only a specific record is desired specifically identify it. For example, you may state, "Fill Weight Records for #2 Filling Machine for the period of 4-15-23 through 6-7-23." See IOM Exhibit 5-2.

21 CFR 108.35(c)(3)(ii) states that commercial processors engaged in thermal processing of low-acid foods packaged in hermetically sealed containers shall provide the FDA with any information concerning processes and procedures necessary by the agency to determine the adequacy of the process. 21 CFR 108.25(c)(3)(ii) requires the same of commercial processors of acidified foods. The information in this regulation is the data on which the processes are based. Many processors will not have this information, and, in fact, 21 CFR 113.83 requires only that the person or organization establishing the process permanently retain all records covering all aspects of establishing the process. The processor should, however, have in their files a letter or other written documentation from a processing authority describing the recommended scheduled process and associated critical factors.

You may encounter situations where you believe control of certain factors is critical to the process, yet there is no evidence to document these factors were considered when the process was established (for instance, a change in formulation that could affect consistency). It is appropriate then to issue a written request for a letter or other written documentation from a processing authority, which describes the recommended scheduled process and associated critical factors. This information should be requested using a FDA 482b (Exhibit 5-3). This represents the processing authority's conclusions and should correlate with the filed process. If you believe control of certain factors are critical to the process and are not described in the process authority's recommendation or the filed process, request all available information about the situation as follows:

> *"As mandated by 21 CFR 108: all documents and records relating to or having a bearing on the adequacy of processes for all Low-Acid Canned Food and/or Acidified Canned Food products produced by this firm."*

You may also identify specific products that you need to review. For example, if only one product had a significant formulation change then you may only need to request details about that one product. Include the name of the person or organization who established the process and the specific practices of the firm. This information should be included in your report and forwarded by your program division to LACFTechnical@fda.hhs.gov for review, as soon as possible. If the process establishment data and information is deemed necessary by the center, they will either request it directly from the processor, or will direct the program division to request it.

5.8.1.2 - Preparation and References

Before conducting a food inspection, refer to the following guidance:

- Acquaint yourself with the firm's inspectional, compliance, personal safety, and recall history; open complaints (see IOM 5.2.3); related firms; responsible persons; trademarks; practices; and products. This review may help reveal or identify products you will want to cover because, for instance, they are difficult to manufacture; or they require special handling, processes, techniques, or specific hours of operation, the latter of which may inform a more effective inspection start day/time and decisions regarding environmental sampling, etc. Determine the type of operation (manufacturer, warehouse, own-label distributor, etc.) to be inspected to ensure you apply of the appropriate regulations. OII has numerous applications available for investigators to use when preparing for an inspection. These include:
- FDA's Online Search and Retrieval System (OSAR), which allows you to quickly perform searches for firm, inspection, remote regulatory assessments, investigations, personal safety, recall, consumer complaint, and citation data in one location. Information accessible through OSAR is curated from multiple OII systems, including Firm Management System (FMS), Compliance Management System (CMS), Online Reporting Analysis Decision Support System (ORADSS), Field Accomplishments and Compliance Tracking System (FACTS), eNSpect, Recall Enterprise System (RES), and Documentum. You can access the OSAR User Guide through the help link located at the bottom of the OSAR homepage.
- Firm360, a module of OSAR that provides you with a comprehensive view of information on a specific firm based on the FDA Establishment Identifier (FEI). You can access the most recent Firm360 User Guide through the help link located at the top right in a Firm360 window. This guide provides an overview of the main site features within Firm360. Under each section in Firm360, you can click on the "+ more/- less" button in the detail column to expand or collapse the subsections for additional details. Investigators performing Human and Animal Food program domestic inspections should pay particular attention to content found within the following sections of Firm360:
  - **"Snapshot"** – This section provides you with information, including, for instance, if the firm you are assigned to inspect has a personal safety alert (PSA).
  - **"Firm Details"** – Here you can find information such as firm registrations, attestations, aliases, FMS firm comments, and district use codes (for example, dual jurisdiction establishment).
  - **"Personal Safety" –** This section provides information on firm-related personal safety issues including alerts and personal safety plans. Documents outlining the issue(s) and plan(s) are downloaded here from eNSpect.
  - **"Samples & Lab Analysis"** – In this section you can quickly sort data using the lab class column to determine if the firm has any recent violative samples or has a history of repeat violative samples.
  - **"Inspections"** – Here you'll find the firm's inspectional history, including past final inspection classifications. Use the "+ more/- less" button to find inspection documents. The inspection documents, if available, provide a hyperlink to download the document or select multiple documents to download into a zip file. You can also find a list of FDA citations linked to the inspection and determine if these were written FDA 483 observations (displays as "Normal Printing") or if they were "Do Not Print" additional observations entered into the firm's Corrective Action Report (CAR).
  - **"Corrective Action Report"** – CAR data is specific to the HFP program. In this section, you'll find all the firm's CAR enabled observations (can be written FDA 483 observations or do not print observations) from past inspections. The correction status column will help you determine if that particular observation has been entered as corrected, not corrected, pending review, etc. However, Firm360 does not provide all information needed to follow-up on the CAR observations. For this, you will need to access CAR information through CMS (search by the firm FEI) to find the firm's corrective action documents, for example, and any additional notes/comments entered by compliance branch. Also, note that state contract inspection PACs are not currently CAR-enabled.

- **"Investigations"** – Here you'll find the firm's investigational history. For each investigation, you can find details such as the investigation reason, investigation findings, and documents uploaded for the investigation (if available).
- **"Remote Regulatory Assessments"** – While not widely common yet in the HFP program, you should determine if the firm you are assigned to inspect has had a recent RRA conducted. If so, you should review the information.
- **"Consumer Complaints"** – This section provides you with consumer complaints associated with the firm. You can find the complaint number, status, product name, injury/illness, and details on the complaint. Use care when determining which consumer complaints need to be followed up on during your inspection. For example, the complaint status may show "closed," but you will need to use the "+ more/- less" button to confirm that a follow-up disposition, and associated date, has been entered. If you review the prior EIR and note the consumer complaint was followed up on, you should speak with your supervisor to determine next steps. Any consumer complaints with a status of Awaiting Follow-up Disposition should be followed up on during your surveillance/routine inspection. You can search individual complaints in CMS to see full complaint data.
- **"Recalls"** – Here you can find a list of recalls associated with the firm, including recalls not necessarily initiated by it). Any recent recalls, or a history of recalls, can help inform or determine which products and/or processes you will want to cover during your surveillance/routine inspection. For example, if a firm has multiple recalls for undeclared allergens due to incorrect labeling, this should lead you to cover a product containing major food allergens, including determining what steps the firm is taking to ensure the product is packaged with the correct allergens declared on the label.
- **"Compliance Cases"** – Here you can see if the firm you are assigned to inspect has a history of regulatory actions (for example, regulatory meetings, warning letters, untitled letters, injunctions, etc.). Clicking on the "Case ID" hyperlink will take you to the case in CMS. There you can find a wealth of information, including communications between the division, program and compliance, for example. Firm360 does not provide a list of withdrawn or disapproved compliance cases. However, this information can be found directly in CMS by searching for the firm by FEI.
- **"Compliance Work Activities"** – Here you can find the last five years of work activities for the firm entered in CMS. While CMS is primarily used by compliance , this system contains information pertinent to investigators too. For example, when you see a "District - Inspection Response (previously District - 483 Response)" work type under this section, click on the "Work ID" hyperlink to be directed to CMS. There, you should have access to the firm's FDA 483 response (for instance, documentation, attachments, and emails sent by the firm to the division) and evaluation of that response by the center compliance office. You will also be able to read any information added to the firm's CAR and associated corrective action documents. **If you are a OII investigator and do not have access to CMS, request access through your supervisor.**

- In addition to the above data systems, you should also plan to review other content, such as information housed in the FDA Unified Registration and Listing System (FURLS) and hardcopy records found in the division files of the firm to be inspected. Determine the status of the firm's food facility registration, as well as the fulfillment of other applicable requirements, such as Food Canning Establishment (FCE) registration and process filings for acidified and low-acid canned foods.
- Conduct an internet search to obtain additional information regarding the firm's operations, marketing practices, distribution patterns, etc. For example, a review of Secretary of State websites and other applicable business databases may reveal if the firm is no longer in operation, is operating under a different name, has moved to a different address, etc. Review the firm's online presence too, including any

websites, social media accounts, multi-level marketing websites, to determine what, if any, promotional claims, or statements are being made about the firm's products. Be aware of claims that can be used on food and dietary supplement labels.

- Become familiar with the relevant Human Food and Animal Food Compliance Programs and Inspection Guides. Become familiar with the applicable Compliance Policy Guides (CPG). In addition, the Resource Library offers a "one-stop shop" for relevant inspection resources for human and animal food investigators.
- Review the inspectional assignment, if one exists, and follow all of its instructions, including arranging any pre-inspectional meetings, following up on any specific issues or concerns, etc.
- Ensure that all necessary training that may be required has been received. Consult your supervisor with questions.
- Consult Exhibit 5-19 for applicable biosecurity measures if you are assigned to inspect a facility, including a private residence, that is engaged in any plant- or animal-related activities, such as the growing of crops or produce, or the housing or transporting of any domestic or wild animals. Accordingly, consult CP 7303.836 (Inspection of Egg for Monitoring Compliance with Egg Safety Rule) for applicable biosecurity measures if assigned to inspect an egg farm or commercial poultry operation.
- Review FD& C Act Chapter 9, Subchapter IV: Food.
- Review and become familiar with the appropriate parts of 21 CFR pertaining to foods. All CFRs can be found here.

Food for Human Consumption	21 CFR 100-190
Animal Drugs, Feeds, and Related Products	21 CFR 500-589
Control of Communicable Disease	21 CFR 1240
Interstate Conveyance Sanitation	21 CFR 1250

- Review implementation dates of regulations to ensure application of the appropriate regulations.
- Review reference materials on food technology and other subjects.
- Review the most current "Food Code" and be trained in its use if you are assigned to inspect retail foodservice establishments associated with a National Special Security Event or other special event. All Retail Food Specialists and some Interstate Travel Program Specialists are standardized in use of the Food Code.
- Be familiar with the Food Chemicals Codex. See IOM 5.8.4.3.
- Review the IOM Safety Chapter (IOM Chapter 10) as it pertains to your inspection. You should anticipate, recognize, evaluate, and apply control strategies to eliminate or minimize hazardous conditions and unsafe practices that may, even potentially, be encountered.

5.8.1.3 – You've Arrived at the Firm: Now What?

This section provides tips on beginning the inspection and conducting your walk-through of the facility. This information is not meant to be all-inclusive or prescriptive in nature.

When you arrive at the firm to conduct an inspection, introduce yourself, show your credentials, and issue an FDA 482, Notice of Inspection (for domestic inspections only) to the owner, operator, or agent-in-charge (OOAC) at the facility at the time of your arrival. Typically, while introducing yourself and issuing the FDA 482, you will also briefly explain the purpose of your visit (for example, "Good morning, my name is Sidney Rogers. I'm an investigator with the U.S. Food and Drug Administration, and I'm here to conduct a routine inspection of your food manufacturing facility."). When issuing the FDA 482, be sure to use the OOAC's legal name (including their middle initial if they have one). Also, use the firm's legal business name. Do not use an alias or doing-business-as (DBA), for example.

Once you have properly displayed your credentials and issued the FDA 482 to the OOAC, your inspection can officially begin.

Usually you'll want to keep your "opening meeting" with the firm brief to expedite proceeding with the "walk-through" of the facility. Topics you choose to cover in the opening meeting will depend on several factors, including if the inspection is a routine, for-cause, compliance follow-up, etc. For newer investigators, many of the inspections will be routine. Initial questions you ask during the opening meeting should help you confirm that the facility is a workload obligation (for instance, is the firm primarily retail?), is subject to FDA jurisdiction (e.g., what are the products handled), what the scope of your inspection will be (e.g., qualified facility, limited scope, etc.), and if there are any other regulators on site. For example, if you determine the firm only manufactures USDA-regulated products, you will collect the information needed by your division to update FMS. Depending on your experience and division practices, you'll then know not to proceed with inspecting the facility. You should confirm with your supervisor before ending the inspection.

Once you confirm the facility is subject to FDA regulation and a workload obligation, you'll want to ask additional questions to ascertain hours of operation, sanitation schedule(s), and what operations are occurring during the time you plan to be in the facility. Depending on the firm's inspectional history and purpose of the inspection, the opening meeting may take additional time. For example, if you are following up on a consumer complaint, you may want to conduct a quick review of complaints or adverse events received by the firm before selecting the product(s) to cover or conducting the walk-through. Typically, the opening meeting should be kept as brief as possible to allow you to proceed with the walk-through and determining the process flow/products to cover.

While there isn't a prescribed approach to conducting your walk-through of a facility, it is common practice to follow the product process from receipt of ingredients (or packaged products in the case of warehouse/distributors) to storage and distribution of products. You'll be observing the firm's processes, manufacturing, procedures, and employee practices as you proceed. There may be situations where your walk-through begins with the "clean" side of the facility, such that the first area you observe would be staging/warehousing of packaged product and the end of your walk-through would be at receipt/storage of ingredients. This may be beneficial, for example, if you are following-up on a sanitation problem in the finished product warehouse, and you prefer to start there rather than at incoming raw ingredients. During your walk-through, you may review written procedures and records and may speak with employees to help determine to what extent processes and procedures are being implemented. You should also remain flexible. Know that you may begin the walk-through with the intent to proceed from "start to finish," but this could change depending on what you observe or learn along the way.

Unless you are directed to follow a specific product(s) or process during the inspection, you'll want to use the opening meeting and walk-through to identify which product(s) you will want to cover during your inspection. For most routine inspections, you'll want to pick the highest risk product/process to cover. For this determination, you'll draw on your knowledge of the regulation(s), compliance program your covering, commodity area, and any associated hazards. For example, if the firm manufactures both ready-to-eat (RTE) and non-RTE products, in most situations, you'll want to cover an RTE product. Be reassured that if you are a new investigator, or are new to a commodity area, there are numerous resources available to guide you in deciding what products and/or processes are wisest to cover. These resources include, but are not limited to, your supervisor, other investigators, and technical assistance networks/SMEs.

5.8.1.4 - Food Defense Inspectional Activities

Food defense inspectional activities should be conducted during all routine food safety inspections. During the normal course of the inspection be alert to opportunities for improvement or enhancement of the firm's food defense preventive measures, as compared to those recommended in the guidance documents described below.

You should not perform a comprehensive food defense audit of the firm or conduct an extensive interview of management or employees to determine the level of adoption of preventive measures listed in the guidance. The goal is to facilitate an exchange of information to heighten awareness about food defense.

5.8.1.4.1 – Food Defense

Inspectional activities related to food defense for routine food establishment inspections should include:

- Discussions with firm management regarding relevant FDA guidance documents including:
  - FDA Firm Resources
  - Human food manufacturing facilities: Draft Guidance for Industry: Mitigation Strategies to Protect Food Against Intentional Adulteration.
  - Retail Food Stores and Food Service Establishments: Guidance for Industry: Food Security Preventive Measures Guidance for Retail Food Stores and Food Service Establishments. (**Note:** FDA does not have food defense requirements for retail food establishments)
  - These documents should be used as references during inspections, as appropriate. If firm management does not already have a copy of the relevant guidance documents, provide them with hard copies or information on how to obtain the guidance from FDA's web site.
- Identification of opportunities for improvement or enhancement of the firm's food defense preventive measures, as compared to those recommended in the guidance documents, and encouragement of management to make such improvements or enhancements to their system.

Keep in mind that guidance does not represent mandatory conditions or practices; some of the recommended food defense preventive measures may not be appropriate or practical to the specific operation; and other means of achieving the goals of the preventive measures listed in the guidance may be more suitable for the specific operation than those cited as examples. The important message for management is for them to consider the goals of the food defense preventive measures; evaluate the goals relative to the specifics of their operation; and address those that are relevant to the extent practical.

Food defense observations should not be listed on form FDA 483, Inspectional Observations, unless they likewise constitute deviations from Current Good Manufacturing Practice. Discussions of these observations should be handled discretely and should only involve management of the firm.

The fact that the discussion took place and, if applicable, that a copy of the guidance document(s) was provided, should be recorded in the administrative data section of the EIR. For example, under a section heading titled "Food Defense" you should only state, "A copy of the FSMA Final Rule for Mitigation Strategies to Protect Food Against Intentional Adulteration documents were provided to and food defense issues were discussed with (name of firm official)." The details of inspectional findings should **NOT** be recorded. You should also minimize the quantity and detail of notes taken relative to the firm's food defense program, recording only items needed to serve as a "memory jog" during the discussion with management. If during the inspection or your review of the food defense program, you determine that a reconciliation exam should be conducted for cause or if directed by the assignment or your supervisor to conduct a reconciliation exam see Exhibit 5-24.

5.8.1.5 - Food Registration

See IOM subchapter 3.10.1 for more information on this topic.

Regulatory submissions (for instance, registrations, process filings, pre-market notifications) are required for certain food-related facilities and firms. You should refer to the relevant HFP and CVM Compliance Program and specific Guidance for Industry to help you determine what submissions may be required and what exemptions may

exist. See the Registration of Food Facilities and Other Submissions website, which provides guidance and instructions to industry on specific regulatory submission requirements and voluntary submissions.

As covered in 5.8.1.2, you should review FURLS when you are preparing to conduct a food inspection to familiarize yourself with the firm's registrations and listings (for example, its Food Facility Registration, Acidified/Low-Acid Canned Food Registration and Process Filing, and Qualified Facility Attestation).

Beginning January 4, 2020, an owner, operator, or agent-in-charge of a facility must submit their registration to FDA electronically, unless FDA has granted a waiver under 21 CFR 1.245 (see 21 CFR 1.231(a)(2)). If the firm needs to submit a waiver request, inform them that they may obtain a copy of this registration form to complete and submit by mail.. Also encourage the firm to submit the optional information on the registration form to assist and facilitate FDA's future communications with the firm.

If a regulatory submission is required, but the firm is found to be operating without it, provide the firm with the Registration of Food Facilities and Other Submissions website and any relevant Guidance for Industry for information on how to make the required submissions, as well as information about applicable penalties. If you find a firm has failed to submit Food Facility Registration per section 415 of the FD&C Act, or if you find a firm has a current registration but information obtained during the inspection/investigation is different from the information in FFRM, you must send an email to FoodFacilityRegistration@fda.hhs.gov with the Official Establishment Data Collection Form (FORM-000173) attached, with all the required fields completed (1-32, 42-48). Make sure that the firm's management is aware of the food facility registration requirement to submit an update to the facility's registration within 60 calendar days of any change to any of the required information (21 CFR 1.234(a)).

5.8.2 – Personnel

5.8.2.1 – Management

Follow the guidance described in IOM 5.6.3 when documenting individual responsibility, including obtaining the full name and title of the following individuals:

- Owners, partners, or officers.
- Other management officials or individuals supplying information.
- Individuals to whom credentials were shown and the FDA 482 Notice of Inspection, FDA 482d Request for Foreign Supplier Verification Program (FSVP) Records, and other inspectional forms issued.
- Individuals refusing to supply information or to permit an inspection.
- Individuals with whom inspectional findings were discussed or recommendations made.

Certain regulations require management of an establishment to take reasonable measures and precautions to ensure control of communicable disease, employee cleanliness, appropriate training of key personnel, and compliance by all personnel with the applicable requirements (as found in21 CFR 117.10, 117.4, 112 Subpart C, 113.10, 114.10, and 111 Subpart B).

Determine if adequate employee supervision is provided for critical operations where violations are likely to occur if tasks are improperly performed.

5.8.2.2 – Employees

Improper employee practices may contribute to violative conditions in an otherwise satisfactory plant. Use multiple approaches to determine an employee's duties or work functions. You can observe the employee as they perform their duties, interview the employee to have them explain their duties to you, and review records/documentation that provide direct or indirect evidence of an employee's duties. You should also observe the actions of employees during all phases of the inspection.

Note whether or not employees working in direct contact with food, food-contact surfaces, or food-packaging materials are following appropriate food hygiene and food safety practices while on duty. For example, are the employees:

- wearing outer garments suitable to the operation in a manner that protects against allergen cross-contact and contamination of food?
- maintaining adequate personal cleanliness?
- storing personal items properly?
- eating, chewing gum, drinking beverages, or using tobacco while in areas where food may be exposed or where equipment or utensils are washed?

Determine if hand washing and sanitizing, if necessary, is adequate, and performed at the appropriate times and intervals. Unsecured jewelry and other objects should be removed, covered, or sanitized as appropriate. Gloves, if they are used in food handling, shall be maintained in an intact, clean, and sanitary condition. Hair nets, headbands, caps, beard covers, or other effective hair restraints should be worn, where appropriate, in an effective manner. Determine disease control practices, if there is a reasonable possibility of food, food-contact surfaces, or food-packaging materials becoming contaminated. For example, if employees are shown to have or appear to have an illness; open lesion, including boils, sores, or infected wounds; or any other abnormal source of microbial contamination, they should be excluded from any operations that may be expected to result in contamination.

Special note: Under no circumstance should you swab a sore, touch or remove a bandage from an employee in an attempt to obtain bacteriological evidence. To do so is a violation of personal privacy, possibly hazardous to you and/or the employee, and usually provides little useful data.

Observe employee traffic patterns to determine how they affect possible routes of contamination. (See IOM 5.8.7.2 for additional information on routes of contamination.) During inspections of produce farms, evaluate practices for growing, harvesting, packing, and holding practices of covered produce to prevent contamination of covered produce and food contact surfaces.

Observe and document insanitary employee practices or actions showing employees handling or touching insanitary or dirty surfaces, and then contacting food products or direct food contact surfaces. (See IOM 5.8.7.2 for additional information on how employee practices can become routes of contamination.) Such practices might include employees spitting, handling garbage, placing their hands in or near their mouths, cleaning drains, handling dirty containers, etc., and then handling food product(s) without washing and sanitizing their hands. Observe whether employees comply with plant rules such as, "No smoking," "Keep doors closed," "Wash hands before returning to work," etc.

Be alert to employees handling insanitary objects, then quickly dipping their hands in sanitizing solutions without first washing them. Depending upon the amount and type of filth deposited on the hands during the handling of insanitary objects, such attempts at sanitizing are questionable at best. Note, too, that sanitizers work most effectively on hands that have first been cleaned by washing with soap and water.

Conducting conversations with employees doing the work may provide information on both current and past objectionable practices, conditions, and circumstances. Be sure to document these conversations in your regulatory notes.

Determine employee education and training as appropriate to the regulation you are covering during the inspection. Determine the type, duration, and adequacy of the firm's training programs, if any, to prepare employees for their positions and to maintain their skills.

5.8.3 – Plants and Grounds

The plant and grounds must be kept in a condition that will protect against the contamination of food. Outbuildings and structures used for equipment or storage must be appropriately maintained. Plant employees must have control of their grounds and outbuildings, regardless of the specific food being produced or held, because litter, waste, weeds, and grass can all attract and harbor pests, and the first step for pest control in the plant is to avoid attracting pests. If the plant grounds are bordered by grounds not under the operator's control, care must be exercised in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth that may be a source of food contamination. Environmental factors such as proximity to swamps, rivers, wharves, city dumps, drain fields, runoff, concentrated animal feeding operation (CAFO), compost operations, manure operations, etc., may also contribute to rodent, bird, insect, or other sanitation problems.

Note: Buildings on produce farms may include fully- or partially enclosed structures (such as structures that have a roof but no walls) and fields. These buildings can be permanent or temporary structures.

5.8.3.1 – Plant Construction, Design and Maintenance

The plant must be suitable in size, construction, and design to facilitate maintenance and sanitary operations for food-production purposes (manufacturing, processing, packing, and holding). Determine the approximate size and construction (for example, brick and concrete block) of building(s) housing the firm and if suitable in size, construction, and design to facilitate maintenance and sanitary operations.

Buildings, fixtures, and other physical facilities must be maintained in a clean and sanitary condition and must be kept in repair adequate to prevent food from becoming adulterated. Check placement of equipment, storage of materials, lighting, ventilation, and placement of partitions and screening to eliminate product contamination by bacteria, birds, vermin, etc. You should determine any construction defects or other conditions (for instance, broken windows, cracked floorboards, sagging doors, gaps/holes to the outside environment), which may permit pest entry or harborage.

Also, determine if drip or condensate from the plant fixtures, ducts, and pipes could potentially contaminate food, food handling areas, or equipment.

Determine who is responsible for buildings and grounds maintenance. Many facilities such as docks, wharves, or other premises are owned and maintained by other firms, municipalities, or individuals for lease for manufacturing operations. Determine who is legally responsible for repairs, maintenance, rodent proofing, screening, etc. Document evidence that demonstrates the mindset and behavior of firm management/employees towards maintenance and cleaning operations. For example, are there procedures in place to routinely monitor the condition of floors, walls, and ceilings? What actions were, or were not, taken in response to needed repairs? If you bring issues to management or the employees’ attention, what is their response?

5.8.3.2 – Waste Disposal

Waste and garbage disposal poses a problem in all food operations depending upon plant location and municipal facilities available.

Check the effectiveness of waste disposal on the premises and ensure it does not cause violative conditions or contribute toward contamination of the finished products. Check for in-plant contamination of equipment and/or product, if its water is supplied from nearby streams, springs, lakes, or wells.

If you suspect the firm is dumping sewage effluent into nearby streams, lakes, or bay waters near water intakes, speak to your supervisor and explain what evidence (for instance, via photographs, documents, statements from firm management/employees) you have indicating the firm could be dumping sewage effluent inappropriately. You may be instructed to conduct a test using water-soluble fluorescein sodium dye for tracking the sewage effluent

from the firm to the nearby stream, lakes, etc. If this is the case, you should place approximately two ounces of the water-soluble fluorescein dye, which yields a yellowish red color, into the firm's waste system and/or toilets, as applicable, and flush the system. The discharge area of the effluent becomes readily visible by a yellowish-red color on the surface of the water as the dye reaches it. Take photographs to document the contamination.

Determine collecting or flushing methods used to remove waste from operating areas. If water is used, determine if it is recirculated and thus able to contaminate equipment or materials.

Determine the disposition of waste materials that should not be used as human food such as rancid nuts, juice from decomposed tomatoes, etc.

Determine the disposition of waste, garbage, etc., that contains pesticide residues. Determine how this material is segregated from waste material that contains no residues, and that which may be used for animal feed.

5.8.3.3 – Plant Services

If applicable, check steam generators for capacity and demand. Demand may reach or exceed the rated capacity, which could affect adequacy of the process. Check boiler water additives if steam comes in direct contact with foods. Boiler additives for steam that comes into contact with food must be approved as direct food additives under 21 CFR 173.310.

Check central compressed air supply for effective removal of moisture (condensate) and oil. Determine if any undrained loops in the supply line exist where condensate can accumulate and become contaminated with foreign material or microorganisms.

5.8.4 – Raw Materials

Raw materials and other ingredients must be inspected and segregated or otherwise handled as necessary to ascertain that they are clean and suitable for processing into food. Raw materials must be stored under conditions that will protect against allergen cross-contact as well as microbial, chemical of physical contamination and stored in a manner to minimize deterioration.

List in a general way the nature of raw materials on hand. Itemize and describe those, which are unusual to you, or involved in a suspected violation (copy quantity of contents and ingredient statements, codes, name of manufacturer or distributor, etc.). Be alert for additives and preservatives. Evaluate the storage of materials. Determine the general storage pattern, stock rotation, and general housekeeping. The plant must provide sufficient space for storage of materials as is necessary for the maintenance of sanitary operations and the production of safe food. Thoroughly check ceilings, walls, ledges, and floors in raw material storage areas for evidence or rodent or insect infestation, water dripping or other adverse conditions.

5.8.4.1 – Handling Procedure

Determine if growing conditions relative to disease, insects, and weather are affecting the raw material. Check measures taken for protection against insect or rodent damage. Raw materials may be susceptible to decomposition, bruising or damage, e.g., soft vegetables and fruits delivered in truckload lots. Determine the holding times of materials subject to progressive decomposition. Review storage practices for ingredients that require time / temperature control such as bulk silos or in-process batters and slurries.

5.8.4.2 – Condition

Evaluate the firm's acceptance examination and inspection practices including washing and disposition of rejected lots. Examine rejected lots and, if you encounter a raw material that is potentially adulterated or misbranded, consider collecting a sample and ensure the information is reported to the appropriate OII Division. If the documentation shows the product was imported, then you should review FIRM 360 for the product manufacturer

to determine if the product is subject to Import Alert and work with Division management to contact your corresponding import division to determine appropriate follow-up.

Determine the general acceptability of raw materials for their intended use and their effect on the finished product. Raw stocks of fruits or vegetables may contribute decomposed or filthy material to the finished product. Be alert for use of low quality or salvage raw materials. Check bags, bales, cases, and other types of raw material containers to determine signs of abnormal conditions, indicating presence of filthy, putrid, or decomposed items. Check any indication of gnawed or otherwise damaged containers, to ascertain if material is violative. Be alert to contamination of raw materials by infested or contaminated railroad cars or other carriers.

Document by photographs, exhibits, or sketches any instances where insanitary storage or handling conditions exist.

5.8.4.3 – Food Chemicals Codex

Any substance used in foods must be food-grade quality. FDA regards the applicable specifications in the current edition of the publication Food Chemicals Codex as establishing food-grade unless FDA publishes other specifications in the Federal Register.

5.8.5 – Equipment and Utensils

By arriving before processing begins, you can evaluate conditions and practices not otherwise observable before plant start-up. This includes adequacy of clean-up, where and how equipment is stored while not in use, how hand sanitizing solutions and food batches are prepared and if personnel sanitize their hands and equipment before beginning work as appropriate.

Dirty or improperly cleaned equipment and utensils may be the focal point for filth or bacterial contamination of the finished product. Examine all equipment and utensils to determine the following: design, materials, workmanship, materials, maintenance, suitability, and ease of cleaning and sanitization. Determine if equipment is constructed or covered to protect contents from dust and environmental contamination. Open inspection ports to check inside only when this can be done safely. Notice whether inspection ports have been painted over or permanently sealed.

Containers and equipment used to convey or hold human food by-products for use as animal food before distribution must be designed, constructed of appropriate material, cleaned as necessary, and maintained to protect against the contamination of human food by-products for use as animal food.

5.8.5.1 – Filtering Systems

Observe the firm's filtering systems and evaluate the cleaning methods (or replacement intervals of disposable filters) and schedules. Check types of filters used. There have been instances where firms have relied on household furnace type filters.

5.8.5.2 – Cleaning and Sanitization of Equipment and Utensils

Cleaning and sanitizing of utensils and equipment must be conducted in a manner that protects against allergen cross-contact and against contamination. Utensils and equipment must be cleaned as frequently as necessary to protect against allergen cross-contact and against contamination of food.

Check the sanitary condition of all machinery used in manufacturing, processing, packing, or holding food. Determine if equipment is cleaned prior to each use and the method of cleaning. Observe how cleaning occurs and if there is a possibility of aerosol contamination of food contact surfaces. For example, the use of high-pressure hoses on one system that is idle may contaminate an adjacent system that is operational. If the firm rents or leases equipment on a short-term basis, report prior cleaning procedures. Equipment may have been used for pesticides, chemicals, drugs, etc., prior to being installed and could therefore be a source of cross-contamination.

5.8.5.3 – Conveyor Belt Conditions

Equipment used to convey, hold, or store raw materials and other ingredients, work-in-process, rework, or other food must be designed / constructed and of such material / workmanship as to be adequately cleanable /maintained to protect against allergen cross-contact and against contamination during manufacturing, processing, packing, and holding.

Inspect conveyor belts for build-up of residual materials and pockets of residue in corners and under belts. Look in inspection ports and hard-to-reach places inside, around, underneath, and behind equipment and machinery for evidence of filth, insects, and/or rodent contamination. Chutes and conveyor ducts may appear satisfactory, but a rap on them with the heel of your hand or a rubber mallet may dislodge static material, which can be examined. See IOM 4.3.6.6.3 for procedure on taking In-line Sample Subs.

5.8.5.4 – Utensils

Determine how brushes, scrapers, brooms, and other items used during processing or on product contact surfaces are cleaned, sanitized, and stored. Evaluate the effectiveness of the practices observed.

5.8.5.5 – Mercury and Glass Contamination

Be alert for improper placement or inadequately protected mercury switches, mercury thermometers, or electric bulbs. Breakage of these could spray mercury and glass particles onto materials or into processing machinery.

5.8.5.6 – UV Lamps

If firm is using ultraviolet (UV) lamps for bacteria control, check if it has and uses any method or meters to check the strength of UV emissions. If so, obtain methods, procedures, type equipment used, and schedule for replacement of weak UV bulbs. Please note that disinfection may no longer occur beyond the manufacturers recommended replacement schedule.

5.8.5.7 – Chlorine Solution Pipes

In plants where chlorine solution is piped, check on type of pipe used. Fiberglass reinforced epoxy pipe has been observed to erode inside through the action of the chlorine solution. This poses a threat of contamination from exposed glass fibers. Pipes made with polyester resin do not deteriorate from this solution.

5.8.5.8 – Sanitation Practices

Overall sanitation must be under the supervision of one or more competent individuals assigned responsibility for this function. Observe sanitizing practices throughout the plant and evaluate their effectiveness, degree of supervision exercised, strength, time, and methods of use of sanitizing agents. Determine the use, or absence of, sanitizing solutions both for sanitizing equipment and utensils as well as for hand dipping. (Note: Not all operations require the use of sanitizer. Check the requirements for the specific regulation you are inspecting under.) 21 CFR 178.1010 describes sanitizing solutions that may be safely used (under the conditions prescribed in this part of the regulation) on food-processing equipment and utensils, and on other food-contact articles. Confirm the firm is following the manufacturer’s instructions for use on the sanitizer label or accompanying documentation. If the firm is using, typically a concentration of 50 ppm - 200 ppm free chlorine should be used for equipment and utensils, while a 100-ppm free chlorine will suffice for hand dipping solutions. Many sanitizing solutions rapidly lose strength with the addition of organic material. The strength of the solution should be checked several times during the inspection. Sanitizers including peracetic acid (PAA) and chlorine dioxide may be used in post-harvest agriculture water as a treatment for bacteria in the water. Ensure any sanitizers used are food grade and manufacture’s labeled instructions are followed.

5.8.6 – Process and Controls

All operations must be conducted in accordance with adequate sanitation principles. All operations must be conducted under such conditions and controls necessary to minimize the potential for the growth of microorganisms, allergen cross-contact, contamination of food, and deterioration of food. These operations include manufacturing, processing, packing, and holding of food.

Fans and other air-blowing equipment should operate in a manner that minimizes the potential for allergen cross-contact and for contamination.

Where helpful to describe equipment and processes, draw flow plans or diagrams to show movement of materials through the plant. Generally, a brief description of each step in the process is sufficient. List all quality control activities for each step in the process and steps where food safety hazards are controlled or minimized. Provide a full description when necessary to describe and document objectionable conditions, or where the assignment specifically requests it. Observe whether hands and equipment are washed (and sanitized as appropriate) after contact with insanitary objects. For example:

- Workers do general work, then handle the product;
- Containers contact the floor, then are nested or otherwise contact product or table surfaces;
- Workers use common or dirty clothes or clothing for wiping hands; or
- Product falls on a dirty floor or a floor subject to outside foot traffic and is returned to the production line.

Be alert for optimum moisture, time, and temperature conditions conducive to bacterial growth.

Keep in mind that in agricultural practices, some buildings may not be fully enclosed. This is a normal part of operations and may not indicate insanitary conditions. Evaluate the farm's operations including the process controls and cleaning operations.

In industries where scrap portions of the product are reused or reworked into the process (e.g., candy and macaroni products), observe the methods used in the reworking and evaluate from a microbiological standpoint. Reworking procedures such as soaking of macaroni or noodle scrap to soften or hand kneading of scrap material offers an excellent seeding medium for bacteria. Determine if work-in-process and rework materials are handled in a manner to protect against allergen cross-contact, contamination, and growth of undesirable microorganisms.

When a product is processed in a manner which destroys microorganisms, note whether there are any routes of recontamination from the "raw" to the processed product (e.g., dusts, common equipment, hands, flies, etc.).

5.8.6.1 – Ingredient Handling

Raw materials and ingredients must be inspected and segregated or handled so they are clean and suitable for processing and must be stored under conditions that will protect against allergen cross-contact and against contamination and minimize deterioration. Water reused for washing, rinsing, or conveying food must not cause allergen cross-contact or increase the level of contamination of the food.

All food that has become contaminated to the extent that it is adulterated must be rejected, or if appropriate, treated or processed to eliminate the contamination.

21 CFR 117.100(b) further prohibits the mixing of a food containing defects at levels that render that food adulterated with another lot of food. This practice would render the final food adulterated, regardless of the defect level of the final food. Examples of defect action levels that may render food adulterated can be found in the Food Defect Levels Handbook.

Material scheduled for rework must be identified and held to protect against allergen cross-contact and against contamination. This includes holding at proper temperatures and relative humidity and in such a manner as to prevent the food from becoming adulterated.

Observe the method of adding ingredients to the process. Filth may be added into the process stream from dust, rodent excreta pellets, debris, etc. adhering to the surface of ingredient containers. Evaluate the effectiveness of cleaning and inspectional operations performed on the materials prior to or while adding to the process. Determine specific trimming or sorting operations on low quality or questionable material. Observe and report any significant lags during the process or between completion of final process and final shipping. For example, excessive delay between packing and freezing may be a factor in production of a violative product.

5.8.6.2 – Formulas

The Act does not specifically require management to furnish formula information except for human drugs, restricted devices, and infant formulas. Nonetheless, they should be requested especially when necessary to document violations of standards, labeling, or color and food additives. Management may provide the qualitative formula but decline to provide the quantitative formula.

If management declines to provide formula information, attempt to reconstruct formula by observing:

- Product in production,
- Batch cards or formula sheets, and
- Raw materials and their location.

5.8.6.3 – Food Additives

Refer to the food additives programs in CP 7309.006 (page 9) for instructions on conducting establishment inspections of firms manufacturing food additive chemicals. Information is also available in OII's Guide to Inspections of Manufacturers of Miscellaneous Food Products - Volume II.

On food inspections, direct your evaluation of food additives only to those instances of significant violation, e.g., failure to declare sulfiting agents on finished product labels, when required, or gross misuse.

Routine inspectional coverage will be directed primarily to the following two types of additives:

- Unauthorized and illegal as listed in the Food Additive Status List (safrole, thiourea, et al), and
- Restricted as to amount in finished food.

Because of special problems, exclude the following additives from coverage during routine inspections:

- Packaging materials,
- Waxes and chemicals applied to fresh fruit and vegetables (unless covered under the Produce Safety Regulation),
- Synthetic flavors and flavoring components except those banned by regulations or policy statements (these products will be covered under other programs), and
- Food additives in feeds (these products will be covered under other programs).

Substances Added to Food (formerly The Everything Added to Food in the United States (EAFUS contains an alphabetical listing of substances, which may be added directly to foods or feeds and their status under the Food Additives Amendment and Food Standards. In addition, a few unauthorized or illegal substances are included.

You may encounter substances not included in the Substances Added to Food (formerly EAFUS). Such substances will include:

- Safe substances not on the list of items Generally Recognized as Safe (GRAS) which are not published in the regulations, i.e., salt, cane sugar, corn syrup, vinegar, etc.;

- Synthetic flavoring substances because of their indefinite status;
- Substances pending administrative determination, or
- Substances granted prior sanction for specific use prior to enactment of the Food Additives Amendment.

Give primary attention to unauthorized substances. Document and calculate levels of restricted-use additives in finished food only where gross misuse or program violations are suspected as follows:

1. List ingredients, which may be restricted substances or food additives, and determine their status by referring to the current Substances Added to Food. Document labeling on containers of these substances.
2. Obtain the quantitative formula for the finished product in question.
3. Determine the total batch weight by converting all ingredients to common units.
4. Calculate the theoretical levels in the final product of all restricted or unauthorized ingredients from the formula by using the Food Additives Nomographs. See IOM Exhibit 5-11.
5. Determine probable level of restricted ingredients by observing the weight of each ingredient put into the batch.

5.8.6.4 – Color Additives

Evaluate the status of color additives observed during each establishment inspection by using the Color Additive Status List and the Summary of Color Additives Listed in the United States in Food, Drugs, Cosmetics, and Medical Devices. Both links can be found at www.fda.gov websites. These lists provide the current status and use limitations of most color additives likely to be found in food, drug, device, or cosmetic establishments.

Determine if certified color additives are declared on finished product labels, when required.

Stocks of delisted and uncertified colors may be found in the possession of manufacturers where there is no evidence of misuse. Advise the firm of the status of these color additives. Note: Delisted colors can be used in lots of food specifically manufactured for export to a country in which its use is legal, provided all the requirements of Section 801(e) of the Act are followed and provided further, that a control system is followed which insures that there is no possibility of diversion by mistake or otherwise to domestic channels, of the food containing the color. If management wishes to voluntarily destroy such colors additives, witness the destruction, and include the facts in your EIR. If the firm declines to destroy the colors additives, determine what disposition is planned (i.e., use in non-food, non-drug, non-cosmetic, or non-medical device products). The validity of certification information can be checked by accessing the Color Certification Lot # Lookup application (also referred to as the Color Certification Database) maintained by the Office of Colors and Cosmetics (OCAC). You will be prompted to request access if you do not already have approval to access the database.

If you encounter the following situations, collect a sample of the finished product for color analysis (see bullet #1, 2, and 4 below for documentation, sample collection, and shipping details).

- Unlisted color additive (e.g., FD&C Red #2)
- Improper use of a listed color additive (e.g., food containing D&C Orange #5)
- Use of a color additive that does not conform to the purity and identity specifications of the listing regulation (e.g., cochineal extract with a pH over 5.5 at 25°C)

When color additive information is not consistent with Color Certification Lot # Lookup, such as different color additive or company, then the color additive may be violative and proceed as follows:

1. Collect an official sample consisting of the finished product suspected of containing the violative color additive. Make every effort to collect interstate shipments of the product before attempting to develop a 301(k) or 301(a) case. When regulatory action is an alternative, obtain sufficient interstate records to cover both the color additive and the basic ingredients of the manufactured product. Refer to IOM Sample Schedule, Chart 9 – Sampling Schedule for Color Containing Products for guidance.

2. Document the use of violative color additives. Documentation should include photo of the color additive label, batch formula cards, employee statements, code marks indicating date of manufacture, color certification number, and purchasing, shipping, and receiving documents for the color additive. Presence of a color additive in the finished product will be confirmed by the Office of Laboratory Operations and Applied Science (OLOAS) servicing laboratory.
3. If the violative color additive(s) where the certification information is not consistent and is available for sampling at the same time as the finished product, email the Director for OCAC's Division of Color Certification and Technology Branch (HFS-105) prior to collecting the color additive. If instructed to collect the color additive, refer to IOM Sample Schedule, Chart 9 – Sampling Schedule for Color Containing Products for guidance.
4. When collecting only the finished product for color analysis, ship the officially sealed sample to the appropriate OLOAS servicing laboratory (refer to the LST Dashboard). When collecting the finished product and the color additive, ship the samples as follows:
    a. **It is imperative to link the finished product sample to the color additive sample in FACTS as related samples (see IOM 4.6.2.41).** Identify the finished product sample as the "lead" sample and include in the collection remarks field on each C/R how the samples are related (e.g., sample # [enter sample number] of [name of finished product] is suspected of containing [name of color additive] under sample # [enter sample number].
    b. Ship the officially sealed finished product sample to the appropriate OLOAS servicing lab for color analysis (refer to the LST Dashboard).
    c. For certified color additive samples, see Compliance Program 7309.006 for shipping details.
    d. For the color additive sample, select "HFP-LABS" under the physical sample sent to field in FACTS. Also, include the sample is to be analyzed by the Color Certification Lab in the Collection Remarks section.
    e. Email the servicing lab and color certification staff (color.cert@fda.hhs.gov) to ensure they are aware of how the two samples are related to each other. Provide the shipping information and both sample numbers. Use the following in the email subject line: "Samples shipped to Color Certification Lab and the servicing lab for color additive analysis".

5.8.6.5 – Quality Control

Appropriate quality control operations must be employed to ensure that food is suitable for human consumption and that food-packaging materials are safe and suitable. The objective of quality control is to ensure the maintenance of proper standards in manufactured goods, especially by periodic random inspection of the product. Chemical, microbial, or extraneous-material testing procedures must be used where necessary to identify sanitation failures or possible allergen cross-contact and food contamination. Your inspection should determine if the firm's quality control system accomplishes its intended purpose.

The manufacturer, processor, packer, and holder of food must utilize quality control operations that reduce natural or unavoidable defects to the lowest defect action level currently feasible. More information of defect levels can be found here: Food Defect Levels Handbook | FDA.

Establish responsibility for specific operations in the control system. Determine which quality controls are critical for the safety of the finished product. These controls may include process control points, sanitation control points, allergen control points or other controls intended to ensure a safe product is manufactured.

5.8.6.5.1 – Inspection system

Determine what inspectional control is exercised over both raw materials and the processing steps. Such inspection may vary from simple visual or other organoleptic examination to elaborate mechanical

manipulation and/or laboratory tests. Determine what inspection equipment is used, i.e., inspection belts, sorting belts, grading tables, ultraviolet lights, etc.

Ascertain its effectiveness, maintenance, or adjustment schedules. Where indicated, determine the name of the manufacturer of any mechanical inspection device and the principles of its operation.

Evaluate the effectiveness of the personnel assigned to inspection operations. Determine if the inspection belts or pick-out stations are adequately staffed and supervised.

Determine the disposition of waste materials, which are unfit for human or animal food purposes.

5.8.6.5.2 – Laboratory Tests

Describe routine tests or examinations performed by the firm's laboratory and the records maintained by the firm. Tests may include in product testing, finished product testing or environmental monitoring. Determine what equipment is available in the laboratory and if it is adequate for the purpose intended. If the firm uses a consulting laboratory, determine what tests are performed and how often. Review laboratory records for the period immediately preceding the inspection.

5.8.6.5.3 – Manufacturing code system

Obtain a complete description of the coding system with any necessary keys for interpretation, or the need of ultra-violet light for visibility. (Specific requirements exist for codes applied to Low Acid Canned Foods (LACF) and Acidified Foods (AF)). Refer to 21 CFR 113.60(c) and 114.80(b)).

5.8.6.6 – Packaging, Labeling, and Packing

Evaluate packaging, packing, and labeling operations. “Packaging” is the processes and procedures used to place product into its immediate container. “Packing” refers to how packages or secondary packages are placed and configured for storage, shipping, and distribution.

Evaluate storage of packaging materials including protection from contamination by rodents, insects, toxic chemicals, or other materials. Appraise the way containers are handled and delivered to the filling areas. Determine if there is likelihood of chipping of glass or denting, puncturing, tearing, etc., of packaging materials. Observe the preparation of containers prior to filling. Consider any washing, steaming, or other cleaning process for effectiveness. Determine, in detail, the use of air pressure or other cleaning devices.

5.8.6.6.1 – Quantity of contents

If slack fill (21 CFR 100.100(a)) is suspected, weigh a representative number of finished packages. See IOM 4.3.7.1 for net weight procedure. Sets of official weights are available in the division servicing laboratory. These may be used to check the accuracy of firm's weighing equipment.

5.8.6.6.2 – Labeling

Check the sanitary condition of labelers and equipment feeding cans to, and away from, the labeler. Evaluate the firm processes for product label changeover or refilling to ensure the proper labels are used. Check availability of floor drains in the labeling area. Absence of floor drains could indicate infrequent cleaning of the equipment unless it is physically moved to another area for cleaning.

For human food by-products for use as animal food, ensure the labeling that identifies the by-product by the common or usual name is affixed to or accompanies the product when distributed.

Determine what labels and labeling are used. Document any applicable labeling agreements in place. Determine what labeling accompanies and/or promotes the product, including information on the establishment’s internet website. Depending upon the claims made in promotional material, a food product may be a dietary supplement or drug product. Consult your supervisor with questions about claims. Obtain

specimens of representative labels and labeling including pamphlets, booklets, and other promotional material as necessary.

5.8.6.6.3 – Nutritional and allergen labeling

If the products contain allergens, ensure that the firm has controls in place to accurately identify the label declaration and procedures to ensure proper application to the final packaging. Review product labels to ensure major food allergens are properly declared in the ingredient list or in a "Contains" statement. Check for listing of sub-ingredients that may contain allergens. See Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA) requirements for guidance.

For products that bear voluntary gluten-free claims, refer to the Gluten- Free Labeling of Foods page for guidance. Such claims must meet the requirements in the Gluten-Free labeling of foods regulation (21 CFR 101.91).

Refer to the Industry Resources on the Changes to the Nutrition Facts Label and 21 CFR 101.9 to ensure product labels meets the requirement for the Nutrition Facts label as applicable to the firm (does the firm qualify for an exemption).

5.8.6.6.4 – Labeling violations

21 CFR 101 is the primary reference for labeling requirements for conventional foods and dietary supplements. Refer to 21 CFR Part 112 for information on labeling requirements covered under the Produce Safety rule. Collect and review labels as required by a particular assignment. See IOM 4.4.7 for more information on labels and labeling. For routine inspections, collecting labels is not required unless significant violations are noted.

5.8.6.6.5 – Qualified exempt produce labeling

When a food packaging label is required on food that would otherwise be covered produce it must include prominently and conspicuously on the food packaging label the name and the complete business address of the farm where the produce was grown.

When a food packaging label is not required on food that would otherwise be covered produce, it must prominently and conspicuously display, at the point of purchase, the name and complete business address of the farm where the produce was grown, on a label, poster, sign, placard, or documents delivered contemporaneously with the produce in the normal course of business, or, in the case of Internet sales, in an electronic notice.

For additional information on qualified exempt produce and labeling, refer to 21 CFR 112 Subpart A.

5.8.7 – Sanitation

Documented observation of the conditions under which food products are manufactured, processed, packed, or held is essential to the proper evaluation of the firm's compliance with the law. This involves the determination of whether insanitary conditions contribute to the product being adulterated with filth, rendered injurious to health, or whether it consists in whole or in part of a filthy, putrid, or decomposed substance.

Observations that dirt, decomposed materials, feces, or other filthy materials are present in the facility and there is a reasonable possibility these filthy materials will be incorporated in the food are also ways of determining products may have become contaminated.

5.8.7.1 – Sanitary Operations and Sanitary Facilities

Buildings, fixtures, and other physical facilities must be maintained in a clean and sanitary condition and must be kept in repair adequate to prevent food from becoming adulterated.

Substances used in cleaning and sanitizing must be free of undesirable microorganisms and be suitable under the conditions of use. Toxic compounds, e.g., detergents, sanitizers, and pesticides, must be properly stored and used per manufacturer instructions.

Effective measures must be taken to exclude pests from the manufacturing, processing, packing, and holding areas and to protect against the contamination of food on the premises by pests.

Each plant must be equipped with adequate sanitary facilities and accommodations including the following: water supply, plumbing, sewage disposal, toilet facilities, hand washing facilities and rubbish and offal disposal.

Inspect toilet facilities for cleanliness, adequate supplies of toilet paper, soap, towels, hot and cold water, and hand washing signs. Check if hand washing facilities are hidden, or if located where supervisory personnel can police hand washing.

Determine if there is backflow from, or cross connections between, piping systems that discharge wastewater or sewage and piping systems that carry water for food or food manufacturing.

5.8.7.2 – Routes of Contamination

It is not sufficient to document only the existence of insanitary or filthy conditions. You must also demonstrate how these conditions contribute or may contribute to contaminating the finished product. Investigate and trace potential routes of contamination and observe all means by which filth or hazardous substance may be incorporated into the finished product. For example, defiled molding starch in a candy plant may contribute filth to candy passing through it, splash or overspray from cleaning operations may contaminate food and food contact surfaces, or filth in insect or rodent contaminated raw materials may carry over into the finished product. Document evidence of insanitary / filthy conditions, as appropriate, through observations, photographs, and sample collections. IOM Section 4.3.6 contains instructions on sample collection techniques for adulteration violations, including instructions for field exams and sample collections to document evidence of rodent, insect, etc., contaminated lots, and instructions for in-line sampling, including bacteriological samples. Finished product sample sizes for filth and micro collections can be found in the applicable food CPs or Inspection Guides. Consult with your supervisor prior to collecting samples.

5.8.7.2.1 – Insects

Insect contamination of the finished product may result from insect infested raw material, infested processing equipment or insanitary practices, and by insanitary handling of the finished product. When evidence of contamination with insect filth is encountered, broadly identify the type of insects found (e.g., apparent weevils, beetles, moths, etc.), its quantity, location, affected product, and other pertinent information. Explain its significance and potential for product contamination. See IOM Exhibit 4-22 for information on collecting insect evidence.

5.8.7.2.2 – Rodents

Rodent contamination of the finished product may result from using rodent defiled raw materials, exposure to rodents during storage or processing, and by rodent depredation of the finished product. When evidence of rodents is encountered, you should describe the type of contamination (e.g., apparent rodent excreta pellets, gnaw marks, etc.), its quantity, location, affected product(s), and other pertinent information. Explain its significance and potential for product contamination. See IOM Exhibit 4-22 for information on collecting rodent evidence.

5.8.7.2.3 – Pesticides and Industrial Chemicals

Pesticide and industrial chemical contamination of the finished product may be the result of mishandling of food products at any stage (e.g., growing, manufacturing, storage). The use of pesticides and chemicals in a

manner, which may result in contamination, constitutes an insanitary condition. Additional information can be found in 21 CFR as follows:

- Part 117.10(b)(9) – Personnel
- Part 117.20(b)(2) – Plant Construction and Design
- Part 117.35(b) – Sanitary Operations
- Part 117.35(c) – Pest Control
- Part 117.40(a)(2) – Equipment and Utensils

Additional information can be found in 40 CFR Part 180 – Tolerances and Exemptions for Pesticide Chemical Residues in Food administered by the Environmental Protection Agency as follows:

- Part 180.521 – Fumigants for grain-mill machinery; tolerances for residues, and
- Part 180.522 – Fumigants for processed grains used in production of fermented malt beverages; tolerances for residues.

All firms should have Safety Data Sheets for all chemicals used onsite. When evidence of contamination with chemical or pesticides is encountered, you should determine the chemical, quantity used, location, affected product(s), and other pertinent information. In addition, for pesticides determine:

- Who administers the firm's rodent and insect control program,
- responsibility for the careless use of toxic materials,
- Name of exterminator and contract status,
- Name of pesticide,
- Name of pesticide manufacturer,
- EPA registration number,
- Active ingredients, and
- Any significant markings on pesticide containers.

Examples of misuse or possible cross contamination include:

- Possible PCB polychlorinated biphenyls (PCB) contamination. Articles containing PCBs (e.g., transformers, PCB containers stored for disposal, electrical capacitors) must be marked with prescribed labeling to show they contain PCBs. No PCB-containing heat exchange fluids, hydraulic fluids, or lubricants are allowed to be used in food production and storage areas. All PCB storage areas must be marked to show the presence of PCBs. Observe food plant transformers for possible leakage. If observed, determine if food items are stored in the area, and sample for PCB contamination. If PCBs are encountered in a food establishment, immediately advise management this is an objectionable condition and advise your supervisor.
- Possible mix-up of pesticides or industrial chemicals with food raw materials.
- Improperly stored pesticides or industrial chemicals (lids open, torn bags near foods, signs of spillage on floors, pallets, shelves, etc.).
- Incorrect application methods including excessive use. Many pesticide labels give instructions for use and precautions on the container.
- Improper disposal or reuse of pesticide or industrial chemical containers.
- Evidence of tracking powder or improper use of bait stations or baited traps.
- Improper handling of equipment. Movable or motorized equipment used for handling possible chemical contaminants should not be used for handling food products unless they are thoroughly decontaminated. For example, fork-lifts moving pallets of pesticides should not also be used to move pallets of flour, etc.

- Use of unauthorized pesticides.
- Use of foods treated with pesticides and marked "Not for Human Consumption" (e.g., Treated seed wheat, etc.).
- Noticeable odor of pesticides.
- Careless use of machinery lubricants and cleaning compounds.
- Chemical contaminants in incoming water supply.



Arsenic, lead, mercury, and cadmium, sometimes referred to as heavy metals or toxic elements, may occur naturally in the environment and are often at higher levels from past industrial uses and pollution. When inspecting products with a known potential for contamination with heavy metals, determine whether the firm has evaluated the hazard and if they test for such contamination in raw materials as appropriate for the regulation(s) they must comply with.

If samples are to be collected to document pesticide or industrial chemical misuse, exercise caution to prevent contamination of the immediate area of use, product, or yourself. See IOM 10.14.2-10.14.4.

Please refer to the Compliance Program 7304.019 Toxic Elements in Food and Foodware, and Radionuclides in Food – Domestic and Import and Compliance Program 7304.004 Pesticides and Industrial Chemicals in Food - Domestic and Import for additional information.

5.8.7.1.4 – Other

Contamination of food products by bats, birds, and/or other animals is possible in facilities where food and roosting facilities are available. Birds and other animals are normal in farm operations. Evaluate the farm's wildlife management and their actions if there is any contamination or concerns.

Examine storage tanks, bins, and warehousing areas, as appropriate, to determine condition and history of use. There have been instances where empty non-food use containers were used for food products.

5.8.7.3 – Microbiological Concerns

During the inspection, identify likely sources and possible routes of contamination of the product with pathogenic microorganisms. Identify any vectors of contamination (e.g., birds, rodents, insects, foot traffic, etc.), and describe sources and the routes of contamination from them to the product. Support this with your actual observations.

See IOM sections 4.3.6.6 and 4.3.6.7 for microbiological and viral sampling guidance.

You should become familiar with the flow of the process and determine the potential trouble spots, which may be built into the operation. To document the establishment is operating under insanitary conditions which may result in the presence of pathogens in food, it is necessary to show that the manufacturing process may have or has contributed to the bacterial load of the product. (s)If there are several products being prepared at once, do not try to cover the entire operation during one inspection. Select the product which has the greatest potential for bacterial contamination, or which poses the greatest risk for the consumer.

It is extremely important for each EIR to contain complete, precise, and detailed descriptions of the entire operation. The EIR must be able to stand alone without the analytical results, which serve to support the observations.

Observations made during the inspection must be written in clear and concise language. The EIR will be reviewed in conjunction with analytical results of in-line, environmental, and finished production samples collected. Based on this review and other information which may be available, the program division must then decide if the total package will support a recommendation for regulatory action.

Each inspection/process will be different, but the techniques for gathering the evidence will be the same. However, the critical points in the operation should always be defined and special attention given to these areas.

Depending on the type of product being produced and the process being used, it may be useful to record the time each critical step takes, encompassing the entire processing period from beginning to end, with correlating temperature measurements. This should be done especially for products which may support the growth of microbial pathogens. During the entire inspection, be aware of and document delays in the processing of the product (e.g., temperature of product prior to, during, and after a processing step, and the length of time the product has been delayed prior to the next step). Be aware of and document potential routes of environmental contamination.

Some products receive a thermal process at the end of production, which may reduce bacterial counts to or near zero, although post process contamination is still possible through cross-contamination from the environment. Include detailed observations of heating step, temperature, length of time, controls, and documentation used/not used by the firm. Even in the presence of end-product thermal processing, there is a regulatory significance to insanitary conditions prior to cooking, coupled with increases in bacterial levels demonstrated through in-line sampling.

5.8.7.3.1 – Processing equipment

Document the addition, or possible addition of pathogenic microorganisms from accumulated material due to poorly cleaned and/or sanitized processing equipment. All food-contact surfaces must be cleaned as frequently as necessary to protect against allergen cross-contact and against contamination of food.

Observe and report the firm's cleaning and sanitizing procedures and the condition and cleanliness of food contact surfaces before production starts, between production runs and at the end of the day. Document any residue on food contact surfaces of equipment, especially inside complex equipment not easily cleaned and sanitized. Report firm’s clean-up procedures in depth, since it may lend significance to insanitary conditions of residues on the plant machinery which are left to decompose overnight or between shifts. Where possible, observe equipment both before and after cleaning to assess its adequacy. Observations of residues on plant machinery can dramatically document the addition of pathogenic microorganisms, if present, into the product.

5.8.7.2.2 – Employee practices

Document any poor employee practice and how they have or would provide a route for contaminating the product with microorganisms. For example, did employees (number/time of day) fail to wash and sanitize their hands at the beginning of processing, after breaks, meals, or after handling materials likely contaminated with a microbial pathogen, etc., and then handle the finished product or touch RTE food contact surfaces. Did employees handle product in an insanitary manner (cross contaminating raw product with cooked product, etc., how many, how often).

5.8.7.4 – Storage

Evaluate the storage of finished products in the same manner as for raw materials. Determine if products are stored to minimize container abuse, facilitate proper rotation, and adherence to the storage requirements. This includes refrigeration temperatures, critical temperature tolerance, aging of products, and proper disposition of distressed stock.

During holding, human food by-products that are destined for use as animal food must be accurately identified.

5.8.7.4.1 – Food transport vehicles

FDA’s final rule establishing 21 CFR Part 1, Subpart O (Sanitary Transportation of Human and Animal Food, also known as the Sanitary Transport (ST) rule, created new requirements for the sanitary transportation of human and animal food by motor vehicle and rail vehicle to ensure that transportation practices do not create food safety risks. Unless excluded or subject to a wavier, the ST rule applies to shippers, receivers, loaders, and carriers who transport food domestically by motor or rail vehicle, whether or not the food is offered for or

enters interstate commerce. The rule does not apply to transportation of food by barges, ships, or aircraft. As explained in Compliance Program 7303.040 (Preventive Controls and Sanitary Human Food Operations), divisions will be notified of the need to perform surveillance ST inspections via the annual work plan and Food Safety Modernization Act (FSMA) inventory. However, the Compliance Program also provides a list of circumstances when ST inspections should be performed for-cause.

In addition to the ST rule, there are other FDA regulations covering sanitary transportation of food. For example, 21 CFR 118.1(b) and 118.4(e) established requirements for refrigeration of shell eggs during storage and transportation. For links to existing regulations and guidance documents that address food transportation see FDA's Sanitation & Transportation Guidance Documents & Regulatory Information webpage. In addition, FDA's Guidance for Industry: Sanitary Transportation of Food contains an appendix listing regulations and guidance documents addressing food transportation and provides a list of problem areas where food may be at risk for physical, chemical, or biological contamination during transport.

The type of transportation operations covered will depend on several factors including the type of inspection and food commodity area. Speak to your supervisor if you are unsure what transportation operations to cover. Refer to IOM 5.2.2.2 regarding issuance of FDA 482, Notice of Inspection, while inspecting vehicles. In general inspections of the transportation operations will evaluate for evidence of insanitary conditions, physical defects in the transport vehicle, poor industry handling practices, or conditions which might lead to food adulteration. The type of transport vehicles (both refrigerated and non-refrigerated) covered during your inspection could include railroad boxcars/hopper cars, trucks, and farm vehicles used in covered produce activities. Use extreme caution if it is necessary to inspect tank railcars or tank trucks. Usually, this coverage will be limited to determining what was transported in the tank previously and was the tank cleaned and/or sanitized as necessary between loads.

Regulatory actions are possible if, for example, unfit transportation vehicles are loaded and, because of loading, adulteration occurs. Fully document any violations noted with appropriate evidence such as photographs. When vehicle insanitation is observed, it is imperative to document the carrier's and shipper's responsibility for the food adulteration with appropriate evidence, such as:

- The nature and extent of the conditions or practices.
- The mechanical or construction defects associated with the food transport vehicle.
- Individual responsibility for vehicle or trailer cleaning, vehicle assignments, load assignments, etc.

For the ST rule, CP 7303.40 provides some examples of conditions that may warrant regulatory action, depending on firm history, inherent risk of the food, and corrective action/response to observed conditions.

5.8.7.4.2.1 – Vehicles at receivers

When it comes to inspecting vehicles at receivers, you should refer to the regulation and compliance program you are covering to determine what to evaluate and how in-depth to go. In general, when inspecting receivers of food products, examine the food transport vehicle prior to or during unloading. Make a preliminary assessment of food product condition, then inspect the vehicle after unloading to determine its condition and whether the unloaded food may have been contaminated during shipment. If the food appears to have been adulterated, speak to your supervisor to determine if sample collection is warranted. You may also collect documentary (DOC) samples from the vehicle to substantiate the route of contamination.

5.8.7.4.2.2 – Vehicles at shippers

When it comes to inspecting vehicles at shippers, you should refer to the regulation and compliance program you are covering to determine what to evaluate and how in-depth to go. In general, when

inspecting shippers of food products, examine the food transport vehicle just prior to loading to determine its sanitary/structural conditions. If the vehicle has significant sanitation or structural deficiencies, notify the shipper of these conditions and of the possibility of product adulteration. If the shipper loads food aboard the vehicle, alert your supervisor so they can contact the FDA program division where the consignee is located for possible follow-up. You may also collect evidence of the conditions observed.

5.8.8 – Distribution

Report the general distribution pattern (i.e., direct sales to consumer; states, regions, and/or receiving countries) of the firm and how the products reach the firm customers (i.e., firm truck, common carrier truck, rail, vessel, air freight, etc.). Review interstate shipping records or invoices to report shipment of specific lots. If access to invoices or shipping records is not possible, observe shipping cartons, loading areas, order rooms, address stencils, railroad cars on sidings, etc., to determine customer names, addresses and destination of shipments. If no products are suspect, obtain a listing of the firm's larger consignees.

5.8.8.1 – Promotion and Advertising

Determine the methods and patterns used to promote or advertise products (e.g., websites, social media, oral presentations, printed materials, etc.). Determine what promotional materials are used and whether they accompany the products or are distributed under a separate promotional scheme.

5.8.8.2 – Recall Procedure

Determine the firm's recall procedure. Audit enough records to determine the effectiveness of established procedures. Firms that are subject to preventive controls have specific requirements for recall plan. Refer to 21 CFR 117.139, as applicable, for firms subject to 21 CFR 117, Subpart C

Note: Many firms are not required to have a recall procedure, such as produce farms.

5.8.8.3 – Complaint Files

Review the firm’s complaint files Include a summary of each significant complaint in the EIR. During the inspection, identify who reviews complaints and their qualifications. Describe the criteria used by the firm in evaluating the significance of complaints and how they are investigated.

Determine if records are kept of oral and telephone complaints. See IOM 5.5.4 for discussion of complaints with management and IOM 5.7.1.4.10 for reporting of complaints in the EIR.

Complaints may not be filed in one specific file, but may be scattered throughout various files under other subject titles including Product name; Customer name; Injured party name; Adjustment File; Customer Relations; Repair orders, etc.

During the inspection investigate all complaints received by FDA since the last inspections, or that were not covered during the previous inspection. See IOM 5.2.3, 5.5.4 and 5.7.1.4.10. Complaints can be accessed by doing a fast search for the complaint number in CMS, or by clicking the “Firm 360” link in OSAR of the associated firm.

5.8.9 – Other Government Inspection

See IOM Chapter 9 for general procedures on cooperating with other federal, state, and local officials.

During establishment inspections when other government officials are onsite, document their agency, name, and title.

- Federal – See IOM 9.2. Information specific to USDA can be found under IOM 9.2.1.
- State and local – See IOM 9.3.

5.8.9.1 – Grade A Dairy Plant Inspections

If you are assigned to conduct an inspection or sample collection at a milk plant that is covered under the Grade A Milk program, which has milk and milk products labeled and sold as Grade A, you should verify the need to complete the assignment with your supervisor and a milk specialist. Grade A milk plants, milk, and milk products labeled as Grade A are inspected by state inspectors and check rated by ORA's Office of State Cooperative Programs (OSCP) milk specialists and you should not inspect these Grade A milk and milk products. Milk plants in the Grade A Milk program and covered by the Interstate Milk Shippers (IMS) program are identified in the Interstate Milk Shippers List of Sanitation Compliance and Enforcement Ratings. This reference lists the specific milk plant and each milk and milk product covered under the IMS program. These Grade A milk and milk products are covered by a Memorandum of Understanding (MOU) between the FDA and the states, which places primary inspectional responsibility with the state.

There are situations where you will need to conduct an inspection in a Grade A milk plant and cover products they manufacture which do not carry the "Grade A" designation (such as juices). Prior to conducting an inspection at a Grade A plant, you should contact the FDA milk specialist for the state. A list of the FDA milk specialists can be found on the Interstate Milk Shippers List.

Fluid milk and milk products, cultured/ acidified milk and milk products, eggnog, cream(s), sour cream, and yogurt are all considered Grade A and are required to be labeled as Grade A. The Grade A milk plant may also manufacture milk and milk products which are optional for the Grade A designation, depending upon the state. Cottage cheese is considered a Grade A optional milk product. If the state does not require the Grade A designation for cottage cheese, then the cottage cheese will not be included in the IMS listing of Grade A milk and milk products for that specific milk plant. If the Grade A milk plant is manufacturing condensed or dried milk or milk products or condensed or dried whey or whey products, which are optionally labeled as Grade A, then those milk or milk products must be IMS listed and are covered under the Grade A Milk Program. Note: This same Grade A milk plant may also be manufacturing non-Grade A versions of these condensed/dried milk or milk products or condensed/dried whey or whey products.

5.8.10 – Pesticides

Most farm investigations into pesticide residues are conducted by the states and your first contact should be your state liaison and/or emergency response coordinator via your immediate supervisor. See Exhibit 5-22 (Pesticide Inspections/Investigations) for information on inspection and investigation activities related to pesticides.

5.8.11 – Foreign Supplier Verification Program

See IOM 6.8 Foreign Supplier Verification Program for inspectional instructions.

5.8.12 – Standards of Identity for Food

See Exhibit 5-23 for information on inspection activities related to standards of identity for food.

5.9 – Cosmetics

5.9.1 – Cosmetics Inspections

NOTE: While Subchapter 5.8 refers specifically to food inspections, general guidance concerning sanitation, routes of contamination, etc., can be applied to all commodities. Consumer safety officers conducting cosmetics inspections should be familiar with that subchapter.

Cosmetic inspections are conducted to ensure the safety of cosmetics through the evaluation of the firms' compliance with applicable statutory and regulatory requirements.

See the SharePoint site for the Office of Chief Scientist (OCS) Regulatory Policy and Compliance Team (RPCT) for the most current resources (e.g., active assignments and assignment resources). Additional resources can be found at the SharePoint site for the Office of Cosmetics and Colors, which is the office responsible for developing guidelines, regulations, and policies for cosmetics and color additives.

There is currently no FDA pre-approval for cosmetic products or ingredients, except for color additives. However, cosmetic firms are responsible for marketing safe and properly labeled products. Inspections can identify adulterated and misbranded cosmetics as defined in Sections 601 [21 U.S.C. 361] and 602 [21 U.S.C 362], respectively, of the FD&C Act. Inspections cover three major areas:

- Control of processes and quality of products – Products are manufactured in an adequate state of control to meet the firm's established quality standards.
- Sanitation, cleanliness, and hygiene – The facility is clean and orderly, sanitary conditions are being maintained and workers are attentive to preventing contamination.
- Labeling – Products are labeled in compliance with regulations and are accurately labeled to reflect contents.

FDA inspections can reveal use of prohibited ingredients, noncompliance with requirements related to color additives, failure to adhere to requirements for tamper-resistant packaging where needed, and violations involving labeling without necessarily performing an on-site inspection. Assurance of cosmetic product safety also depends upon control of microbiological product quality during manufacturing and distribution of products. An on-site inspection is the only means by which FDA can determine if cosmetics are being manufactured under insanitary conditions whereby cosmetics may be contaminated with objectionable microorganisms. (See 5.9.1.3 (Contaminated Cosmetics) and 5.9.1.6 (Specific Types of Cosmetic Safety Concerns))

5.9.1.1 – Preparation and References

Before conducting a cosmetic inspection, refer to IOM 5.8.1.2 (information in bullets 1-3 and 4-8 as applicable) and additional resources below:

- Review FD&C Act Chapter 9, Subchapter VI: Cosmetics, 21 CFR 700-740 (Cosmetics), and the Fair Packaging and Labeling Act .
- Determine if the firm has registered. For questions on registration and listing, contact the office of Cosmetics and Colors at ERLC@fda.hhs.gov and allow 5 business days for a response.
- Refer to Compliance Program 7329.001 (Cosmetics – Import and Domestic) and IOM Chapter 5 All Program Sections.
- Additional resources include the Guidance for Industry: Registration and Listing of Cosmetic Product Facilities and Products, the Decision Tool (a tool to help industry decide if they are required to register), Draft Guidance for Industry: Cosmetic Good Manufacturing Practices, the Cosmetics Labeling Guide, import alerts relevant to cosmetics, and cosmetics recalls / alerts.

5.9.1.2 – Documents and Records

While there is no requirement for the firm to provide records for your review, it is important to review documents and records, to determine if the site has adequate procedures and systems for manufacturing and monitoring to ensure production and distribution of safe cosmetic products. Therefore, make a request to review processing records, packaging and labeling records, raw material records, and any records pertinent to the manufacture, packaging, labeling and distribution of the cosmetic product, including finished product testing, batch release, complaints and/or adverse events.

5.9.1.3 – Contaminated Cosmetics

Inspect the firm's methods for preventing and controlling microbial and other forms of contamination and review records that may indicate batches that were manufactured and distributed in violation of any of the cosmetic adulteration provisions of the Act.

Typical causes of product adulteration are manufacturing under insanitary conditions, improper storage conditions, and product design flaws and/or defects (i.e., ingredients, packaging) including use of an ineffective preservative system (see below). Observe and document when any of the following present a potential cause of insanitary conditions:

- Overall cleanliness of the facility and sanitation practices, including programs and systems for pest control and waste disposal.
- Personal hygiene and employee health, including training of staff and monitoring of employees by supervision.
- Handling of ingredients, materials, and products by employees; including procedures for making transfers, training, and use of Personal Protective Equipment (PPE).
- Microbiological quality of ingredients, including whether ingredient batches received from suppliers are tested by the manufacturer and how ingredients are stored (see next section on raw material quality).
- Water systems, including system design and control and monitoring of microbiological quality.
- Equipment design, including potential for stagnant water.
- Cleaning and sanitization of equipment surfaces contacting process stream or products, including utensils and shared equipment.
- Buildup of previous batches of material on equipment surfaces during prolonged manufacturing campaigns.

Susceptibility of cosmetic products to microbiological growth is governed the by water activity of the formulation. Preservatives are added to mitigate the risk of microbial growth, but each preservative system's capability has unique limitations. As proof of effectiveness of preservation, the formulation can be subjected to microbial challenge testing. Check to see if the manufacturer (or product distributor) has performed and retained documentation of preservative efficacy testing on its cosmetic product formulations. See CP 7329.001 section on adequacy of preservation for more information. Also refer to sections 5.8.7 for more information about documenting routes of contamination and microbiological concerns. While Subchapter 5.8 refers specifically to food inspections, general guidance concerning sanitation, routes of contamination, etc., can be applied to all commodities.

See CP 7329.001 Part V.1.c. for more information on current policy on microbiological quality of cosmetics, including products and levels of concern constituting potential health hazard.

5.9.1.4 – Cosmetic product labels or labeling making drug claims

See CP 7329.001 (Part III.A. and III.B.1) to determine if there is cause to collect evidence supporting that a cosmetic is to be considered a drug. 21 CFR 701 contains information on cosmetic labeling requirements and 21 CFR 740 describes requirements for cosmetic product warning statements. Examples of products marketed strictly as cosmetics but making drug claims include those which claim to promote hair growth, prevent baldness, prevent, or treat dandruff, enhance eyelash growth, and treat skin diseases such as acne.

Collect the following as evidence that could enable FDA to consider such a product an illegally marketed drug:

- Product labels, including outer containers and all inserts.
- Promotional material in written and/or electronic format.

If the product is suspected to contain an active pharmaceutical ingredient associated with drug claims also collect:

- Samples of product.
- Samples of the active ingredient used in the cosmetic and ingredient certificate of analysis.
- Records showing usage of the active ingredient in manufacturing of a cosmetic product batch.

(NOTE: The Center for Drug Evaluation and Research and OCS have concurrent jurisdiction over any product purported as a cosmetic that meets the legal definition of a drug.)

5.9.1.5 – Cosmetic Ingredients

Determine if the manufacturer has suitable procedures for supplier selection and qualification and adequate controls for chemical, microbial, and physical contamination to ensure the ingredients are suitable for use in cosmetics. If the manufacturer uses ingredients that have been reconditioned or reprocessed, determine if there is adequate documentation to justify such use. Determine who (e.g., the firm's quality department, the product distributor) decides to approve suppliers, and accept or reject ingredient batches from suppliers. Determine if ingredients (and packaging materials) are stored and handled properly to prevent mix-up and contamination; and if there are suitable systems to identify and trace ingredients and packaging materials used in cosmetic products.

5.9.1.6 – Specific Types of Product Safety Concerns

You should be aware of certain cosmetic products that OCS/OCAC has identified as posing unusual safety hazards due to concerns about the product ingredients. Examples include:

- Tattoo inks.
- Ingredients or products labeled "organic" or "natural".
- Products lacking traditional preservatives.
- Products containing stem cells or human tissue.
- Wet wipes (used by infants/children and adults).
- Cosmetic non-alcohol oral care products.
- Eye area products.
- Potential use by immuno-suppressed or institutionalized individuals.

There are currently no prohibitions on the use of many of these ingredients and FDA's regulatory policy is still in development. OCAC will provide training on these specific topics and others that may emerge in the future. If in doubt about the status of a particular ingredient or type of product you encounter on an inspection, contact OCS/OCAC.

5.10 - Drugs

5.10.1 - Drug Inspections

5.10.1.1 - Pre-Announcements

If a program division believes pre-announcing an inspection of an establishment will optimally facilitate the inspection process, then the respective procedures for conducting pre-announcement for drug inspections should be followed. OII's primary purpose for pre-announcing is to ensure the appropriate records and personnel will be available to us during the inspection. It is not to make an appointment for the inspection, nor should it be referred to as an "appointment" to inspect. When doing a pre-announcement, it is important you communicate to the establishment the purpose of the inspection and a general idea of the records you may wish to review. If you find neither the appropriate personnel, nor records available, note this in your Establishment Inspection Report

(EIR). For pre-announced foreign drug inspections, the pre-announcement will be conducted by the Division of Human and Animal Drugs Foreign Inspectorate (DHADFI) as part of the inspection planning process.

In the case of drug inspections, if efforts to schedule a pre-announced inspection are met with unreasonable delays by the establishment, including a request for a later start date without a reasonable explanation, it may constitute a delay of an inspection under Section 501(j) of the FD&C Act [21 U.S.C. 351(j)]. The FDA will make reasonable accommodations for potentially interfering local conditions such as weather, holidays, or, where appropriate, manufacturing campaign schedules; however, if faced with an unreasonable delay by the establishment, you may call the responsible person's attention to 501(j) of the Act. Talk with your supervisor to determine whether the length of a particular delay may be considered unreasonable, even in cases in which the explanation given for the delay may seem reasonable. The program division may use this data in the future when considering whether this establishment should be eligible for pre-announced inspections.

Guidance using eNSpect: In the eNSpect "Pre-Announced / Unannounced to Firm" field, select "Unannounced" when no notification was provided to the firm in advance of arrival at the firm for inspection. Select "Pre-announced" when the firm was notified of the inspection prior to the CSO arrival at the firm for the inspection. See IOM 5.2.6 for general guidance on Pre-Announcement.

5.10.1.1.1 - Basic Premises

Pre-announcement of inspections is to be applied only to establishments that meet specific criteria. Pre-announcement may be considered for establishments that manufacture both drugs and devices or biologics and devices. The eligibility of an individual establishment for pre-announced inspection is at the discretion of the inspecting division using clearly described criteria. (See 5.2.6.1 Criteria for Consideration) The program division does not have the discretion to decide the types of establishments eligible for pre-announcement, but may decide the specific establishments' eligibility because they meet the criteria.

The pre-announcement should generally be no less than five calendar days in advance of the inspection. Should a postponement be necessary, the decision as to rescheduling rests with the investigator/team, but the new inspection date should not be later than five calendar days from the original date. Inspections may be conducted sooner than five calendar days, if requested by or acceptable to the establishment, and if this date is acceptable to the investigator/team.

To participate in a pre-announced inspection, establishments are expected to meet the commitment to have appropriate records and personnel available during the inspection.

Pre-announced inspections should be as thorough as necessary, and, in no way limit an investigator's authority to conduct the inspection.

5.10.1.1.2 – Criteria for Consideration

Certain criteria determine whether an establishment requires or qualifies for a pre-announced inspection (see section 5.2.6.1 Pre-Announcement). Examples include:

- Foreign inspections, unless conducted as part of a "For Cause" assignment or as part of the "foreign un-announced inspection pilot."
- Specific kinds of inspections as instructed by the Compliance Program, assignment, or directive (for example, per 56006P, positron emitting tomography (PET) drug production facilities, unlike other commercial production facilities, generally employ a few operators each of whom must perform certain operations and checks quickly, without disruption, so that the drug product can be distributed promptly to pharmacies and waiting patients. For this reason, Divisions are to schedule PET inspections in advance with the firm to allow the facility time to ensure appropriate staff is available to enable an efficient and complete inspection. When scheduling the inspection with the firm, the investigator may

obtain information about the planned times of key operations and time their arrival accordingly. Note that the investigator may also need to accommodate the typical PET establishment's early hours of operation. "For cause" inspections, however, need not be scheduled in advance.

- Inspections conducting during a health emergency crisis, like an epidemic or pandemic.

5.10.1.1.3 - Procedures

Procedures:

1. The investigator or designated FDA official should contact the most responsible individual at the facility. You should leave a message requesting a return call if the most responsible person at the facility is unavailable at the time the call is made. If this is the case, the program division should use good judgment in determining what constitutes a reasonable time frame to await the return call.
2. Keep changes in dates to a minimum. If a change is made, a new date should be provided as soon as possible that still facilitates an effective inspection and accommodates your schedule. The establishment should also provide a valid reason for requesting a change in the start date. (A valid reason should be the same as you would accept if presented with the information during an unannounced inspection.)
3. Inform the establishment as to the purpose, estimated duration, and the number of agency personnel expected to take part in the inspection. The products or processes to be covered should be described if this will facilitate and be consistent with the objectives of the inspection.
4. When appropriate, request access to any relevant specific records and/or personnel at the time the inspection is pre-announced.
5. Be as specific as reasonably possible in your notification, including an exact date for the start of the inspection.
6. If it is a pre-approval inspection, you should notify the pre-approval manager, and CDER's Office of Pharmaceutical Manufacturing Assessment (OPMA), with the inspection dates or altered pre-approval inspection dates.

Special notes regarding the EIR: Include in your report whether or not the inspection was pre-announced, as well as information on any difficulties you experienced in notification, or while accessing records or personnel that should have been freely available as a result of pre-announcing the inspection. Also, if an establishment should become ineligible for pre-announcement, the endorsement of the EIR should reflect this statement. This information will be necessary for making any future determinations regarding pre-announced inspections of the establishment. In addition, you should inform the establishment during the current, and subsequent inspections, of the action(s) that may have caused them to be ineligible for pre-announcement.

5.10.2 - Drug Inspections

As a reminder, our authority for conducting inspections is discussed in IOM 3.2. FD&C Act Sections 501(a) through (d) and 501(j) [21 U.S.C. 351(a) through (d) and 351(j)] describe the ways in which a drug may be or may become adulterated. Section 502 of the FD&C Act [21 U.S.C. 352] does the same, with respect to misbranding. Section 505 of the FD&C Act [21 U.S.C. 355] requires that new drugs be approved by the FDA. With these authorities, laws, and regulations in mind, the purposes of a drug inspection are to execute and fulfill the following:

1. Evaluate a firm's adherence to the concepts of sanitation and good manufacturing practices, such that production and control procedures take into account all reasonable precautions needed to ensure the identity, strength, quality, and purity of the finished products and active pharmaceutical ingredients.
2. Identify deficiencies that could lead to the manufacturing and distribution of products in violation of the Act, (for example, non-conformance with Official Compendia, super/sub potency, or substitution).

3. Determine whether a firm is distributing drugs that lack required FDA approval, including counterfeit or diverted drugs.
4. To obtain correction to identified deficiencies.
5. Determine if drugs are manufactured by the same procedures and formulations as specified in the associated Drug Application documents.
6. Determine the drug labeling and promotional practices of the firm.
7. Ensure the firm is reporting NDA field alerts as required by 21 CFR 314.81, and Biological Product Deviation Reports (BPDRs) for therapeutic biological products as required by 21 CFR 600.14;
8. Determine if the firm is complying with the requirements of the Prescription Drug Marketing Act (PDMA) and associated regulations.
9. Determine the disposition of Drug Quality Reports (DQRS) received from the Drug Surveillance and Data Reporting Branch (DSDRB)/CDER.
10. Determine if the firm is complying with any relevant post-market Adverse Drug Experience reporting requirements, as required by 21 CFR sections 310.305 (prescription drugs without approved NDA/ANDA), 314.80, 314.98, and 314.540 (application drug products), 514.80 (applicable for animal adverse events) and 600.80 (therapeutic biological products); Section 760 of the FD&C Act (non-application nonprescription products) [21 U.S.C. 379aa];. and Section 503B (b)(5) [21 U.S.C. 353b(b)(5)] of the FD&C Act (registered outsourcing facilities).
11. Determine, for pharmacy compounding inspections, if compounded drug products meet the conditions of section 503A or 503B of the FD&C Act.

5.10.2.1 - Preparation and References

During your preparation for an upcoming assignment, you should become familiar with current programs related to drugs. You should also determine the nature of the assignment, for instance, does it relate to a specific drug problem? Or is it a routine inspection?). If necessary, consult other program personnel, such as chemists, microbiologists, and other subject matter experts, or center personnel, such as office of compliance staff, to aid your understanding. You should also review the establishment program files of the firm to be inspected, including, any:

- Establishment Inspection Reports
- Inspection Coversheets
- Firm Profiles
- OTC monographs and other pertinent references for non-application products
- Drug Applications (new, abbreviated and investigational) and the Knowledge Transfer Memo, if the Center has provided it for a specific pre-approval inspection
- Therapeutic Biologics License Applications
- Sample results, where applicable
- Complaints and Recalls
- Regulatory files
- CMS Files/FEI Information
- Drug Quality Reports (DQRs), NDA Field Alert Reports (FARs), and Biological Product Deviation Reports (BPDRs)
- Drug Registration and Listing
- Inspection Protocols (NIPP) and their questions where appropriate
- Facility Dossier, where applicable
- Inspection Assignment memo, where applicable.

During your review of these documents, you should also pay special attention to and identify products that:

- Are difficult to manufacture
- Are complex dosage forms
- Require special tests or assays, or cannot be assayed
- Require special processes or equipment
- Are new drugs and/or potent low dosage drugs
- Are misbranded, unapproved, fraudulent, or are compounded human drug products that do not meet the conditions of section 503A or 503B of the FD&C Act
- Are manufactured for vulnerable populations (such as, pediatric or geriatric)

You should also review the factory jacket, OEI and registration/listing data, CMS, OSAR, and all complaint reports that are marked follow-up next inspection. These complaints are to be investigated during the inspection and discussed with management. (See IOM 5.7.1.4.14.)

Become familiar with current regulations and programs relating to drugs, CP 7356.002, and similar resources. When preparing for CGMP inspections, discuss with your supervisor the advisability of consulting a microbiologist, analyst, engineer, or other subject matter expert to aid in evaluating those areas of the firm germane to their expertise. Review the FD&C Act, Chapter V, Drugs and Devices. Review parts of 21 CFR 210/211/212 applicable to the inspection involved and Bioavailability (21 CFR 320).

In the case of APIs, review FD&C Act section 501(a)(2)(B) [21 U.S.C 351(a)(2)(B)] and the ICH industry's Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients.

Review the current editions of the United States Pharmacopeia (USP), and Remington's Pharmaceutical Sciences for information on specific products or dosage forms. (See IOM 2.2.3 Authority to Inspect and 3.10 Regulatory Submissions for special regulatory information by product category.)

Review 21 CFR 203 "Prescription Drug Marketing," 21 CFR 205 "Guidelines for State Licensing of Prescription Drug Distributors," and CP 7356.022, Enforcement of the Prescription Drug Marketing Act (PDMA).

Before conducting drug pre-approval inspections (CP 7346.832), it is important to be familiar with the application, and coordinate accomplishment of Center goals as communicated by (1) Division Preapproval Manager, (2) inspectional memos, (3) pre-inspection briefings, and/or (4) Center participation on the inspection team.

The Office of Manufacturing Quality (OMQ) in CDER has established two digital resources for you to obtain technical assistance before, during, or after an inspection:

1. The OMQ SharePoint site, which contains organizational charts, names, and phone numbers of OMQ individuals identified as technical specialists in various areas.
2. The Questions and Answers on Current Good Manufacturing Practices for Drugs forum, which is intended to provide timely answers to questions about the meaning and application of CGMPs for human, animal, and biological drugs, and to share these widely. Questions and answers found here generally clarify statements of existing requirements or policies.

Section 704(a)(4) of the Act provides for a records request or other information in advance of an inspection. This section will not discuss the legal aspects of in lieu of an inspection but addresses in advance of an inspection. The issuance of a 704(a)(4) request must follow established procedures. Please see QMiS DIR- 000087 for OPQO procedures.

5.10.2.2 - Inspectional Approach

Review and follow Compliance Program Guidance Manual (CPGM) 7356.002 and others as appropriate when conducting drug CGMP inspections. The in-depth inspection of all manufacturing and control operations is usually

not feasible or practical, as such, a risk-based systems audit approach is recommended in which higher-risk, therapeutically significant, medically necessary, and difficult-to-manufacture drugs are covered in greater detail during an inspection. (Note: The status of a drug as "medically necessary" is determined by CDER. For more information, contact Office of Compliance/Recalls and Shortages Branch at cderrecalls@fda.hhs.gov) This group of drugs includes, but is not limited to, time-release and low-dose products, metered-dose aerosols, aseptically processed drugs, and formulations with components that are not freely soluble. If the inspection is conducted for a CDER-led combination product, see also IOM 5.16 Combination Products.

CPGM 7356.002 incorporates the systems-based approach to conducting an inspection and identifies six systems in a drug establishment for inspection: Quality, Facilities and Equipment, Materials, Production, Packaging and Labeling, and Laboratory Control. The full inspection option includes coverage of at least four of the systems; the abbreviated inspection option covers at least two systems. In both cases, CPGM 7356.002, indicates the Quality System be selected as one of the systems being covered. During your evaluation of the Quality System, it is important to determine if top management makes science-based decisions and acts promptly to identify, investigate, correct, and prevent manufacturing problems likely to, or have led to, product quality problems.

When inspecting drug manufacturers that market a number of drugs meeting the earlier-mentioned risk criteria, consider doing the following to help you identify suspect products:

1. Review the firm's complaint files early in the inspection to determine relative numbers of complaints per product.
2. Inspect the quarantine, returned, reprocessed, and/or rejected product storage areas to identify rejected products.
3. Identify those products that have process control problems and batch rejections by reviewing processing trends and examining reviews performed under 21 CFR 211.180(e).
4. Review summaries of laboratory data (for instance, laboratory workbooks), OOS investigations, and laboratory deviation reports.

5.10.2.3 - Drug Registration & Listing

Keep in mind the following requirements and other information regarding registration and listing:

- Registration and listing is required whether or not interstate commerce is involved. (See Exhibit 5-12 and IOM 3.10.2.1 for additional information.)
- Two or more companies occupying the same premises and having interlocking management are considered one establishment and usually will be assigned a single registration number. (See IOM 5.1.4.3.3 - Multiple Occupancy Inspections for additional information.)
- Independent laboratories providing analytical or other laboratory control services on commercially marketed drugs must register.
- FACTS FMS, eDRLS, and CMS will indicate if the establishment is registered for the current year. If you determine registration and listing is required, advise your supervisor. After checking for past registration, cancellation, etc., the program division will provide the firm with the proper forms and instructions.
- Each establishment is required to list with the FDA every drug in commercial distribution, whether or not the output of such establishment or any particular drug so listed enters interstate commerce. During the establishment inspection, you should remind the firm of its responsibilities for ensuring its drug listing accurately reflects the current product line, and updating its listing as necessary to include all product changes, NDC changes, and discontinuations in accordance with 21 CFR 207. If registration and listing deficiencies are found, document it in your EIR, collect a documentary sample and/or contact your supervisor.

- During foreign inspections, the investigator should verify the information for the U.S. agent. A U.S. Agent is a person residing or working in the Unites States who is designated as such by a foreign establishment registered for drugs. A U.S. agent is responsible for: 1) reviewing, disseminating, routing, and responding to all communications from the FDA; 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 registered foreign establishment directly or quickly, the agency may provide the information and/or documents to the U.S. agent, who is considered equivalent to providing the same information and/or documents to the registered foreign establishment (21 CFR 207.69). This information is critical to ensure the safety of the supply chain and to ensure that the FDA has appropriate contact information for any emergency or recall situations.

5.10.3 - Counterfeit Drug Authority

Section 702(e) of the FD&C Act [21 U.S.C. 372(e)] contains certain authorities relating to counterfeit drugs including the authority to seize ("confiscate") counterfeit drugs and containers, counterfeiting equipment, and all other items used or designed for use in making counterfeit drugs prior to the initiation of libel proceedings. This authority has been delegated, with certain restrictions, to holders of official credentials consistent with their authority to conduct enforcement activities. Additional authorities in 702(e), to make arrests, to execute and serve arrest warrants, to carry firearms, and to execute seizure by process under Section 304 of the FD&C Act [21 U.S.C. 334], have not been delegated.

The agency does intend to utilize the authority contained in Section 702(e) to execute and serve search warrants, but such use does not require delegation from OII's Associate Commissioner Inspections and Investigations.

Section 702(e)(5) contains authority for such delegated persons to confiscate all items which are, or which the investigator has reasonable grounds to believe are, subject to seizure under Section 304(a)(2). Items subject to seizure, and thus to confiscation under Section 702(e)(5), includes most things associated with counterfeit drugs. Confiscation authority does not, however, extend to vehicles, records, or items (for instance, profits) obtained as a result of counterfeiting.

5.10.3.1 - Scope

Under this delegation, with supervisory concurrence and prior to the initiation of libel proceedings, investigators and inspectors are authorized to confiscate:

1. Any counterfeit drug
2. Any container used to hold a counterfeit drug
3. Any raw material used in making a counterfeit drug
4. Any labeling used for counterfeit drug
5. Any equipment used to make a counterfeit drug including punches, dies, plates, stones, tableting machines, etc.
6. Any other item which you have reasonable grounds to believe is designed or used in making a counterfeit drug.

NOTE: You and your supervisor must remain vigilant regarding the potential dangers involved in confiscating property from individuals. Special care should be taken to ensure your safety. See to IOM 10.3 for information on personal safety and speak to your supervisor about creating a personal safety plan. Arranging for teams of investigators to conduct the investigation, or arranging for assistance by local police, or other agencies with police powers, should be considered in planning the confiscation of counterfeit materials.



5.10.3.2 - Inspectional Guidance

Guidance provided for implementing the authority to confiscate drug counterfeits is as follows:

1. The authority is not to be utilized unless there has been an agency determination that the drug to be confiscated is a counterfeit and is a drug that "without authorization, bears a trademark, *** or any likeness" of a legitimate product. The determination usually is based upon evidence supplied by the firm whose product is being counterfeited. A written agency determination will issue to the Division Director Office of Import Operations), in conjunction with CDER or CVM.
2. When engaged in counterfeit investigations, you should proceed as follows when encountering items to be confiscated:
    a. Evaluate your safety needs and check the physical location to ensure it is safe to proceed. Do not attempt to remove an item by force. If it appears there will be resistance, contact the local police, or other agencies with police powers, for backup, if not already done in advance. (See IOM 10.3 for information on personal safety and speak to your supervisor about creating a personal safety plan.)
    b. Inventory the items to be confiscated.
    c. Prepare a written receipt and offer it to the person in charge.
    d. Remove the items, if possible, from the premises (if they cannot be removed, secure them under seal).
    e. Place all items removed, under lock, at a secure location. In most cases, confiscated items will be stored at the program division or resident post office until they are seized.

5.10.3.3 - Follow Up Guidance

After items are confiscated, certain actions must be taken to bring confiscated items under the control of the court. You should proceed as follows:

1. Immediately notify your supervisor after an item has been confiscated.
2. Supervisors must then notify the appropriate compliance units of the items confiscated.
3. Compliance units should initiate seizure proceedings against any items confiscated.
4. Medical Products Inspectorate (MPI) should be advised of any action utilizing this authority.

5.10.3.4 - Search Warrants

Section 702(e)(2) contains authority to execute and serve search warrants. Proceed as instructed by your program division after a search warrant has been obtained.

5.10.4 - Promotion and Advertising

5.10.4.1 - Promotion and Advertising

The jurisdiction of FDA drug promotion and advertising falls to two regulatory agencies: the FDA and the Federal Trade Commission.

If you should come across any drug advertisement or promotional labeling that is potentially a violation of the FD&C Act, collect that labeling or advertisement for further review. Collect, or document, the drug advertisement and promotional labeling as a photo, screenshot, or PDF. Keep in mind that any hyperlinks associated with a drug or firm website are often temporary and may not capture changes made to the website after the potential violation was observed. Your intent should be to capture labeling of potential misbranding/unapproved new drug adulteration violations. Once collected, that evidence, with your supervisor’s approval, should be sent to compliance for evaluation.

(For more important information about how a drug is promoted, see section 21 CFR 201.128, which defines the intended use of the drug product.)

5.10.5 - Labeling

See section IOM 4.4.7 for the definition of product labeling and the method of collection.

Product labeling includes the product labels (the label on the immediate product container and packaging or outer box) that describes the intended use of a drug product and lists active and inactive ingredients and concentration of each active ingredient. The product label may also reference website(s) for additional information for the intended use (such as treatment of a medical condition). OTC drug manufacturers may also manufacture dietary supplements and cosmetics. Information on the product label differentiates whether a product is an OTC drug product, a dietary supplement, or a cosmetic product. (See 21 CFR 201.66 OTC Drug Labeling.)

During GMP inspections of OTC drug manufacturers, you should collect and review product labeling (product label and internet website) of each drug product to determine conformance with the OTC drug monographs found in 21 CFR 310.519 - 548 (negative monograph or new drugs) and 21 CFR 331 - 358 (final monograph) in order to consider whether any unapproved new drug and misbranding charges apply to the firm's OTC products. Please ensure that photocopies or photographs of all sides of the product label show legible texts. You should also document interstate shipment(s) of the distributed OTC product to support an unapproved new drug charge. (See CPGM 7361.003 OTC Drug Monograph Implementation for inspectional guidance.)

5.10.6 – Guaranties and Labeling Agreements

You should determine the firm's policies relative to receiving guaranties for raw materials and issuing guaranties on their products. Also determine firm's practices regarding shipment of unlabeled drugs under labeling agreements. (See IOM 5.6.10.2.)

5.10.7 - Other Inspectional Issues

5.10.7.1 - Intended Use

Please see the discussion of jurisdiction in section IOM 5.7.1.4.5.

5.10.7.2 - Drug Approval Status

You should ascertain whether the drugs manufactured by the firm are covered by an NDA, ANDA, NADA, ANADA, OTC monograph, or marketed under a claim of DESI or another exemption status.

5.10.7.3 - Drug Status Questions

If you have questions about misbranding, new drug status, API/finished drug product status, drug/cosmetic, or drug/food (dietary supplement) status, contact the Office of Unapproved Drugs and Labeling Compliance (OUDLC) in CDER's Office of Compliance at 301-796-3100 or CDEROUDLCPMTRACK@CDER.FDA.GOV.

If you have questions about the status of compounded human drugs products, contact the Office of Compounding Quality Compliance in CDER's Office of Compliance at 301-796-3100 or Compounding@fda.hhs.gov.

5.10.7.4 - Verification of Compliance with PDMA Requirements

You should ascertain whether a manufacturer uses samples of prescription drugs to market its products. If so, it must be in compliance with the regulations at 21 CFR 203 Subpart D – Samples. (Refer to CP program 7356.022, Enforcement of the Drug Sample Distribution Requirements of the Prescription Drug Marketing Act (PDMA).) If you have questions concerning this portion of an inspection, contact Office of Compliance at 301-796-3100 or DrugSupplyChainIntegrity@fda.hhs.gov.

5.10.7.5 - Drug/Dietary Supplement Status

In instances where the drug/dietary supplement status of a product is unclear, you should collect all related labeling and promotional materials, including pertinent websites. Such labeling, promotional materials, and

websites are often useful in determining the intended use of a product, as they may, for example, contain or advertise disease claims, that can be used to determine the intended use of a product and, therefore, if it is a dietary supplement or a drug and an unapproved new drug. (See 21 CFR 201.128).

5.10.7.6 - Approved Drugs

Check the current programs in your CPGM, Section 505 of the FD&C Act [21 U.S.C. 355] and 21 CFR part 314 for required information. You may also ask your designated pre-approval manager for CMC information of the targeted drug application. Document and report all deviations from representations in the NDA or ANDA, even though they may appear to be minor. You can access applications through the Lorenz docuBridge application.

5.10.7.7 - Investigational Drugs

Follow the instructions in pertinent programs in your CPGM, or as indicated in the specific assignment received.

5.10.7.8 - Clinical Investigators and/or Clinical Pharmacologists

Inspections in this area will be on specific assignment previously cleared by the agency. Follow guidance in the CPGM or assignment.

5.10.7.9 - Delaying, Denying, Limiting or Refusing Drug Inspections

Use reasonable discretion when discerning whether action taken by a drug firm during an inspection constitutes delaying, denying, limiting, or refusing a drug inspection. If you are unsure whether an action taken by a firm constitutes delaying, denying, limiting, or refusing drug inspection, consult with your supervisor.

As needed, refer to the Guidance for Industry – Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection, for examples of firm actions that may cause a drug to be deemed adulterated under FD&C Act section 501(j). Remember, however, that these examples are not exhaustive, and that guidance documents do not establish legally enforceable rights or responsibilities and are not legally binding on the firm or the agency. (See IOM 3.2.3.2)

5.10.8 – Drug Inspection Reports

See IOM 2.4 – English Language Requirement, the requirements in IOM 5.7.1.4 and any applicable CP, as well as New Inspection Protocol Project (NIPP), can be used to help you prepare your report.

Guidance here does not cover the reporting requirements for a directed inspection with a narrow focus, such as a complaint follow-up or investigation into a recall. In those cases, use your judgment and the guidance found in IOM 5.7.1.1 about the depth of reporting required. And follow the instructions and format for a human drug inspection report as contained in IOM 5.7.1.4.

The human drug inspection report does not require full and detailed narratives for every area for every inspection. The firm's state of compliance, the previous inspectional report and information, complexity of operations, type of inspection, and other aspects all are determinants in how much reporting will be necessary. In many cases, brief summaries addressing the format areas will be sufficient.

5.11 - Animal & Veterinary

5.11.1 - CVM Website

The Center for Veterinary Medicine (CVM) website contains a listing of current and planned Guidance Documents, on-line access to the Animal Drugs FDA Database listing new animal drug approvals, and a variety of current information regarding medicated and nonmedicated animal feed and pet food. It also hosts a "search" feature allowing you to search for documents containing various words or phrases. The website also contains

organizational information for CVM and an explanation of the various laws and regulations that the Center enforces. Information on the website can provide guidance for inspectional efforts related to CVM obligations.

5.11.2 - Veterinary Drug Activities

CVM is responsible for work-planning inspections of therapeutic and production drugs, and Active Pharmaceutical Ingredients (APIs). Therapeutic drugs are used in the diagnosis, cure, mitigation, treatment, and/or prevention of disease. Production drugs are used for economic enhancement of animal productivity and include drugs that address such industry issues and objectives as, growth promotion, feed efficiency, and increased milk production.

Pre-approval inspections are conducted pursuant to pending NADA or ANADA applications. (CVM's Compliance Program 7368.001 addresses: New Animal Drug Applications (NADA), Abbreviated New Animal Drug Applications (ANADA) Investigational New Animal Drug (INAD) Applications, Generic Investigational New Animal Drug (JINAD) Applications and Conditional New Animal Drug Applications (CNADA).)

Post-approval inspections of veterinary drugs are conducted to determine compliance with the Current Good Manufacturing Practices (CGMPs) for Finished Pharmaceuticals under 21 CFR Part 211. These cGMPs apply to both human and veterinary drugs. Information on approved veterinary drugs can be found in the "Green Book" database accessed through CVM's website.

APIs are active pharmaceutical ingredients. Many of the APIs used to manufacture dosage-form drugs are imported from foreign countries. The intended source for an API must be indicated in NADA/ANADA submissions for new animal drug approvals. Any change in a source for an API would require a supplement to the application.

The goal of CVM's Compliance Program 7371.001 – Animal Drug Manufacturing Inspection is to minimize animals' exposure to adulterated drugs and human exposure to adulterated food resulting from animals treated with adulterated drugs. This includes APIs and finished-dose form (sterile and non-sterile) animal drugs.

The CGMPs for Type A Medicated articles are found under 21 CFR Part 226 and can also be found in the "Green Book." CVM's Compliance Program 7371.005 – Type A Medicated Articles provides guidance for implementing the strategies and explains risk-based inspectional requirements for Type A Medicated Article drug manufacturing.

Extra-label drug use refers to the regulations in 21 CFR Part 530 codified as a result of the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994. These regulations set forth the requirements that veterinarians must meet to prescribe extra-label uses of FDA-approved animal and human drugs. The regulations also define what constitutes a valid veterinary-client-patient relationship, as well as what is considered illegal extra-label use. 21 CFR Part 530 addresses issues regarding extra-label use in non-food as well as food-producing animals. 21 CFR 530.41 contains a list of drugs that cannot be used in an extra-label manner in food-producing animals. During an inspection or investigation, if you encounter any situations relating to suspected illegal extra-label use of any FDA approved animal or human drugs, or those prohibited for extra label use in food animals, you should contact CVM's Division of Drug Compliance (HFV-210).

21 CFR Part 530 also addresses compounding of products from approved animal or human drugs by a pharmacist or veterinarian. The regulations clearly state compounding is not permitted from bulk drugs. This would include APIs. CVM has an existing GFI-256 which addresses Animal Drug Compounding. The Division of Drug Compliance (HFV-210) has issued assignments to conduct inspections of firms, including internet pharmacies, who may be engaged in the practice of manufacturing under the guise of pharmacy compounding.

OII drug investigators should send their correspondence about general pharmacy compounding issues to oiicompounding@fda.hhs.gov (OII-Compounding) for proper response and routing. OII-Compounding should contact the Division of Drug Compliance (HFV-210) at cvmcompounding@fda.hhs.gov to report instances of animal drug

compounding, or to seek guidance on inspectional issues, or regulatory and enforcement policies relating to animal drug compounding.

5.11.3 - Animal Food Activities

Animal food is defined under Section 201(w) of the FD&C Act [21 U.S.C. 321 (w)] as "food for animals other than man intended for use as a substantial source of nutrients in the diets of the animal, this includes raw materials and ingredients used to manufacture animal food." As such, CVM is responsible for oversight of the following animal food programs:

- Medicated animal feed
- CGMP and Preventive Controls for animal foods
- Pet foods and treats
- Feeds containing Veterinary Feed Directive (VFD) drugs
- Prohibited Materials in Ruminant Animal Food (BSE)
- Sanitary Transportation Requirements (Directed Only)

The regulations for these programs can be found here:

CGMPs for medicated feed	21 CFR Part 225
CGMPs/PC for non-medicated feed and pet food	21 CFR Part 507
VFD Requirements	21 CFR Part 558.6
BSE Requirements	21 CFR Parts 589.2000 and 589.2001
Medicated Feed Mill Licensure	21 CFR Part 515
Sanitary Transportation	21 CFR Part 1, Subpart O

Your inspections of animal food facilities should include an evaluation of all activities performed at a facility such that you can determine compliance with all animal food regulatory requirements that may apply. CVM's Comprehensive Animal Food Inspection Compliance Program, 7371.000 lays the framework for conducting a comprehensive animal food inspection and provides additional guidance on topics that are ancillary to these inspections (including registration, feed mill licensing, VFD distributor notifications, etc.). The comprehensive inspectional approach serves two purposes: (1) to implement a systems-based approach to evaluate whether a facility is implementing practices necessary to meet all the animal food safety regulatory requirements that apply at their facility; and (2) to efficiently utilize inspectional resources.

Appropriate training must be obtained prior to conducting any animal food inspections.

If you have questions concerning any of the animal food programs, you should contact CVM/Division of Food Compliance at CVMAnimalFoodPrograms@fda.hhs.gov.

(The regulations for animal food labeling are found in 21 CFR Part 501. Guidance on pet food labeling requirements can be found on CVM's website www.fda.gov/animal-veterinary/animal-food-feeds/pet-food.)

5.11.4 - Biosecurity Procedures for Inspections at Poultry Facilities and Farms

Biosecurity continues to be a high priority when conducting animal food inspections. Given our experiences with pathogenic animal viruses, such as porcine epidemic diarrhea virus (PEDV) and highly pathogenic avian influenza (HPAI), we expect everyone conducting animal food inspections on FDA's behalf to observe simple, routine, biosecurity precautions for all routine animal food inspection work. In addition to FDA's biosecurity guidance and procedures, you should:

1. Follow the biosecurity plan for the facility being visited if it has one.

2. Plan your daily activities and movements so that you do not carry contamination from one location to another. As much as possible, plan to work from the cleanest to the dirtiest site on a given day, whether this is within a single facility, or across multiple facilities.
3. Wear clean shoes and clothes and use clean equipment.
4. Practice good personal hygiene, such as handwashing and bathing.
5. Change or clean your shoes between inspection sites if they get dirty or soiled or wear disposable shoe coverings.
6. Avoid making contact with animals during on-farm feed inspections, a practice generally not required in most situations anyway, unless it becomes necessary.
7. Be cognizant of any recent contact with livestock, poultry, or pet birds owned by you or others, including during activities/hobbies such as hunting.
8. As much as possible, avoid going from one farm to another on a single day. If you need to do so, consider changing clothes and/or shoes, and showering.
9. Make an appointment to conduct routine on-farm inspections.
10. Review and be familiar with all appropriate field alerts and field bulletins.

This information is summarized from Exhibit 5-19, - Biosecurity it is important that you follow biosecurity procedures – during the inspection planned for a given site, as well as for work that may be planned for several days following – and that you are prepared to practice these measures. Therefore, CVM suggests that all routine assigned work (covered in the work-plan or an assignment) involving on-farm animal food inspections be pre-announced. This gives the CSO the opportunity to ask about biosecurity procedures beforehand, including requesting and gaining assurance that someone will be present onsite so that the inspection can be conducted. Regarding for-cause inspections/investigations, pre-announcement is not necessary, but it is essential that you be prepared to address any biosecurity needs and issues you may encounter.

5.11.5 - Drug Residues

The presence of violative drug residues in food from slaughtered animals is a human health concern. Drug residue inspections are performed in response to reports of violative drug residue levels found in tissue sampled at slaughter by the USDA's Food Safety Inspection Service (FSIS).

Drug residues are commonly caused by medicating animals prior to marketing and a failure to follow the drug's approved label directions. When a new animal drug is approved, the approval is very specific in how the drug should be used, the dosage it should be given, route of administration, frequency of use, and reason for use. A drug manufacturer conducts studies to determine withdrawal times, and these times must be followed. Established tolerances for drug residues of new animal drugs in food can be found in 21 CFR Part 556.

Drug residue investigations are unique in comparison to other fieldwork we conduct. Although your investigation may begin at the USDA slaughter establishment, or at a facility for a person named on the USDA/FSIS "Violation Notification Letter", you may inspect and/or visit additional sites as part of your overall investigation. For instance, you may also need to visit an auction barn, dealer, trucker, veterinarian, drug supplier, slaughter facility (USDA firm management or state personnel), etc., as one or more of these establishments may be responsible for the drug residue. As a result, each establishment's activities may warrant a recommendation for regulatory action, such as a Warning Letter, Injunction, etc., where involvement with residue violations is documented.

Upon receipt of a FACTS assignment from CVM to conduct a drug residue follow-up investigation, the program division may also create additional operations, linked to the original CVM assignment, to encompass all operations required to complete the CVM assignment. This could include multiple inspections, sample collections, and/or investigations. In fact, you may not be aware of all the establishments you will need to visit prior to beginning your investigation. This also means you will need to add, or delete, applicable operations to or from the program

division assignment as you proceed with the investigation. Be mindful, too, that each site visit is unique, and produces its own set of unique documents and evidence requiring individual reporting by an establishment. Practice diligence and good judgment during case development to assure you document your investigation thoroughly. Explain the full chain of events and evidence, from the initial drug residue report to any other establishments, and how they were all involved. Collect DOC samples as appropriate (DOC samples are generally only required for violative cases where judicial action is being sought). Consult regularly with your supervisor and/or compliance branch during these operations to ensure all evidence needed to develop a quality case is obtained and submitted in an appropriate format.

Following completion of all operations, you should prepare a Memo of Investigation, referencing the FACTS assignments, for your supervisor's endorsement to the center compliance office, with a copy to the originating CVM office. This memo should summarize each site visit (EI or Investigation), sample(s) collected, and relevance to the overall CVM assignment. A copy of the memo will be routed to each appropriate factory file. The individual operations will then stand alone, and/or may be used together to build one or multiple cases. For example, a site visit to a slaughter facility may yield information about an animal according to USDA inspection personnel on site, as well as verification from management that the establishment ships in interstate commerce. Information obtained at the slaughter facility or other establishments may be documented in an affidavit from each individual providing salient information. A site visit to a veterinarian is required when the drug(s) causing the violative residue was/were prescribed by the veterinarian. When there is reason to believe extra-label use or other activities have occurred, which may warrant a recommendation for regulatory action, an establishment inspection should be conducted, and your evidence included with your report. (Refer to the Compliance Program 7371.006, "Illegal Residues in Meat, Poultry, Seafood and other Animal Derived Foods" (https://www.fda.gov/media/74810/download) for in depth instructions on how to conduct a drug residue inspection.)

For more information on drug residue violations and activities, contact the CVM/Division of Food Compliance (HFV-236) CVMAnimalFoodPrograms@fda.hhs.gov.

5.11.6 - Veterinary Devices

Medical devices for animal/veterinary use are not subject to the premarket approval requirements like human medical devices. Once an animal use device is marketed the Center is concerned with safety and efficacy of the veterinary device. CVM often recommends firms use the human device GMPs in controlling the manufacturing of animal use devices. CVM also suggests labeling be sent in for review by the Division of Drug Compliance (HFV-210) (ASKOSC@fda.hhs.gov) to avoid misbranding. Regulatory questions for veterinary/animal use devices should be directed to the CVM/Division of Drug Compliance (HFV-210) (ASKOSC@fda.hhs.gov.)

5.11.7 - Animal Grooming Aids

Grooming aids for animals formulated and labeled only to cleanse or beautify the animal are not cosmetics within the meaning of Section 201(i) and not subject to the Federal Food, Drug, and Cosmetic Act. Where animal grooming aids are labeled to contain an active drug ingredient or otherwise suggest or imply therapeutic benefit, they may be considered to be drugs and/or new animal drugs as defined by Section 201(v) of the Act (see CPG 653.100).

Questions on labeling and regulatory concerns should be directed to the Division of Compliance (HFV-230) at 240-276-9200.

5.11.8 – Products Intended for Control of Fleas and Ticks

Products for animal use intended for control of fleas and ticks may be regulated as drugs by FDA under the Federal Food, Drug, and Cosmetic Act or pesticides by the Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act. Products registered with EPA as pesticides must have an EPA registration number listed on the label. Questions regarding whether a product intended for control of fleas and ticks is regulated

by FDA or EPA should be directed to CVM, Division of Drug Compliance at CVMCompliance@fda.hhs.gov. Questions regarding EPA-registered pesticide products should be referred to EPA at pesticidequestions@epa.gov or Environmental Protection Agency, Office of Pesticide Programs, 1200 Pennsylvania Ave., Washington, DC 20460.

5.12 - Medical Device and Electronic Radiation Product Controls (EPRC)

5.12.1 - Medical Device Inspections

Medical device inspections will be conducted as assigned and in accordance with applicable Compliance Program(s), for instance, CP 7382.850 Inspection of Medical Device Manufacturers . Types of inspections include surveillance and directed assignments, such as Compliance Follow-Up, For-Cause, Specific Product Risk Assignments (SPRA),Premarket Approval (PMA), and Post-Market inspections. Inspections may also be assigned as combinations of these different types.

If the inspection covers EPRC requirements, see also IOM 5.12.2. If the inspection is conducted for a combination product, see also IOM 5.16.

CAUTION: Investigators should be on the alert for, and avoid contact with, manufacturing materials and hazards associated with the manufacturing of many types of devices, which may present a threat to health, including ethylene oxide, high-voltage electricity, pathogenic biomaterials, etc. (See IOM Chapter 10, including 10.15.2- Radiation Hazards, 10.12.6.3 - Ethylene Oxide (EtO), and 10.15.1.3 - Energy Hazards.)



5.12.1.1 – Inspection Authority for Medical Devices

The term "device" is defined in Sec. 201(h) of the FD&C Act [21 U.S.C. 321 (h)]. In-vitro diagnostics (21 CFR 809) are also devices, as defined in 201(h) of the Act [21 U.S.C. 321 (h)], and may also be biological products, subject to Section 351 of the PHS Act.

The FDA has distinct authority under section 704(e) of the FD&C Act [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)]. Investigators should only collect copies of documents as necessary to support observations or to satisfy assignments. Note that manufacturers who have petitioned for and obtained exemption from the QMSR are *not* exempted from FDA authority to review and copy complaints and records associated with investigation of device failures and complaints. (See IOM 3.2 for discussion of statutory authority to enter and inspect.)

Provisions in the FD&C Act pertaining to FDA review of records are:

1. For restricted devices, the FD&C Act in Section 704(a)(1)(B) [21 U.S.C. 374 (a)(1)(B)] extends inspection authority to records, files, papers, processes, controls, and facilities bearing on restricted medical devices. (See FD&C Act Sec. 704 [21 U.S.C. 374] for a full explanation and for a list of the items, for instance, financial data, which are exempt from disclosure to the FDA.) (Restricted devices, per CFR 807.3(i), are devices for which a requirement restricting sale, distribution, or use has been established by regulation, such as prescription devices.)
2. For all devices, including restricted devices, refer to Section 704(e) of the FD&C Act [21 U.S.C. 374 (e)], which provides for FDA's access to, copying, and verification of certain records.
3. Section 519 of the FD&C Act [21 U.S.C. 360i] requires manufacturers, importers, or distributors of devices intended for human use to maintain such records and provide information as the Secretary may by Regulation reasonably require.
4. Section 520(g) of the FD&C Act [21 U.S.C. 360j (g)] covers the establishment of exemptions for devices for investigational use and the records which must be maintained and open for inspection.

Records showing compliance with the QMSR must be maintained by the firm in accordance with ISO 13485:2016 clause 4.2.5-Control of records and 2 CFR 820.35.

5.12.1.2 - Medical Device Single Audit Program (MDSAP)

The FDA works with other global regulators within the International Medical Device Regulators Forum (IMDRF) for the purposes of leveraging work performed for other medical device regulators to meet FDA inspection obligations. The Medical Device Single Audit Program (MDSAP) allows an MDSAP-recognized Auditing Organization to conduct a single regulatory audit of a medical device manufacturer that satisfies the relative requirements of the regulatory authorities participating in the program. Currently, five countries participate in MDSAP: the United States, Australia, Brazil, Canada, and Japan.

The FDA uses MDSAP audit reports as a substitute for surveillance inspections for firms that volunteer to participate in the MDSAP program. MDSAP audit reports submitted by MDSAP Auditing Organizations, that include the United States as a jurisdiction, are reviewed and classified by the FDA.

Inspections that are conducted "For Cause" or "Compliance Follow-up" by the FDA will not be affected by this program. Moreover, this MDSAP program does not apply to any preapproval or post approval inspections for Premarket Approval (PMA) applications or to decisions under Section 513(f)(5) of the FD&C Act [21 U.S.C. 360c(f)(5)] concerning the classification of a device. Firms with activities related to the Electronic Product Radiation Control (EPRC) provisions of the Act continue to be subject to FDA inspections for the EPRC activities.

You should verify a firm's active status and participation in the Medical Device Single Audit Program (MDSAP) by accessing the MDSAP Master List before conducting any surveillance medical device inspections. You can do so by searching the list for FEI, firm name, and address. Note that firm participation is based on facility/site, so a firm with multiple sites may or may not be participating in MDSAP for all sites. If additional verification or other information is required, contact the MDSAP program via MDSAP@fda.hhs.gov.

When planning an inspection at a firm participating in MDSAP, you should alert CDRH of the planned inspection by sending an e-mail to MDSAP@fda.hhs.gov *prior to scheduling* the inspection if possible, *but no later than five business days* before the scheduled inspection. The e-mail should include the name, address, and FEI of the firm, the type of inspection that will be performed, the estimated inspection dates, and any additional information pertinent to the situation, such as a request for the MDSAP report or a reference number for a Warning Letter, etc.

If the reason for an inspection at an MDSAP-participating firm is related to a specific assignment, generated by either OII or CDRH, the OII Division should email OII's 's OMDRHO Operations at oii-devices-inspection-poc@fda.hhs.gov*at least ten days prior* to initiating the inspection. The email should contain the name, address, and FEI of the firm, planned dates of inspection or investigation, nature of the complaint or quality issue, and any other relevant firm/device information or history, prior to OII investigators conducting the inspection or investigation. In these situations, a teleconference between the CDRH MDSAP SMEs and OII may be needed to discuss the scope of any planned inspection or investigation and allow additional information to be exchanged between CDRH and OII.

5.12.1.3 - Pre-inspectional Activities for Medical Device Inspections

Refer to IOM Section 5.2 for general pre-inspection activities applicable to all inspection types.

5.12.1.3.1 - Assignment Information

The assignment details in eNSpect should be reviewed to determine the scope of the inspection and general information about the firm, Operation Type, PAC, Assigned and Target Date, Priority, and assignment. Foreign trip assignment information is communicated to the traveler via the Foreign Inspection, Planning and Scheduling System (FIPSS).

5.12.1.3.2 - Firm Information

You should review the history of the establishment prior to the start of a medical device inspection. You should also review the previous EIR, inspectional findings, and subsequent correspondence between the establishment and the FDA. Additionally, you should check for and review any consumer complaints where follow-up has not occurred, or recalls, since the last inspection.

You may obtain this information via Firm360, CMS, OII's Online Search and Retrieval (OSAR), and the Online Reporting Analysis Decision Support System (ORADSS). Firm 360 provides a comprehensive history of the firm to include firm registration and listing, previous inspections with exhibits and attachments, OII consumer complaints, recalls, compliance cases, and import alerts. ORADSS extracts data from various FDA systems, and in preparation of an inspection, can be used to query, run canned reports, and analyze retrieved data, such as import activities related to foreign and/or domestic firms.

5.12.1.3.3 - Medical Device Reports (MDRs)

As part of pre-inspectional preparation, you should review the firm's MDR data. MDRs can provide data to assist in determining potential problem areas in the manufacturing process, issues with the design of the device, specific lot/batch issues, and/or adverse events.

MDR information can be accessed through the Manufacturer and User Facility Device Experience (MAUDE) database or Total Product Lifecycle (TPLC). (Additional information about Medical Device Reporting requirements may be found in Compliance Program 7382.850, Inspection of Medical Device Manufacturers.)

5.12.1.3.4 - Registration & Listing

You should review the firm's Registration and Listing information through a resource such as the FDA Establishment Registration and Listing page, to identify the firm's establishment types, device listings, device product codes and regulation numbers, device classifications, Marketing Authorizations, and firm contact information.

5.12.1.3.5 - Marketing Authorizations

510(k) and PMA submission data can also assist you in determining what devices the establishment is manufacturing and whether any devices have been newly designed or changed since the last inspection. This data can also help you identify higher risk devices, for example, Class II or III versus Class I. One way to determine device submissions is to review registration and listing data. If needed, you may also request and obtain additional documents related to the submissions via CDRH.

5.12.1.3.6 – Unique Device Identification

You should review the firm's UDI submissions to the Global Unique Device Identification Database (GUDID) by conducting a search via Access GUDID to confirm the firm has all devices with required UDI information submitted.

5.12.1.4 - Pre-announcement of Medical Device Inspections

As a result of the FDA Reauthorization Act of 2017 (FDARA), the FDA published a guidance document outlining processes and standards for device establishment inspections, including a standardized process for pre-announcement. Certain types of medical device inspections are required to be pre-announced to the owner, operator, or agent-in-charge under this process, while the FDA retains its authority to continue to conduct unannounced for-cause inspections.

The purpose of pre-announcement is to notify the establishment's management of the date and time the investigator will be arriving at the establishment to conduct the inspection. For domestic inspections,

preannouncement is *not* a request to schedule an inspection. See IOM section 5.12.1.4.2 for considerations if a firm requests a change in start date.

5.12.1.4.1 - Criteria for Consideration

You will need to determine whether an establishment requires pre-announcement prior to inspection. Inspections where pre-announcement is appropriate include:

- Surveillance inspections
- Pre-market and post-market inspections (PMA, 510(k))
- Foreign inspections
- When instructed, by directive, procedure, compliance program, or assignment
- Where logistical concerns indicate preannouncement would be beneficial to the inspection, with supervisory concurrence.

5.12.1.4.2 - Procedures

1. Pre-announcement of domestic firms should be no less than five calendar days in advance of the inspection; pre-announcement of foreign firms is generally more than five calendar days due to the requirements for country clearances.
2. For domestic inspections, the investigator designated to conduct the inspection will contact the owner, operator, or agent-in-charge at the facility by phone to pre-announce. Should that person be unavailable at the time the call is made, a message requesting a return call should be left. The program division should use good judgment as to what is a reasonable time frame to await the return call. If after several attempts, acknowledgement of pre-announcement by the owner, operator, or agent-in-charge cannot be obtained, the inspection may proceed as planned.
3. During pre-announcement planning, you should inform the establishment as to the start date, the type/nature of the inspection, estimated duration (to include working hours during which the inspection is likely to take place), and the number of agency personnel expected to take part in the inspection. To the extent possible, you should also provide advance notice of some records that may be requested during the inspection (for instance, certain procedures and any associated records).
4. Changes in dates should be kept to a minimum. Should a postponement be necessary, the decision as to rescheduling rests with the investigator/team, but the new inspection date should not be later than five calendar days from the original date. If an establishment requests a change in start date, it must also provide a valid reason for the request. A valid reason should be the same as an investigator would accept if presented with the information during an unannounced inspection.
5. Include in the EIR whether the inspection was pre-announced, and if not pre-announced, describe briefly in the EIR why not.

5.12.1.5 - Conducting Medical Device Inspections

Medical Device inspections should be conducted in accordance with assignment instructions and Compliance Programs . Specifically, you should be attentive to:

1. Specific instructions in the assignment, if any.
2. The applicable Compliance Program, such as CP 7382.850 Inspection of Medical Device Manufacturers.
3. Guidance documents specific to the firm's operation type(s) and product(s) being reviewed.
4. Guidance from your supervisor.

Brief information is provided in sections 5.12.1.5.1 to 5.12.1.5.4 on regulations commonly reviewed during Risk-Based Medical Device inspections; however, this list is not exhaustive.

5.12.1.5.1 - Quality Management System Regulation (QMSR)

The regulation promulgated under 21 CFR 820 establishes minimum requirements applicable to finished devices, as defined in 820.1(a). This regulation does not generally apply to manufacturers of components or parts of finished devices. In some special cases, such as components that have been classified as finished devices (for instance, dental resins, dental alloys), components may be subject to the QMSR. Consult with your supervisor if you should have any questions about applicability of this regulation.

The preamble to the final rule for the QMSR includes FDA's response to the public comments that were received and explains the agency's thinking on application of the regulation. See preamble and QMSR.

The medical device QMSR does not prescribe in detail how a firm must manufacture a particular device. The regulation provides a framework, with which all manufacturers must comply, to develop and follow procedures that are appropriate to the manufacture of a given device. Use your good judgment in determining compliance with the QMSR, keeping in mind that all requirements may not apply or be necessary. You should also not insist that a manufacturer meet non-applicable requirements. (Refer to IOM Exhibit 5-13 for types of establishments that are required to comply with the QMSR.)

5.12.1.5.2 - Medical Device Reporting (MDR)

The first Medical Device Reporting (MDR) regulation was published on December 13, 1984. Undergoing several changes over time, the latest version of MDR regulation under 21 CFR 803 includes reporting requirements for manufacturers, user facilities, and importers. This regulation generally requires manufacturers of medical devices, including in vitro diagnostic devices, to report to the FDA whenever the manufacturer or importer receives, or otherwise becomes aware of, information that reasonably suggests that one of its marketed devices: (1) may have caused or contributed to a death or serious injury or, (2) has malfunctioned and the device, or any other device marketed by the manufacturer or importer, would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Guidance on the application of this regulation may be found in the guidance document Medical Device Reporting for Manufacturers published in November 2016, and in Compliance Program 7382.850 Inspection of Medical Device Manufacturers.

5.12.1.5.3 - Recalls, Corrections and Removals

The Corrections and Removal regulation, 21 CFR Part 806, took effect on May 18, 1998. The regulation generally requires that device manufacturers and importers promptly report to the FDA any correction or removal of a device undertaken to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by a device which may present a risk to health. Device manufacturers and importers are also required to keep records of all corrections and removals they make, including those not required to be reported to the FDA.

Medical device recalls are usually conducted voluntarily by the manufacturer under 21 CFR 7. In rare instances, where the manufacturer or importer fails to voluntarily recall a device that is a risk to health, the FDA may issue a recall order to the manufacturer under 21 CFR 810, Medical Device Recall Authority.

Guidance on the application of this regulation may be found via the Recalls, Corrections and Removals (Device) page on FDA.gov, and in Compliance Program 7382.845 Inspection of Medical Device Manufacturers.

5.12.1.5.4 - Unique Device Identification (UDI)

The FDA established the Unique Device Identification (UDI) system to adequately identify medical devices sold in the United States, from manufacturing through distribution, under regulations promulgated in 21 CFR 801 (Subpart B) and 21 CFR 830. Device labelers (typically, manufacturers) are generally required to: 1) include a UDI, under a system operated by an FDA-accredited issuing agency, on device labels, device packages, and in

some cases, directly on the device; and 2) submit device information to the Global Unique Device Identification Database (GUDID).

Guidance on the application of this regulation may be obtained from The Unique Device Identifier System: Frequently Asked Questions, Vol. 1, and in Compliance Program 7382.850 Inspection of Medical Device Manufacturers.

5.12.1.5.5 - Considerations for Establishment Types

When preparing for, or during the conduct of, an establishment inspection, you may have questions as to the appropriate areas for inspectional coverage based on the types of operations being conducted at the facility. In these instances, refer to IOM Exhibit 5-13 SUBSTANTIALLY EQUIVALENT MEDICAL DEVICES for guidance. The table includes a list of medical device operation types and indicates whether each operation type is subject to compliance with the Quality Management System Regulation (QMSR). Where not all parts of the QMSR are applicable to a particular operation type, the table identifies those regulations that should be considered for coverage.

For example, Initial importers/distributors (except where distribution is retail only) are required to ciomply with certain QMSR requirements based on the scope of their operations, and must document any requirements which are inapplicable and their justification. When firm management states that they do not have primary responsibility for complaint-handling and medical device-reporting activities, you should verify that the firm has a Quality Agreement in effect (signed and dated by both parties) delineating each parties' responsibilities, including record-keeping and record accessibility requirements.

5.12.1.5.6 – Annotations for Form FDA 483

At the close of the inspection, you should meet with the most responsible person and discuss the observations made during the inspection, if any. For all medical device inspections, whenever reportable observations are issued on a Form FDA 483, Inspectional Observations, the firm must be offered the opportunity to annotate those observations. Annotations are succinct comments about the status of the Form FDA 483 item and include the following selections:

- Reported corrected, but not verified
- Corrected and verified
- Promised to correct
- Promised to correct by [insert date]
- Promised to correct within [time interval; the number of days, weeks, or months]
- Under consideration
- Annotation Intentionally Left Blank

The term "verified" means "to confirm; to establish the truth or accuracy." In this case, the investigator is the one who must do the verification. In some situations, corrective actions cannot be verified unless there is further program division or Center review, or until there is another inspection of the establishment. All corrective actions taken by the establishment and verified by FDA should be discussed in detail in the EIR.

When performing the annotation process, you should ensure that…:

- the firm understands and is offered the opportunity to annotate any Form FDA 483 observations during the final discussion with management.
- the firm understands the annotation process is voluntary.
- the firm is aware that it can annotate each observation differently and is not required to annotate all observations (see below for more information).

When the firm does not wish to annotate the Form FDA 483, the option “no annotation” is selected in eNSpect; if issued outside eNSpect, annotation is not performed. The establishment's stated objections to any given observation, or to the Form FDA 483 as a whole, should not be annotated on the Form FDA 483. Instead, the EIR should reflect the establishment's objections to the observation and the fact that it declined to have the observation annotated.

When an establishment has promised corrections and furnishes a date or timeframe, you should enter the appropriate information after the applicable selection (date or time interval) in the annotation. In instances when you and the establishment disagree about the validity of an observation on the Form FDA, and the establishment is not promising actions to correct the observation, the observation may be annotated as "Under consideration" or with no annotation (Annotation Intentionally Left Blank) based on the establishment's request.

Whether the Form FDA 483 is issued hardcopy or electronically (see IOM 5.5.11.4), you should ensure that the individual to whom the form is addressed receives a copy with all annotations.

5.12.1.5.7 - Form FDA 483 Response Instructions

For inspections in which a Form FDA 483 is issued, you should provide instructions to the firm regarding their options for submitting a voluntary written response through use of one of the following handouts:

- FORM-0002147 OMDRHI Div 1 West Inspectional Handout
- FORM-000300 OMDRHI Div2 South Inspectional Handout
- FORM-000302 OMDRHI Div3 NE Inspectional Handout
- FORM- 002839 OMDRHI Div 4 Midwest Inspectional Handout
- FORM-001247 OMDRHI FDA 483 Responses to Foreign Inspections Handout
- FORM-001676 OMDRHI Mandarin Translation FDA 483 Response for Foreign Inspection

5.12.1.5.8- Medical Devices EIRs

For medical device reports, refer to IOM 5.7.1 for requirements relating to the use of either Summary of Findings or Comprehensive report formats. In addition to these requirements, EIRs utilizing either report format will:

- Include section headings as necessary to report information required by the compliance program or assignment memo.
- For products identified on the FDA 483, include a description of the manufacturing process flow and significant monitoring and measurement activities where appropriate to assist review of the observations in light of the firm’s overall manufacturing processes.
- Ensure that you document at a minimum the following for each Quality Management System (QMS) are and Other Applicable FDA Requirements (OAFR) at a level of detail commensurate with the significance of any findings. This may be reported in the Manufacturing/Design Operations section, if that is present in the EIR.
    - 1. The product(s) selected to evaluate if requirements were met
    - 2.What element(s) were reviewed
    - 3. A brief summary of the data sources, documents reviewed, and other information received from the manufacturer during the inspection.
    - 4. Indicate if any written observations were issued or items discussed with the manufacturer as a result of that area’s review.
    - 5. If one or more QMS area or OAFR was not covered, include why it was not applicable to the inspection site. If applicable, describe the scope of design and development activities occurring

at facilities other than the manufacturing site. Provide the FEI, name, and address for each facility.

5.12.1.6 - Banned Devices

Section 516 of the FD&C Act [21 U.S.C. 360f] provides authority for banning by regulation a device for human use (21 CFR 895) if it presents substantial deception or an unreasonable and substantial risk of illness or injury. You should become familiar with this regulation. If during an inspection or investigation you discover that banned devices are being distributed, you should document their distribution, manufacture, etc., as you would any other violative product and refer them for potential regulatory action(s).

5.12.2 - Electronic Product Radiation Controls (EPRC) Inspections

The Radiation Control provisions of the FD&C Act are located in sections 531 through 542 (see IOM 3.2.3). These authorities apply to any manufactured or assembled product--or component, part, or accessory of such product--which when in operation (i) contains or acts as part of an electronic circuit and (ii) emits (or in the absence of effective shielding or other controls would emit) electronic product radiation. Regulations promulgated to implement the requirements in this portion of the act are contained in 21 CFR 1000 through 1050. These sections of the Act and regulation are referred to as the Electronic Product Radiation Control (EPRC) provisions, and the products subject to these requirements as EPRC products.

All EPRC manufacturers must comply with applicable requirements in 21 CFR 1000, 1002, 1003, 1004 and 1005. If a mandatory radiation safety performance standard applies to a manufacturer's product, then the manufacturer must also comply with 21 CFR 1010, and the product must comply with the requirements of the specific standard found in 21 CFR 1020 – 1050.

EPRC products may be either medical (that is, they also meet the definition of a medical device under the Act) or non-medical. Examples of each:

- Medical: diagnostic x-ray or ultrasound imaging devices, microwave or ultrasound diathermy devices, laser coagulators, x-ray or electron accelerators, sunlamps, ultraviolet dental curing devices
- Non-medical: microwave ovens, televisions receivers and monitors (video displays), entertainment lasers, industrial x-ray systems, laser CD players

5.12.2.1 - Inspection Authority for EPRC products

See IOM Section 5.1.4.3.2 for specific information on the authority to inspect facilities subject to ERPC requirements. As EPRC inspections have authorities separate from section 704 of the FD&C Act, should you encounter a refusal to permit the planned inspection, discuss with your supervisor how best to proceed, depending on the type of assignment and the firm's operations.

Records required by the Radiation Control provisions of the Act must be maintained for five years. 21 CFR 1002(b) requires that upon reasonable notice, manufacturers shall permit inspection of any books, records, papers, and documents relevant to determining whether the manufacturer has acted, or is acting, in compliance with federal standards. Firms may retain records in electronic or photocopy form, provided the copies are true and accurate reproductions.

5.12.2.2 - Pre-inspectional Activities for EPRC Inspections

Prior to inspecting a facility manufacturing an EPRC product, it is important for you to determine whether the firm also manufactures medical devices, or if the product of interest also appears to be a medical device (for example, a medical x-ray, fluoroscopy, or medical laser). If the firm manufactures medical devices, or the product of interest is also a medical device, it is recommended that a joint EPRC/Medical Device inspection be planned. If Medical

Device coverage is anticipated during the inspection, see additionally the pre-inspectional activities outlined within IOM 5.12.1. Guidance for preparing for EPRC inspections is provided based on the product type in the Compliance Programs listed in IOM 5.12.2.3.

Certain required submissions by these firms, such as Annual Reports and Accidental Radiation Occurrences, may also be obtained from queries in the Center Tracking System (CTS).

EPRC inspections, whether or not in conjunction with a medical device inspection, should only be conducted by individuals with appropriate training and experience. Those not trained to conduct EPRC inspections may participate as part of a team with an EPRC-trained investigator. Notify your supervisor prior to pre-announcement if, during preparations, you have questions regarding the training required to complete the operation.

Radiation-emitting devices and substances present a unique hazard and risk potential. Every effort should be taken to prevent any undue exposure or contamination. You should use monitoring devices whenever radiation exposure is possible; for these types of inspections, that may mean bringing along and using more than one dosimeter. To be added to the dosimetry program and obtain appropriate monitoring equipment in advance of an inspection, contact the Ross Dosimetry Program.

If the inspection will be covering medical device requirements, pre-announcement may be required, depending on the nature of the assignment (see IOM 5.12.1.4 to clarify which inspections require pre-announcement). Note that if only EPRC coverage is planned, pre-announcement is not required, but is generally recommended. Such pre-announcement may help facilitate the inspection, ensuring you have access to necessary personnel and records, as well as knowledge, beforehand, of any relevant safety protocols for preventing unintended exposure during the operation. Consult your supervisor if you believe pre-announcement is not warranted for an EPRC inspection.

5.12.2.3 - Inspection of EPRC Facilities

Inspections of facilities manufacturing EPRC products may vary depending on the product type and the nature of the assignment. Guidance for coverage of these operations is provided in these CPGM, accordingly:

Laser Products (Medical and Non-Medical) – 7386.001 Inspection and Field Testing of Radiation-Emitting Electronic Products

Sunlamps – 7386.001 Inspection and Field Testing of Radiation-Emitting Electronic Products

Medical X-Ray Products – 7386.003a Inspection of Domestic and Foreign Manufacturers of Diagnostic X-ray Equipment

Non-Medical X-Ray Products - 7386.001 Inspection and Field Testing of Radiation-Emitting Electronic Products

If during the inspection of a medical device manufacturer, you determine that one or more of their devices emits radiation and is subject to EPRC, consult with your supervisor on whether expansion of the inspection, to include coverage of those requirements, is appropriate.

Significant issues developed during coverage of EPRC requirements should be documented on the Form FDA 483, Inspectional Observations. If both EPRC and medical device observations are being issued on a Form FDA 483, Inspectional Observations, they should be grouped separately on the form using text subheadings.

5.12.3 - Technical Assistance

Each program division has engineers and radiological health personnel available for technical assistance and consultation. Do not hesitate to contact them for further assistance. A list of contacts relevant to types of inspections are located in the associated Compliance Programs.

5.12.4 - Sample Collection During Inspection

Due to the relatively high cost of device samples, you should consider, in consultation with your supervisor, the following factors before collecting a physical sample of a device:

1. Whether or not the sampling, as part of a follow-up to a Quality System observation, demonstrates the issue and/or a defective product. Documentary Samples may be more suitable for Quality System Inspection purposes.
2. The likelihood of the analysis showing the device is unfit for its intended use.
3. The possibility for physical or biological hazards to be present in the collected devices (for instance, returned devices from a patient that may be a biohazard).

Collect the firm's test methods and document the standards used by the firm for any analysis that the FDA will attempt to duplicate.

(Refer to CPGM 7382.845, Inspection of Medical Device Manufacturers, and IOM Chapter 4 for guidance regarding device sample collections.)

5.13 - Biologics

5.13.1 - Definition

A "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide) or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings (Public Health Service Act Sec. 351(i)). Additional interpretation of the statutory language is found in 21 CFR 600.3. Biological products also meet the definition of either a drug or device under Sections 201(g) and (h) of the FD&C Act.

Additionally, veterinary biological products are subject to the Virus-Serum-Toxin Act, which is enforced by the USDA (21 U.S.C. 151-158).

5.13.2 - Biologics Inspections

The periodic CGMP inspections of licensed biological drug products, that include plasma fractionated products, allergenic products, vaccines, and gene and cell therapy products are led by investigators from ORA's Office of Biological Products Operations, Biological Products Inspection Staff (OBPO/BPIS). OBPO Investigation Branch investigators lead inspections of blood and blood components, human cells, tissues, and cellular and tissue-based products (HCT/Ps), source plasma, licensed in-vitro diagnostic devices for donor screening, 510k/PMA, CBER-regulated medical devices (for example, blood establishment software, and NDA/ANDA drug products regulated by CBER.) See IOM 3.2 for a discussion of statutory authority. Generally, CBER maintains the lead for pre-licensing and most pre-approval inspections of biological products, while OII customarily leads PMA/510(k) and NDA/ANDA inspections.

5.13.2.1 - Authority

Biological products are regulated under the authority of Section 351 of the Public Health Service Act and under the FD&C Act, as drugs or devices, with the exception of certain human cells, tissues, and cellular and tissue-based products (HCT/Ps) regulated solely under Section 361 of the Public Health Service Act (see 21 CFR 1271.10). Blood and blood products for transfusion are prescription drugs under the FD&C Act. Under the Act, source plasma and recovered plasma may have the legal identity of either a drug or device depending on their intended use. Section 351(a) of the PHS Act provides for licensure of biological products and inspection of the products covered in 351(d). Most biological drugs are licensed. The investigational new drug application regulations (21 CFR 312) also

apply to biological products subject to the licensing provisions of the PHS Act. However, blood grouping serum, reagent red blood cells, and anti-human globulin in-vitro diagnostic products may be exempted (21 CFR 312.2(b)).

5.13.2.1.1 - Blood and Source Plasma Inspections

For blood bank and source plasma establishment inspections (CP 7342.001 and 7342.002) (CBER compliance programs), use the CGMPs for Blood and Blood Components (21 CFR 606), as well as the general requirements for biological products (21 CFR Part 600), the general biological product standards (21 CFR Part 610), and the additional standards for human blood and blood products (21 CFR Part 640.) This would generally be Parts 606 and 640 of the regulations in the case of blood bank and source plasma establishments. The drug GMPs (21 CFR 210/211) also apply to biological drugs. In the event it is impossible to comply with both sets of regulations, the regulation specifically applicable to the product applies.

4.13.2.1.2 - Human Tissue Inspections

21 CFR Part 1271 contains six subparts and associated topics:

1. Subpart A of part 1271 – general provisions
2. Subpart B of part 1271 – registration
3. Subpart C of part 1271 - screening and testing of donors to determine eligibility
4. Subpart D of part 1271 - provisions on CGTP
5. Subpart E of part 1271 - certain labeling and reporting requirements
6. Subpart F of part 1271 - inspection and enforcement provisions

The subparts apply as follows:

Subparts A through D apply to all HCT/Ps, described in Sec. 1271.10 and regulated solely under section 361 of the PHS Act, and to those regulated as drugs, devices, and/or biological products. Subparts E and F, which pertain to labeling, reporting, inspection, and enforcement, apply only to those HCT/Ps described in Sec. 1271.10 and regulated solely under section 361 of the PHS Act. However, subpart D, with the exception of two provisions (Sec. 1271.150(c) and 1271.155), and subpart E are not being implemented for reproductive HCT/Ps described in 21 CFR 1271.10 and regulated solely under section 361 of the PHS Act.

HCT/Ps subject to the provisions of 21 CFR Part 1271 include, but are not limited to, bone, ligaments, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue.

For HCT/P inspections, use the CP 7341.002, "Inspections of Human Cells, Tissues, and Cellular and Tissue-Based Products."

If the HCT/P does not meet the criteria set out in 21 CFR 1271.10(a), and the establishment that manufactures the HCT/P does not qualify for any exceptions in 21 CFR 1271.15, the HCT/P will be regulated as a drug, device, and/or biological product under the FD&C Act, and/or section 351 of the PHS Act and applicable regulations, including 21 CFR 1271. A premarket review, biologics license application (BLA) or an NDA/ANDA will be required.

5.13.2.2 - Donor Confidentiality

Blood bank, source plasma, and human tissue establishments are typically sensitive about maintaining confidentiality of donor names, though the mere reluctance to provide records is not considered a refusal. The FDA, however, has the authority, under both the PHS and the FD&C Acts, to make inspections, with 21 CFR Part 600.22(g) and 1271.400(d) providing for copying records during an establishment inspection. For prescription

drugs, section 704 of the FD&C Act [21 U.S.C 374] specifically identifies records, files, papers, processes, controls, and facilities as being subject to inspection.

If you encounter problems accessing records, explain FDA's authority to copy these records. IOM 5.5.2 should be followed if a refusal is encountered. When donor names or other identifiers are necessary, they may be copied, but the information must be protected from inappropriate release. (See IOM 5.6.10.4.)

5.13.2.3 - Inspectional Objectives

The inspectional objective for biological products is to assure the products are safe, effective, and contain the quality and purity they purport to possess and are properly labeled (see IOM 5.13.1). The inspectional objective for HCT/Ps regulated solely under 361 of the PHS Act is to assure that HCT/Ps are recovered, processed, stored, labeled, packaged, and distributed, and the donors are screened and tested, in a way that prevents the introduction, transmission, or spread of communicable diseases.

Facilities will be inspected for their conformance with the following:

1. Provisions of the PHS Act and/or FD&C Act
2. Applicable regulations in:
    - 21 CFR 210 and 211
    - 21 CFR Parts 600-680, and
    - 21 CFR Part 820
3. HCT/P regulations in 21 CFR Part 1271.
4. FDA policies, which include guidance to the industry, and the Compliance Policy Guides Chapter 2.

5.13.2.4 - Preparation

As part of your preparation, review the program division files and OSAR of the facility to be inspected, and familiarize yourself with its operation and compliance history. You should also review:

1. Appropriate Compliance Programs and related Compliance Policy Guides (CPG), Chapter 2.
   NOTE: Federal Cooperative Agreements Manual; MOU with the Department of Defense, and MOU with the Centers for Medicare and Medicaid Services (CMS) on transfusion services
2. Correspondence from the firm depicting any changes since the last inspection
3. Firm's registration and product listing information
4. Biological Product Deviation Reports, Adverse Reaction Reports, complaints, recalls, and ECMS, as applicable
5. Consumer Complaints

5.13.2.5 - Inspectional Approach

Consult the Compliance Program (CP) for inspectional instructions and applicable regulations. Give special attention to biological products deviation reports indicative of problematic areas or processes, adverse reactions, transfusion- or donation-associated fatalities, and hepatitis and HIV “lookback” procedures. The follow-up investigations to such reports should also be covered.

- For blood banks and source plasma establishments, refer to CP 7342.001 and 7342.002.
- For HCT/P establishments, refer to CP 7341.002.
- For Biological Drug Products, refer to CP 7345.848.
- For Licensed In-vitro Diagnostic Devices Regulated by CBER, refer to CP 7342.008.
- For 510k/PMA devices regulated by CBER, refer to CP 7382.845 (PACs 42845A, 42845B, 42845C)
- For NDA/ANDA drug products regulated by CBER, refer to CP 7356.002A (PACs

At each inspection, you should provide the current FDA contact information found in the OBPO Domestic or Foreign Inspection Handouts, which includes the post-inspectional correspondence e-mail oiiobibiologicsinspectionpoc@fda.hhs.gov .

QMiS links to the OBI Domestic and Foreign Inspection Handouts:

- OBI and CVM Inspection Handout (FORM-002810)
- OBI and CBER Inspection Handout (FORM-002811)

5.13.2.5.1 - Access of Electronic Databases and Queries

Providing oversight of firm personnel while they access their system for data/records you are requesting is not always practical. For this reason, if *all* the following criteria are met, OBI investigators are permitted, when necessary, to access a firm's records using a read-only account, dummy terminal, or comparable mechanism:

- Responsible management at the firm is agreeable to allowing read-only access to electronic systems and/or databases;
- Access to electronic systems/databases is read- only and will not permit you to change or alter data or programming in any manner;
- The firm has a representative that will be available to initially describe and review the layout of their records, and make themselves available throughout the inspection as additional information or copies of records are needed; AND
- You document this read-only access in your regulatory notes, EIR, or investigational memorandum, accordingly.

5.13.2.6 - Regulations, Guidelines, Recommendations

Guidance documents for industry are made available to the public in accordance with good guidance practice regulations found at 21 CFR 10.115. The contents of most of these documents are incorporated into the establishment's SOPs and/or license applications or supplements.

Deviations from guidance documents must not be referenced on an FDA 483. However, since these documents are often related to specific GMP requirements, in most cases, deviations can be referenced back to the corresponding GMP. If a deviation is observed during an inspection and the investigator relates it to the regulations or law, then the item may be reported on the FDA 483. In addition, during the discussion with management, the relationship of the deviation to the regulation or law, should be clearly explained.

If an establishment indicates it is not aware of any of these documents, provide them the guidance document(s) or direct them where to find these documents on www.fda.gov. Provide the firm with this email address to obtain additional information from CBER at industry.biologics@fda.hhs.gov.

If a firm claims approval for an alternative procedure, verify this by reviewing the firm's written approval letter. Approved alternative procedures may also be verified by contacting CBER/Division of Blood Applications, or the appropriate CBER product office.

5.13.2.7 - Technical Assistance

National Experts and Program Experts in OII are available to assist you, by telephone and/or on-site consultation, with regards to challenges and problem areas you may encounter.

5.13.2.8 - Biologics Establishment Inspection Reports

(See IOM 2.1.4.1) You should write your EIR following the guidance found in IOM 5.7.1.2, 5.7.1.3, 5.7.1.4, and 5.7.1.5. Section headings can be added to address the needs of a specific Compliance Program referenced in conducting the inspection. Where applicable, and per the CP, the report should state the levels of the inspection and systems that were covered. The reasoning for the level and systems covered should also be reported, as

directed in the CPs. The report should also include a summary, the FDA 482, the FDA 483 (if issued), and the required eNSpect record in OSAR.

The scope of the reporting should reflect requirements and regulations for each area, the firm's state of compliance, previous inspectional report(s) and information, complexity of operations, and other aspects that may affect the reporting that will be necessary.

For directed inspections with a narrow focus, include information to appropriately cover the assignment. Follow specific assignment instructions included in any associated assignment memorandum or included in the eNSpect assignment details (Program Directives and Background).

5.13.3 - Registration, Listing and Licensing

5.13.3.1 - Registration and Listing

See IOM 3.10.6.1 for registration and listing requirements for Human Blood and Blood Products and for Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/PS).

Facilities manufacturing biological drug products regulated by CBER must register as a human drug facility, see IOM 3.10.2.1.

Facilities manufacturing medical devices regulated by CBER must register as a device establishment, see IOM 3.10.4.1.

5.13.3.1.1 – Transfusion Services

Transfusion services may be exempt from registration under 21 CFR 607, except for firms that conduct operations as described in section Part II, C. 7. of the CP. This includes facilities that are certified under the Clinical Laboratory Improvement Amendments of 1988 [42 U.S.C. 263a] and 42 CFR Part 493 to perform the FDA-required tests on blood or has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services and are engaged in the compatibility testing and transfusion of blood and blood components, but which neither routinely collect nor process blood and blood components.

Note that all VA Blood Banks and Hospital Transfusion Services must register with FDA since they are not inspected by CMS.

5.13.3.1.2 - HCT/Ps

Establishments manufacturing HCT/Ps (human cells, tissues, or cellular or tissue-based products) as defined in 21 CFR 1271.3(d) must register and list using form FDA 3356. Examples of HCT/Ps include, but are not limited to, bone, ligament, skin, cornea, hematopoietic stem cells derived from peripheral and cord blood, manipulated autologous chondrocytes, and semen or other reproductive tissue.

Establishments that only manufacture investigational HCT/Ps under an IND or IDE are not required to register and list until the HCT/P has been licensed, approved, or cleared by the FDA. Establishments manufacturing HCT/Ps regulated as drugs and/or biological products must register and list with the FDA pursuant to 21 CFR 207. Establishments manufacturing HCT/Ps regulated as medical devices must register and list with the FDA pursuant to 21 CFR 807.

5.13.3.1.3 - Military Blood Banks

Inspection of military blood banks is an OII responsibility. These facilities are required to meet the same standards as other blood banks, although military emergencies may require deviations from the standards. A separate license is held by each branch of the service; and while each individual establishment may be licensed or unlicensed, all are required to register. Program divisions should notify the appropriate military liaison(s) 30 days before inspection of a military facility.

For additional information on inspection of government establishments, see Compliance Program Guidance Manual 7342.001, the Federal Cooperative Agreements Manual, and the MOU with Department of Defense Regarding Licensure of Military Blood Banks.

Special notes: Foreign notification of Military Blood Banks is done by the Trip Planner in preparation of the international trip. Field Management Directive 92, Agency Establishment Registration and Control Procedures, details the registration process within the agency. It's best practice to ensure that the firm's current registration forms reflect actual operations.

5.13.3.2 - MOUs

Under the 1983 Memorandum of Understanding (MOU) between the FDA and the Centers for Medicare and Medicaid Services (CMS, formerly Health Care Financing Administration - HCFA), CMS agreed to survey those facilities that engage in minimal manufacturing to minimize duplication of effort and reduce the burden on the affected facilities while continuing to protect transfusion recipients. However, no transfer of statutory functions or authority is made under the MOU and the FDA retains legal authority to inspect these unregistered transfusion services whenever warranted. When appropriate, program divisions should conduct inspections jointly with the CMS regional liaison. If you determine during a routine inspection an establishment is a CMS obligation under the MOU, you should terminate the inspection and report the status to the OBI OEI Coordinator. (See Federal Cooperative Agreements Manual – FDA/HCFA MOU.)

5.13.3.3 - Biologics License

See IOM 3.10.6.2. A biologics license application (BLA) shall be approved only after inspection of the establishment(s) listed in the application and upon a determination that the establishment complies with the standards established in the BLA and the requirements prescribed in applicable regulations (21 CFR 601.20(d)). CBER maintains the lead for pre-license (PLI) and pre-approval (PAI) inspections of biological products. These inspections are part of the review of a BLA or BLA supplement. CBER identifies the scope of the inspection and invites OII to participate in, or, in some instances, may request OII lead the PLI or PAI.

Copies of CBER's PLI and PAI inspection reports are forwarded to the Program Divisions and are stored in the firm's eCMS file. You can also find these inspection reports in eNSpect and OSAR.

5.13.3.4 - Approval of Biological Devices

There must be a pre-approval inspection (PAI) of the establishment for compliance with the QS/GMP regulation and the firm's PMA. For licensed devices, CBER conducts the pre-license inspection (PLI). Devices used in the collection and testing of blood for transfusion are approved/cleared through the PMA/510(k) authorities. OII OBI Investigators customarily inspect the CBER-regulated devices, which are subject to PMA/510(k) applications.

5.13.4 - Other Inspectional Considerations

5.13.4.1 - Testing Laboratories

Blood bank, source plasma, and HCT/P establishments may use outside testing laboratories to perform required testing.

Laboratories conducting testing for licensed blood banks are usually licensed. CBER may approve the use of a non-licensed laboratory to do required testing, provided the lab is capable of performing the tests and the lab registers with CBER prior to CBER approving the licensing arrangement.

Laboratories performing required testing for source plasma manufacturers must either be:

- licensed, or

- certified to perform such testing on human specimens under the Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 263a) and 42 CFR part 493 or have met equivalent requirements as determined by CMS.

Instructions for inspecting testing laboratories are included in the appropriate CP. You should coordinate the inspection of non-registered laboratories with CMS regional office contacts. If a testing laboratory is located outside of the program division, request an inspection by the appropriate program division office, where appropriate.

(See updated information on: Donor Screening Assays for Infectious Agents and HIV Diagnostic Assays; and HCT/P donors for Relevant Communicable Disease Agents at FDA.gov.)

5.13.4.2 - Brokers

Blood establishments may use brokers to locate buyers for products such as recovered plasma or expired red blood cells. These articles are used for further manufacturing into products, such as clinical chemistry controls and in-vitro diagnostic products not subject to licensure. Fractionators also use brokers to locate suppliers of plasma under the short supply provisions (21 CFR 601.22). During your inspections, you should determine if the facility is selling products to any brokers. If brokers are used, determine if the brokered products are shipped to a facility operated by the broker, or directly to the consignee.

Brokers who take physical possession of blood products and engage in activities considered manufacturing or labeling are required to register and are included in the OEI for routine inspection under the blood bank compliance program. Brokers who only arrange sales of, or store, blood and blood components, but do not engage in manufacturing activities, are not required to register.

5.14 - Bioresearch Monitoring (BIMO)

Inspectional activities in the bioresearch monitoring program involve all product areas and centers. BIMO inspections are conducted to determine the reliability of data submitted in support of premarket and pre-license applications, as well as to ensure the rights and safety of research subjects are protected. Types of establishments inspected include Sponsors, Monitors, Contract Research Organizations, Clinical Investigators, Sponsor-Investigators, Institutional Review Boards, Radioactive Drug Research Committees, In Vivo Bioavailability/Bioequivalence Clinical and Analytical Sites, and Nonclinical Laboratories. Office of Bioresearch Monitoring Inspectorate (OBMI) inspections also include Postmarketing Adverse Drug Experience (PADE) reporting and Risk Evaluation and Mitigation Strategies (REMS) reporting, both of which are post approval activities.

5.14.1 - BIMO Establishment Type Definitions

Clinical Investigator – A person who conducts a research study (that is, recruits study subjects, administers the investigational product to humans or animal subjects or uses a device on subjects, prepares and maintains case history reports, etc.).

Contract Research Organization (CRO)- A person/entity that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, for example, the design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the FDA. When operating under a written agreement for transfer of regulatory obligations, the CROs are subject to the same regulatory actions as sponsors for any failure to perform any of the obligations assumed. The medical device regulations do not define responsibilities for CROs; therefore, device sponsors are held responsible for any regulatory noncompliance by a CRO.

Monitor – An entity employed or contracted by sponsors or CROs to oversee the progress of an investigation. A monitor is not a regulated entity unless the regulatory obligations have been transferred from the sponsor in writing.

In such case, the monitor is regulated as a CRO. However, device sponsors are held responsible for any regulatory noncompliance by a CRO.

Institutional Review Board (IRB) – Also known as "Institutional Review Committee for Human Studies" and "Independent Ethics Committee" internationally. An IRB reviews protocols for studies and evaluates informed consent documents and risk/benefit decisions made regarding study procedures. An IRB may or may not be affiliated with an institution such as a hospital.

In Vivo Bioavailabilty/Bioequivalence Clinical Site – A facility or individual involved in the screening and/or dosing of human subjects for obtaining biological specimens (for example, blood, saliva, urine, feces) for analysis of investigational product content to define absorption, distribution, metabolism, and/or elimination characteristics of the investigational product, or to establish its equivalency with a defined standard.

In Vivo Bioavailability/Bioequivalence Analytical Site – A laboratory involved in the analytical testing of human biological specimens for levels of investigational product content, or the in vitro testing of investigational products to establish equivalency with a defined standard. These facilities may be integrated with, or separate from, clinical sites obtaining human specimens.

Nonclinical Laboratory – A laboratory that conducts in vivo or in vitro experiments in which investigational products are studied prospectively in test systems under laboratory conditions to determine their safety in accordance with the good laboratory practice (GLP) regulations. Nonclinical studies do not include studies utilizing human subjects or clinical studies or field trials in animals. Nonclinical studies also do not include basic exploratory studies carried out to determine whether an investigational product has any potential utility, or to determine physical or chemical characteristics of an investigational product.

Sponsor – A person or establishment that initiates, supports, and usually monitors an investigational study on FDA-regulated products, but who does not actually conduct the study.

Sponsor-Investigator – An individual who both initiates and conducts an investigational study. This person has the responsibilities of both a sponsor and a clinical investigator.

Postmarketing Adverse Drug Experience (PADE) – PADE inspections are conducted at pharmaceutical establishments, which may be the manufacturing site, but most often are at a corporate headquarters facility. The inspection is conducted where the complaint-handling unit/department responsible for evaluating and reporting adverse drug events is located. The purpose of the inspection is to ascertain whether the firm is complying with the evaluation and reporting requirements.

Risk Evaluation and Mitigation Strategies (REMS) - A (REMS) is a required risk management plan that uses tools, as specified in the FDA Amendments Act of 2007 (FDAAA), beyond routine professional labeling (the package insert) necessary to ensure that the benefits of a drug outweigh its risks. The purpose of a REMS inspection is to verify the REMS is implemented and functioning in accordance with the FDA-approved REMS and to verify information in the REMS assessment report.

Radioactive Drug Research Committee (RDRC) –An Institutional Review Board subcommittee or branch, which is FDA approved, who reviews and approves certain research uses of radioactive drugs that are generally recognized as safe and effective (GRASE).

5.14.2 - BIMO Assignments

Workplan assignments are issued by the product centers to OII. These assignments are primarily issued to conduct inspections of entities engaged in clinical or nonclinical research, who were involved in studies submitted as part of an application for approval of a new product. Typically, inspections are conducted after a clinical or nonclinical or clinical

study has been completed. Inspections may also be conducted of ongoing research. Assignments may also be issued for-cause, for allegations of potential noncompliance and to conduct investigations and sample collections.

Each assignment will identify the establishment type to be inspected. In BIMO the compliance programs are based upon the establishment type, so they will provide instruction on what should be covered during the inspection. The areas of coverage relate to the specific regulatory requirements of each establishment type.

Centers prepare assignment memos using a template that was harmonized across all centers for the BIMO program. This assignment memo identifies the following: type of establishment to be inspected, the relevant Compliance Program, the Program Assignment Code, background information, general instructions, and any special instructions for inspectional coverage. Assignments are issued to the BIMO inspection POC team, reviewed, and then assigned to the appropriate division. Assignments are received by the division director and then disseminated to the appropriate branch for assignment to an investigator.

Occasionally, center personnel will participate in inspections with field investigators, serving as subject matter expert on products and/or processes that are the focus of nonclinical or clinical research. In these cases, the BIMO investigator will serve as the lead investigator. (See IOM 5.2.9 – Team Inspections.)

BIMO assignments typically include an assignment memo and specific background materials accessible through a link to the Enterprise Content Management Server/System (ECMS). The background materials may include the protocol for the assigned study and selected data line listings from the application, such as reported adverse events and measurements obtained during the study. When particular areas require focused attention or specific data points need verified during the inspection, the assignment memo will specify these priority areas.

Centers have final classification authority for inspections in the BIMO program. When inspections are completed and the EIR has been reviewed by your supervisor, an initial inspection classification will be assigned through eNSpect. The centers will then determine and document the final classification for the inspection after they complete their review of the EIR and all evidence collected.

5.14.2.1 - Read-Only Access to Electronic Databases During Bioresearch Monitoring Inspections

Clinical and non-clinical trials are increasingly moving toward 100 percent electronic data capture--including electronic case report forms, medical records, patient-reported outcomes, informed consent systems and other electronic study records. It is necessary for bioresearch monitoring investigators to have access to these electronic systems and databases to perform inspections effectively and successfully. Overseeing the firm’s personnel while they access their electronic systems is not always practical in BIMO inspections.

- Access to electronic systems/databases is to be read-only and not permit you to change or alter data or programming in any manner.
- The firm should have a representative that will be available to initially describe and review the layout of their records. They should be available throughout the inspection as additional information or copies of records are needed.
- Document that you had read-only access in your establishment inspection report or investigational memorandum accordingly.

While you may complete a form needed by the firm to obtain read-only access, such as an account request form, you *will not* sign such form as per IOM section 5.5.6. You may acknowledge by email that you have completed any required training necessary for access. When signing in to access a system, you may check a box and/or enter your name to acknowledge or accept the user agreement.

If you foresee that you will need to access the electronic database remotely (e.g., from the office or hotel room) during the inspection, discuss this with firm management. Review of documents away from the firm should not be counted as an inspection day, for example, if a firm is closed and you are reviewing documents in the office.

If it is necessary to print or download a document you are reviewing remotely, you must ask the firm to print or download it for you, just as you would for any other exhibit.
During the close-out meeting, remind the firm's management that your read-only access is to be terminated once the inspection is closed; document this request in your establishment inspection report. You shall not attempt to access a firm's database once the inspection is closed.

5.14.2.2 - Regulatory Notes For BIMO Operations

As per section 2.1.4.3, regulatory notes may be either handwritten in a bound notebook or in electronic format. eNSpect will be used for all electronic regulatory notes in the BIMO program.

5.14.3 – BIMO Compliance Programs

BIMO Compliance Programs are posted on the internet. Compliance Programs in BIMO are designed to focus on the establishment type, as clinical and nonclinical research crosses all product areas.

- 7348.003 In Vivo Bioavailability-Bioequivalence Studies– Clinical
- 7348.004 In Vivo Bioavailability-Bioequivalence Studies– Analytical
- 7348.007 Inspection of Nonclinical Laboratories Conducting Animal Rule-Specific Studies
- 7348.808 Good Laboratory Practice (Nonclinical Laboratories)
- 7348.808A Good Laboratory Practice Program (Nonclinical Laboratories) EPA Data Audit Inspections
- 7348.809 Institutional Review Board
- 7348.809A Radioactive Drug Research Committee
- 7348.810 Sponsors and Contract Research Organizations
- 7348.811 Clinical Investigators and Sponsor- Investigators
- 7353.001 Postmarketing Adverse Drug Experience (PADE) Reporting Inspections
- 7353.001C Risk Evaluation and Mitigation Strategies (REMS) Reporting Inspections

5.14.4 - Postmarketing Adverse Drug Experience (PADE) Reporting Inspections

Section 760 of the FD&C Act [21 U.S.C. 379aa] and 21 CFR sections 310.305, 314.80, 314.98, 314.540, and 329.100 require reporting of adverse events associated with the use of human drug products, and section 21 CFR 600.80 requires reporting of adverse events associated with the use of biological products (including therapeutic biological products). Responsible firms include holders of applications (NDAs, ANDAs, or BLAs) and manufacturers, packers and distributors that are named on the labels of all FDA approved drug products, all prescription drug products, and OTC monograph drug products. Both foreign and domestic firms are required to develop written procedures and to maintain records related to adverse events. Firms must evaluate adverse event data to determine if the event has had a serious outcome--such as death, disability, hospitalization, or was life-threatening--and if the event was expected (labeled) or unexpected (unlabeled) for the product. Responsible firms must also submit adverse event information to the FDA in expedited or periodic reports in an electronic format as described in the regulations. This information should be complete and accurate based on the data received.

(Refer to (CP) 7353.001 and the assignment for the description of the program and for detailed instructions for conducting inspections.)

5.14.5 - Risk Evaluation and Mitigation Strategies (REMS) Reporting Inspections

Section 505-1 of the FD&C Act [21 U.S.C. 355-1] gives the FDA the authority to require Risk Evaluation and Mitigation Strategies (REMS) for certain drugs to ensure that the benefits outweigh the risks. REMS are required risk management plans that use risk minimization strategies, beyond the professional labeling, to ensure benefits of certain prescription drugs outweigh their risks. An applicant may be required to establish a REMS as part of the approval process (or when new safety data for an approved product arises), and an inspection will focus on the applicant's adherence to the REMS. Each REMS is unique, can be used for a single drug or class of drugs, and may include one or more of the following: a medication guide, communication plan, elements to assure safe use (ETASU), and implementation plan. REMS must also include a timetable for submission of assessments.

REMS are subject to inspection and are enforceable under section 505(o) of the FD&C Act [21 U.S.C. 355(o)] as amended by the FDAAA.

REMS inspections are conducted to verify that the REMS is implemented and functioning according to the FDA-approved REMS document and to verify the information provided to the agency in the REMS assessment report. Since every REMS program varies, the detailed instructions for conducting inspections will be given to the investigator prior to each inspection. (Refer to (CP) 7353.001C and the assignment for the description of the program and for detailed instructions for conducting inspections.)

5.14.6 - BIMO Establishment Inspection Reports (EIRs)

Regardless of the format used for BIMO EIRs, it is important that they be concise. Reports should avoid redundancy and not include unnecessary detail when no problem is observed.
All BIMO reports should include the following:

- BIMO program-specific information (that is, the data requested in post-inspection email summaries provided to center points of contact, with additional details that may add value to the review process):
  - Protocol – including name, number, and sponsor
  - Number of Subjects Screened/Consented/Enrolled/Randomized/Completed (use most appropriate descriptions)
  - Records Reviewed (including Subjects) and Recordkeeping Practices
  - Adverse Events
  - Primary Endpoints
  - Discussion Items (including minor protocol deviations and/or recordkeeping issues)

In general, refer to IOM 5.7.1 for reporting requirements following BIMO inspections, with a few exceptions as follows:

Summary of Findings Format

- The Summary of Findings format may be used for BIMO EIRs when it is not the initial inspection of the establishment, and the inspection will have a recommended classification of NAI or VAI.
- Summary of Findings BIMO EIRs will include section headings as needed to include information required by compliance program or assignment memo.

Comprehensive Report Format

BIMO inspections not meeting the above criteria will utilize the Comprehensive Report format but must also include content required by compliance programs and specific assignment instructions. This content should be included by adding the headings that are listed in the compliance program, for example, Authority and Administration, Protocol, Institutional Review Board, Subjects' Records, etc. would be added for a clinical investigator inspection report.

Even when using the comprehensive report format, there are a few section headings that may be deleted as they are not generally applicable to BIMO inspections. If you are creating your report in eNSpect and the system does not

allow you to delete the heading, simply insert “N/A” within that section of the report. Headings that may be deleted for OBMI EIRs include:

- Manufacturing/Design Operations
- Manufacturing Codes (*although may be applicable for Bioequivalence)
- Recall Procedures

All other headings should be included. If they do not apply to your inspection (for instance, Sample Collection and Refusals), simply insert “N/A” into that section, but do not delete it.

5.14.7 – BIMO Complaints

Complaints related to the BIMO program may be received from various sources such as sponsors, Institutional Review Boards, study subjects, and other firms. BIMO complaints are evaluated by the Center responsible for review of the product that is the subject of the complaint. The Center may issue a for-cause inspection assignment to follow-up on a complaint. CSOs may also be assigned to interview complainants or confidential sources, and to report coverage/follow-up of any complaints, including any associated complaint number(s) in the EIR or a memorandum. If you receive a complaint involving an FDA-regulated product directly, contact your supervisor so that the complaint can be routed to the appropriate Center/Office. (See also IOM 5.5.4 (Consumer Complaints) and IOM 5.4.1 (Interviewing Confidential Sources and Informants).)

5.15 - Tobacco Products

5.15.1 - Definitions

The term "tobacco product" is defined in Section 201(rr) of the FD&C Act [21 U.S.C 321] and means any product made or derived from tobacco, or containing nicotine from any source, that is intended for human consumption, including any component part, or accessory of a tobacco product (except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product.) The term "tobacco product" does not mean an article that is a drug under section 201(g)(1) of the FD&C Act, a device under section 201(h) of the FD&C Act, or a combination product described in section 503(g) of the FD&C Act. The term ‘‘tobacco product’’ does not mean an article that is a food under section 201(f) of the FD&C Act, if such article contains no nicotine, or no more than trace amounts of naturally occurring nicotine.

The definition of certain tobacco products can be found in the FD&C Act under section 900.

5.15.2 - Tobacco Inspections

(See IOM 3.2 for discussion of statutory authority.)

Inspections involving tobacco product(s) at manufacturing facilities are led by OII’s Tobacco Operations Staff (TOS) within the Medical Products Inspectorate (MPI) and Tobacco Operations and are conducted pursuant to assignments issued by CTP. These assignments are issued to conduct inspections of entities engaged in the manufacture, preparation, compounding, or processing of tobacco products. Inspections may also be conducted to support the pre-market and post-market review process. Assignments may also be issued to conduct investigations and sample collections. CTP Subject Matter Experts may accompany OII’s Tobacco Operations Staff during such inspections. Additional guidance on deemed tobacco products can be found on CTP's Deeming webpage.
https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/fdas-deeming-regulations-e-cigarettes-cigars-and-all-other-tobacco-products

5.15.3 - Retail Compliance Check Inspection Contracts

The FDA issues contracts to assist with compliance check inspections of tobacco retail establishments to help determine a retailer's compliance with federal laws and regulations, including the FD&C Act, as amended by the

Tobacco Control Act, and associated regulations. The FDA has a goal of establishing a contract, where feasible, with every U.S. state and territory, to support such compliance, but some states and territories, for a variety of reasons, have been unable to do so. Therefore, the agency has awarded contracts to third-party entities that are able to hire commissionable inspectors to conduct compliance check inspections of tobacco retailers in those states and territories where the FDA has been unable to contract with a government agency. The FDA has further expanded this program by awarding retail inspection contracts to American Indian and Alaska Native tribes to conduct retail inspections within their jurisdictions. In addition, the FDA may, at any time, also conduct inspections using its own personnel.

5.15.4 - Guidance, Compliance & Regulatory Information

The https://www.fda.gov/about-fda/fda-organization/center-tobacco-products CTP website contains resources for legal, regulatory, and policy issues related to tobacco products and information for small business assistance (SmallBiz.Tobacco@fda.hhs.gov)

5.16 – Combination Products

5.16.1 – Combination Product Inspections

Combination products are defined in 21 CFR 3.2(e). The term combination product includes:

- A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;
- A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or
- Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

These articles retain their regulatory identity when they become constituent parts of a combination product., Accordingly, the authority for inspections of combination products arises from the authorities for drug, device, and biological product inspections as described in IOM 5.10, 5.12, and 5.13, respectively.

All combination products are subject to at least two sets of CGMP requirements. In 21 CFR part 4, subpart A, section 4.3 identifies a streamlined approach to demonstrate compliance with the drug CGMPs (21 CFR part 210 & 211) and the device Quality Management System Regulation (QMSR) (21 CFR part 820) for single-entity and co-packaged combination products that contain a drug or biological product constituent part and a device constituent part. This allows a combination product manufacturing facility to comply either with the drug CGMPs and specific called-out provisions from the device QMSR (drug CGMP-based streamlined approach, see 21 CFR 4.4(b)(1)) or with the device QMSR and specific provisions from the drug CGMPs (device QMSRbased streamlined approach, see 21 CFR 4.4(b)(2)).

Regardless of whether a streamlined approach is used, in addition, for a combination product that includes a biological product, the manufacturer must demonstrate compliance with all applicable CGMP requirements for biological products (including standards) that are found within 21 CFR Parts 600 through 680 (21 CFR 4.3(c)). For a combination product that includes any HCT/P, the manufacturer must demonstrate compliance with all applicable regulations in 21 CFR Part 1271.

5.16.1.1 – Preparation

Identify the combination products manufactured at the facility and, if not already known, identify the lead center. The lead center is the medical product center (e.g., CBER, CDER, or CDRH) that has primary jurisdiction for a specific combination product's review and regulation. Questions on which center is lead for a combination product should be directed to combination@fda.hhs.gov. Typically, the application type for the combination product is aligned with the lead center (for example, generally, PMA and 510(k) products are CDRH-led, and NDA/ANDA products are CDER-led). The lead center serves as the primary point of contact before, during, and after the inspection. For a CDER-led combination product inspection, review IOM 5.10. For a CDRH-led combination product inspection, review IOM 5.12. For CBER-led combination product inspection, review IOM 5.13.

Obtain the following information before the inspection whenever possible:

- The CGMP operating system in use at the facility. Although most combination product manufacturers choose to follow a streamlined approach that aligns with the lead center/ application type (e.g., a facility manufacturing a combination product approved under a PMA follows a device QS regulation-based streamlined approach), they may choose to follow either of the streamlined approaches or full compliance with both sets of regulations.
- Information about the facilities involved in the manufacturing (including design activities) for the combination product and the scope of CGMP responsibilities of the facility to be inspected.
- For pre-announced inspections, confirm that documentation to enable review of compliance with called out provisions will be available or accessible at the site being inspected.
    - Pre-announcement will typically apply to pre-approval inspections for ANDA/NDA/PMA combination products, consistent with the OII inspectional process for the lead center.
    - Pre-licensing inspections for CDER-led BLAs are also typically preannounced.
    - Pre-announcement will apply to surveillance inspections, as appropriate, consistent with the process for the base (Lead Center) compliance program.
    - For non-application combination products concerns, if needed, request a consult for respective lead center via your supervisor.

5.16.1.2 – Inspectional Approach

For combination product CGMP inspections for CDER-led or CDRH-led single-entity or co-packaged combination products, follow Compliance Program 7356.000 and associated commodity-specific compliance programs for pre-approval, post-approval, surveillance, for cause, and other risk-based inspections. For surveillance inspections where combination product coverage is conducted, prioritize combination products recently approved, cleared, or significantly changed (in terms of design) or those that include complex technology or manufacturing considerations. This applies unless there are indicators that there are safety and effectiveness concerns with other products. For CBER-led combination product inspections, contact OBI supervisory staff and CBER for assistance.

5.16.1.3 – Registration and Listing

Combination products are generally registered and listed with the lead Center only. However, they may also be registered with a secondary Center. In both instances, the listing should reflect that the product is a combination product. If potential problems related to registration and listing are identified, contact the lead center for assistance.

5.16.1.4 – Combination Product Establishment Inspection Report

A single EIR and, when applicable, FDA-483 should be used to document all observations made during an inspection at a combination product manufacturer.

OII investigators conducting a combination product inspection should mark the Combination Products as “Yes” from the drop-down menu in eNSpect (Inspection /Coverage and Conclusion).

5.16.1.5 – Limitations on Inspection

The limitations on the agency’s ability to access audit results also apply to an inspection of a combination product manufacturer.

5-1 FORM FDA 482 NOTICE OF INSPECTION

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION	1. DISTRICT OFFICE ADDRESS & PHONE NO. 1431 Harbor Bay Parkway Alameda, CA 94502 (510)337-6700

TO	2. NAME AND TITLE OF INDIVIDUAL Helen E. Castro, President	3. DATE 07/28/13
	4. FIRM NAME ABC Bread Company	5. HOUR 7:30 a.m.
	6. NUMBER AND STREET 579 Main Street	p.m.
	7. CITY AND STATE & ZIP CODE Richmond, CA 94805	8. PHONE NO. & AREA CODE (510)123-4567

Notice of Inspection is hereby given pursuant to Section 704(a)(1) of the Federal Food, Drug, and Cosmetics Act [21 U.S.C. 374(a)][1] and/or Part F or G, Title III of the Public Health Service Act [42 U.S.C. 262-264][2]

As a small business that is subject to FDA regulation, you have the right to seek assistance from the U.S. Small Business Administration (SBA). This assistance includes a mechanism to address the enforcement actions of Federal agencies. SBA has a National Ombudsman's Office that receives comments from small businesses about Federal agency enforcement actions. If you wish to comment on the enforcement actions of FDA, CALL (888) 734-3247. The website address is www.sba.gov/ombudsman.

FDA has an Office of the Ombudsman that can directly assist small business with complaints or disputes about actions of the FDA. That office can be reached by calling (301) 796-8530 or by email at ombuds@oc.fda.gov.

For industry information, go to www.fda.gov/oc/industry.

9. SIGNATURE(S) *(Food and Drug Administration Employee(s))*	10. TYPE OR PRINT NAME(S) AND TITLE(S) *(FDA Employee(s))*
Sidney H. Rogers	Sidney H. Rogers, Investigator

[1] **Applicable portions of Section 704 and other Sections of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374] are quoted below:**

Sec. 704(a)(1) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, tobacco products, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, tobacco products, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any person (excluding farms and restaurants) who manufactures, processes, packs, transports, distributes, holds, or imports foods, the inspection shall extend to all records and other information described in section 414, when the standard for records inspection under paragraph (1) or (2) of section 414(a) applies, subject to the limitations established in section 414(d). In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs, nonprescription drugs intended for human use, restricted devices, or tobacco products are manufactured, processed, packed, or held, inspection shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs, nonprescription drugs intended for human use, restricted devices, or tobacco products which are adulterated or misbranded within the meaning of this Act, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data (other than data as to qualifications of technical and professional personnel performing functions subject to this

(Continued on Reverse)

Act), and research data (other than data relating to new drugs, antibiotic drugs, devices, and tobacco products and subject to reporting and inspection under regulations lawfully issued pursuant to section 505 (i) or (k), section 519, section 520(g), or chapter IX and data relating to other drugs, devices, or tobacco products, which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(j)). A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.

Sec. 704. (a)(2) The provisions of the third sentence of paragraph (1) shall not apply to (A) pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not, either through a subsidiary or otherwise, manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail; (B) practitioners licensed by law to prescribe or administer drugs, or prescribe or use devices, as the case may be, and who manufacture, prepare, propagate, compound, or process drugs, or manufacture or process devices solely for use in the course of their professional practice; (C) persons who manufacture, prepare, propagate, compound, or process drugs, or manufacture or process devices solely for use in research, teaching, or chemical analysis and not for sale; (D) such other classes of persons as the Secretary may by regulation exempt from the application of this section upon a finding that inspection as applied to such classes of persons in accordance with this section is not necessary for the protection of the public health.

Sec. 704. (a)(3) An officer or employee making an inspection under paragraph (1) for purposes of enforcing the requirements of section 412 applicable to infant formulas shall be permitted, at all reasonable times, to have access to and to copy and verify any records (A) bearing on whether the infant formula manufactured or held in the facility inspected meets the requirements of section 412, or (B) required to be maintained under section 412.

Sec. 704(b) Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, tobacco product, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary.

Sec. 704. (c) If the officer or employee making any such inspection of a factory, warehouse, or other establishment has obtained any sample in the course of the inspection, upon completion of the inspection and prior to leaving the premises he shall give to the owner, operator, or agent in charge a receipt describing the samples obtained.

Sec. 704. (d) Whenever in the course of any such inspection of a factory or other establishment where food is manufactured, processed, or packed, the officer or employee making the inspection obtains a sample of any such food, and an analysis is made of such sample for the purpose of ascertaining whether such food consists in whole or in part of any filthy, putrid, or decomposed substance, or is otherwise unfit for food, a copy of the results of such analysis shall be furnished promptly to the owner, operator, or agent in charge.

Sec. 704(e) Every person required under section 519 or 520(g) to maintain records and every person who is in charge or custody of such records shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and to copy and verify, such records.

Section 704 (f)(1) An accredited person described in paragraph (3) shall maintain records documenting the training qualifications of the person and the employees of the person, the procedures used by the person for handling confidential information, the compensation arrangements made by the person, and the procedures used by the person to identify and avoid conflicts of interest. Upon the request of an officer or employee designated by the Secretary, the person shall permit the officer or employee, at all reasonable times, to have access to, to copy, and to verify, the records.

Section 512 (l)(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A), and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m) (4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

[2] Applicable sections of Parts F and G of Title III Public Health Service Act [42 U.S.C. 262-264] are quoted below:

Part F – Licensing – Biological Products and Clinical Laboratories and* * * * * *

Sec. 351(c) "Any officer, agent, or employee of the Department of Health and Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation

(Continued on Page 3)

of any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid for sale, barter, or exchange in the District of Columbia, or to be sent, carried, or brought from any State or possession into any other State or possession or into any foreign country, or from any foreign country into any State or possession."

Part F – * * * * * *Control of Radiation.

Sec. 360 A (a) "If the Secretary finds for good cause that the methods, tests, or programs related to electronic product radiation safety in a particular factory, warehouse, or establishment in which electronic products are manufactured or held, may not be adequate or reliable, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are thereafter authorized (1) to enter, at reasonable times any area in such factory, warehouse, or establishment in which the manufacturer's tests (or testing programs) required by section 358(h) are carried out, and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, the facilities and procedures within such area which are related to electronic product radiation safety. Each such inspection shall be commenced and completed with reasonable promptness. In addition to other grounds upon which good cause may be found for purposes of this subsection, good cause will be considered to exist in any case where the manufacturer has introduced into commerce any electronic product which does not comply with an applicable standard prescribed under this subpart and with respect to which no exemption from the notification requirements has been granted by the Secretary under section 359(a)(2) or 359(e)."

(b) "Every manufacturer of electronic products shall establish and maintain such records (including testing records), make such reports, and provide such information, as the Secretary may reasonably require to enable him to determine whether such manufacturer has acted or is acting in compliance with this subpart and standards prescribed pursuant to this subpart and shall, upon request of an officer or employee duly designated by the Secretary, permit such officer or employee to inspect appropriate books, papers, records, and documents relevant to determining whether such manufacturer has acted or is acting in compliance with standards prescribed pursuant to section 359(a)."

* * * * * *

(f) "The Secretary may by regulation (1) require dealers and distributors of electronic products, to which there are applicable standards prescribed under this subpart and the retail prices of which is not less than $50, to furnish manufacturers of such products such information as may be necessary to identify and locate, for purposes of section 359, the first purchasers of such products for purposes other than resale, and (2) require manufacturers to preserve such information Any regulation establishing a requirement pursuant to clause (1) of the preceding sentence shall (A) authorize such dealers and distributors to elect, in lieu of immediately furnishing such information to the manufacturer to hold and preserve such information until advised by the manufacturer or Secretary that such information is needed by the manufacturer for purposes of section 359, and (B) provide that the dealer or distributor shall, upon making such election, give prompt notice of such election (together with information identifying the notifier and the product) to the manufacturer and shall, when advised by the manufacturer or Secretary, of the need therefore for the purposes of Section 359, immediately furnish the manufacturer with the required information. If a dealer or distributor discontinues the dealing in or distribution of electronic products, he shall turn the information over to the manufacturer. Any manufacturer receiving information pursuant to this subsection concerning first purchasers of products for purposes other than resale shall treat it as confidential and may use it only if necessary for the purpose of notifying persons pursuant to section 359(a)."

* * * * * *

Sec. 360 B.(a) It shall be unlawful–

(1) * * *

(2) * * *

(3) "for any person to fail or to refuse to establish or maintain records required by this subpart or to permit access by the Secretary or any of his duly authorized representatives to, or the copying of, such records, or to permit entry or inspection, as required or pursuant to section 360A."

* * * * * *

Part G - Quarantine and Inspection

Sec. 361(a) "The Surgeon General, with the approval of the Secretary, is authorized to make and enforce such regulations as in his judgment are necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession. For purposes of carrying out and enforcing such regulations, the Surgeon General may provide for such inspection, fumigation, disinfection, sanitation, pest extermination, destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection to human beings, and other measures, as in his judgment may be necessary."

5-2 - FORM FDA 482a

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION	1. DISTRICT ADDRESS AND PHONE NO. 6751 Steger Dr. Cincinnati, OH 45237 (513)679-2700

TO		
	2. NAME AND TITLE OF INDIVIDUAL Michael A. Weston, Plant Manager	3. DATE OF REQUEST 06/20/12
	4. FIRM NAME ABC Food Company	5. TIME OF REQUEST 8:30 ☑ A.M. ☐ P.M.
	6. NUMBER AND STREET 3114 Mapleleaf Avenue	
	7. CITY AND STATE Cincinnati, OH	8. ZIP CODE 45213

Written demand for examination and/or copying of the records required by 21 CFR 113.100, 21 CFR 114 and 21 CFR 500.23 is hereby given, pursuant to 21 CFR 108.25(g), 21 CFR 108.35(h) and 21 CFR 500 for the records described below in order to verify the pH, adequacy of processing, the integrity of container closures, and the coding of the products processed by your firm.

9. RECORDS NECESSARY

All thermal process, production, and quality control / analytical records and maintenance

All thermal process, production, and quality control / analytical records and maintenance records which may document any changes to the equipment, or the thermal process mandated by 21 CFR 108, 113, and 114 [*choose appropriate regulation, 113 LACF or 114 acidified*] for all low acid canned foods and/or acidified food products [*or specify product*] which were produced by this firm since the last FDA inspection.

10. SIGNATURE *(Food and Drug Administration Employee(s))*	11. TITLE FDA EMPLOYEE
Sidney H. Rogers	Investigator

FORM FDA 482a (6/11) PREVIOUS EDITION IS OBSOLETE. **DEMAND FOR RECORDS**

PSC Publishing Services (301) 443-6740 EF

5-3 FORM FDA 482b

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

1. DISTRICT ADDRESS AND PHONE NO.
6751 Steger Dr.
Cincinnati, OH 45237
(513)679-2700

TO

2. NAME AND TITLE OF INDIVIDUAL
Michael A. Weston, Plant Manager

3. DATE OF REQUEST
06/20/12

4. FIRM NAME
ABC Food Company

5. TIME OF REQUEST
8:30 ☑ A.M. ☐ P.M.

6. NUMBER AND STREET
3114 Mapleleaf Avenue

7. CITY AND STATE
Cincinnati, OH

8. ZIP CODE

Written request is hereby given pursuant to 21 CFR 108.25(c)(3)(ii), 21 CFR 108.35(c)(3)(ii) and 21 CFR 500.23 for the information described below, concerning processes and procedures, which is deemed necessary by the Food and Drug Administration to determine the adequacy of the processes for products processed by your firm.

9. RECORDS NECESSARY

All documents and records mandated by 21 CFR 108 relating to or having a bearing on the adequacy of processes for all low acid canned foods and/or acidified food products [*or specify product*] that were produced in this firm since the last FDA inspection.

10. SIGNATURE *(Food and Drug Administration Employee(s))*
Sidney H. Rogers

11. TITLE FDA EMPLOYEE
Investigator

FORM FDA 482b (6/11) PREVIOUS EDITION IS OBSOLETE. **REQUEST FOR INFORMATION**

PSC Publishing Services (301) 443-6740 EF

5-3 INSTRUCTIONS FOR COMPLETING THE FDA 482b, REQUEST FOR INFORMATION

Block 1 – Enter the district address where the firm is physically located, regardless of program area or investigator duty station. Include the district office commercial telephone number and area code.

Block 2 – Enter the complete name and official title of the individual to whom you issue the FDA 482b.

Block 3 – Enter date on which you are requesting the records.

Block 4 – Enter the firm's legal name. This should be the firm's legal name and not the DBA (doing business as), trade name, or alias.

Block 5 – Enter the time of the request.

Block 6, 7, and 8– Enter the number, street, city, state, and zip code of the firm.

Block 9 – Enter a brief description of the processing records and other relevant documents. See example language in the completed FDA 482b below. If specifying the product involved, include the product name and form, container size, and processing method.

Block 10 and 11 – Enter your signature and title.

Once completed, issue the original FDA 482b to the same person to whom the FDA 482, Notice of Inspection, was issued. Submit an exact copy with your EIR.

5-5 FORM FDA 483

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
#1 Industry Information: www.fda.gov/oc/industry	#2
	FEI NUMBER #3

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: #4

FIRM NAME	STREET ADDRESS
#5	#6
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED #7

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED: #8

#9

Add Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
	#10	#11	#12

FORM FDA 483 (9/08) PREVIOUS EDITION OBSOLETE **INSPECTIONAL OBSERVATIONS** Page 1 of 1

COMPLETION OF THE FORM FDA 483

Presently there are three ways to generate an FDA 483.

- eNSpect
- Electronic (non-eNSpect) version
- Handwritten hard copy

Where possible, you should be creating, issuing, and signing the Form FDA 483 via the eNSpect method. Many of the fields in the form are either partially or fully automated when using this method.

When using an electronic (non-eNSpect) or handwritten hard copy of the FDA 483, the current version must be used.

The sections of the Form FDA 483 are identified below, with numbers corresponding to the preceding blank version of the form.

1 - District Office Address and Phone Number - Legibly print the home District address where the **firm** is physically located, regardless of program area or investigator duty station. Include the district office commercial telephone number and area code. If using eNSpect for the FDA 483, select the home district of the firm.

For example, if a firm is located in Little Rock, Arkansas, then the district office would be Dallas District Office. See Appendix E for boundary maps.

For foreign inspections, the address to be used for this box will be provided as part of the assignment.

2 - Date(s) of inspection - Enter actual or inclusive date(s) of inspection.

3 - FEI Number - If the FDA Establishment Identifier is on the assignment, enter it here. If not readily available, leave blank.

4 - Name and Title of individual to whom report is issued - Enter legal first name, middle initial and last name and full title of the person to whom the form is issued.

5 - Firm Name - Enter full, legal name of the firm, including any abbreviations, quotation marks, dashes, commas, etc.

6 - Street address, city, state and Zip Code-Enter Street address, city, state, and Zip Code. (Not P.O. Box unless P.O. Box is part of the address such as on a Rural Route).

7 - Type of establishment inspected - Enter the type of the establishment, such as bakery, cannery, wholesale warehouse, drug repacker, salvage warehouse, contract manufacturer, specification developer, or medical device manufacturer.

8 – **Medical Device Specific Text** – For inspections of medical device firms, the following language should be inserted on the FDA 483 after the paragraph explaining how the firm may contact FDA and immediately above the statement "During an inspection of your firm (I)(We) Observed":

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

9 - Observations – See IOM 5.5.11 for information about what observations are considered "reportable" and may be listed on the Form FDA 483. Enter your reportable observations succinctly and clearly. Conditions listed should be significant and relate to an observed or potential problem with the facility, equipment, processes, controls, products, employee practices, or records. "Potential problems" should have a reasonable likelihood of occurring based upon observed conditions or events. Do not cite deviations from policy or guidance documents on your FDA 483.

Where applicable, when formulating each FDA 483 observation, answer Who (using titles or initials when necessary), What, When, Where, Why, How Much and How Often? Challenge each observation by asking "So What"? (regarding its significance).

As appropriate, FDA 483 observations should include relationship of observations to a given population, for example, "Two out of 50 records examined were * * *" or "4 out of 12 bags examined were ***." When appropriate, an FDA 483 observation may refer to inadequate situations as long as you provide supporting facts (examples) or explanation as to why the condition, practice or procedure observed is inadequate.

It is preferred not to identify individuals or firms by name (e.g., suppliers and consignees) within the FDA 483. Where appropriate to support the FDA 483 observation, identify the individual(s) or firm(s) by substituting other non-specific identifying information as below. Document your evidence in your EIR, fully explaining the relationship(s).

a. The lot number for a component received from or shipped to firm "A".
b. The invoice number for a shipment from or to firm "A".
c. A patient #, record #. See IOM 5.2.3.3 item 7.
d. The study number for a particular Clinical Investigator site.
e. Other necessary but non-specific identifying information to show the observation's relationship to a particular firm and/or individual.

10 - Employee(s) signature

Everyone present under FDA inspectional authority at issuance signs the FDA 483. However, absence of a team member at the conclusion of an inspection need not prevent issuance of the form (see IOM 5.1.2.5.1). If signing the FDA 483 digitally using eNSpect, the lead CSO's signature will appear on all pages of the FDA 483 and the remaining team members' signature will appear on the last page. When it is necessary to use pen to sign the form (e.g., when issuing a handwritten hard copy version), each person signs the first and last pages of the FDA 483 and initials each intervening page in the signature block.

When using eNSpect to sign the Form FDA 483, the system will retain a copy of the digitally signed form automatically. If you do not use eNSpect to digitally sign the document, assure you retain a digitally signed copy. If using a pen to sign the form, make a photocopy or carbon copy of the signed form. An unsigned photocopy or printed duplicate is unacceptable to maintain with the division's files. See IOM 5.2.3.6.2.

11 - Employee(s) name and title

The names of everyone who participated in the inspection with the issuance of an FDA 482 should be listed on the FDA 483, even if they are not available to sign the document.

12 - Date Issued - Enter the date the form is actually issued to the firm's management.

The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

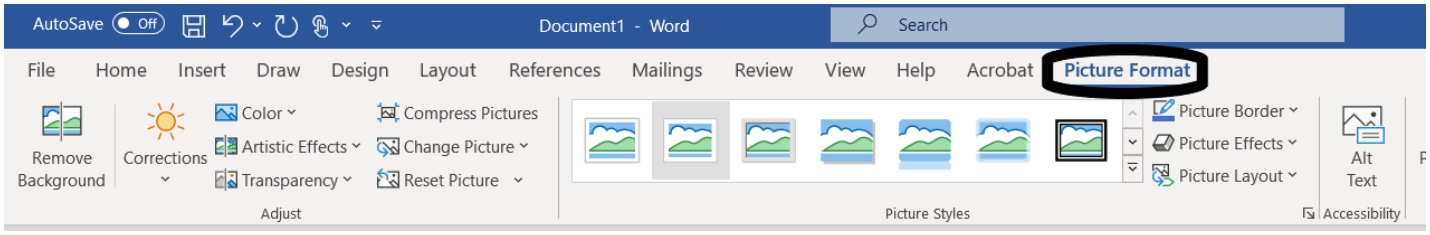
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."

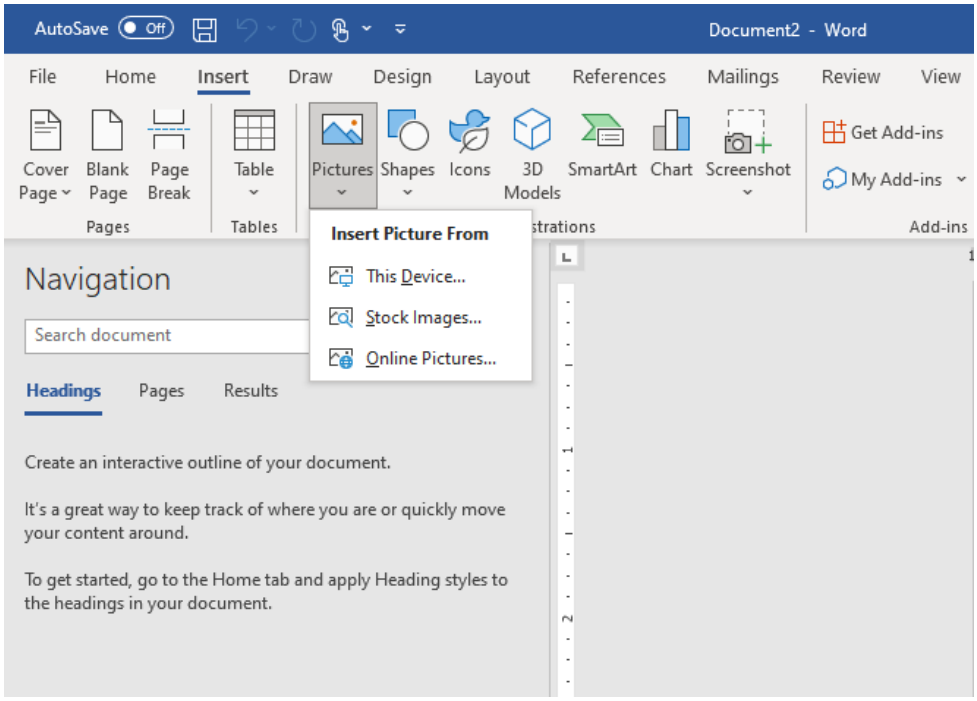
FORM FDA 483 (9/08)

5-6 INSERTING DIGITAL PHOTOS INTO eNSpect (RESIZE PHOTO)

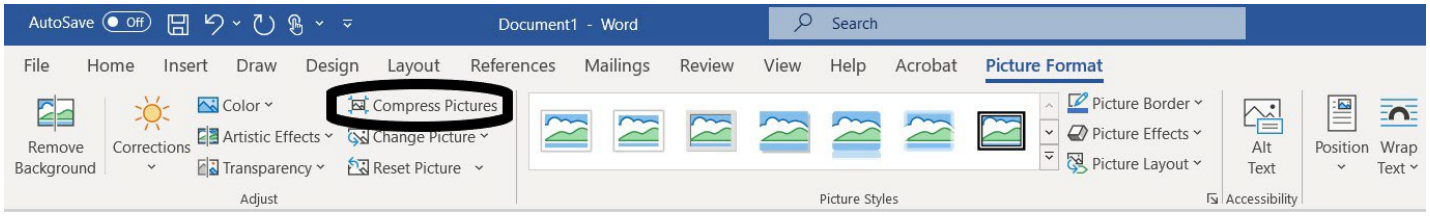


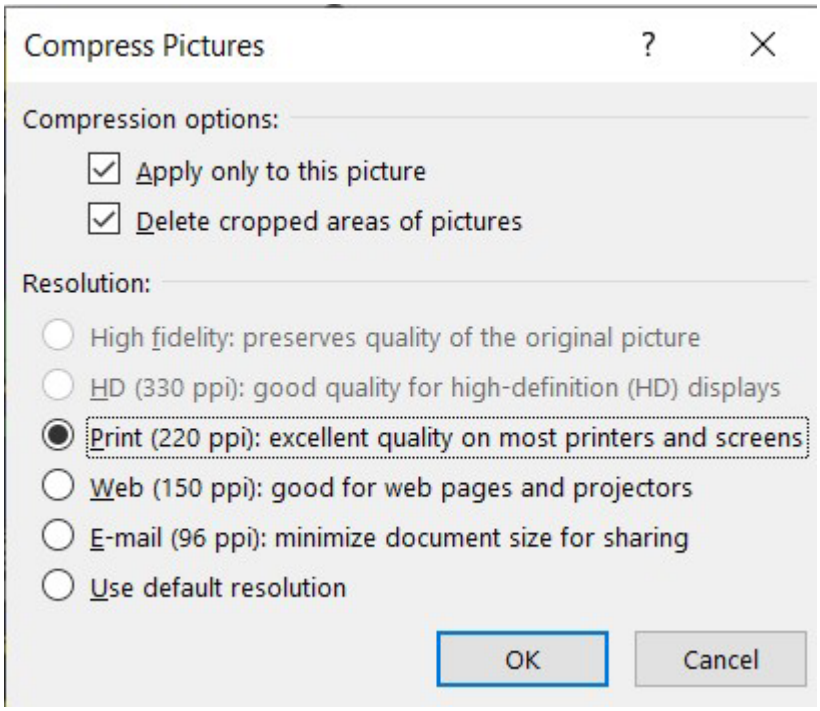
5-7 INSERTING DIGITAL PHOTOS INTO eNSpect (INSERT PHOTO)

Inserting a resized picture into Microsoft Word.

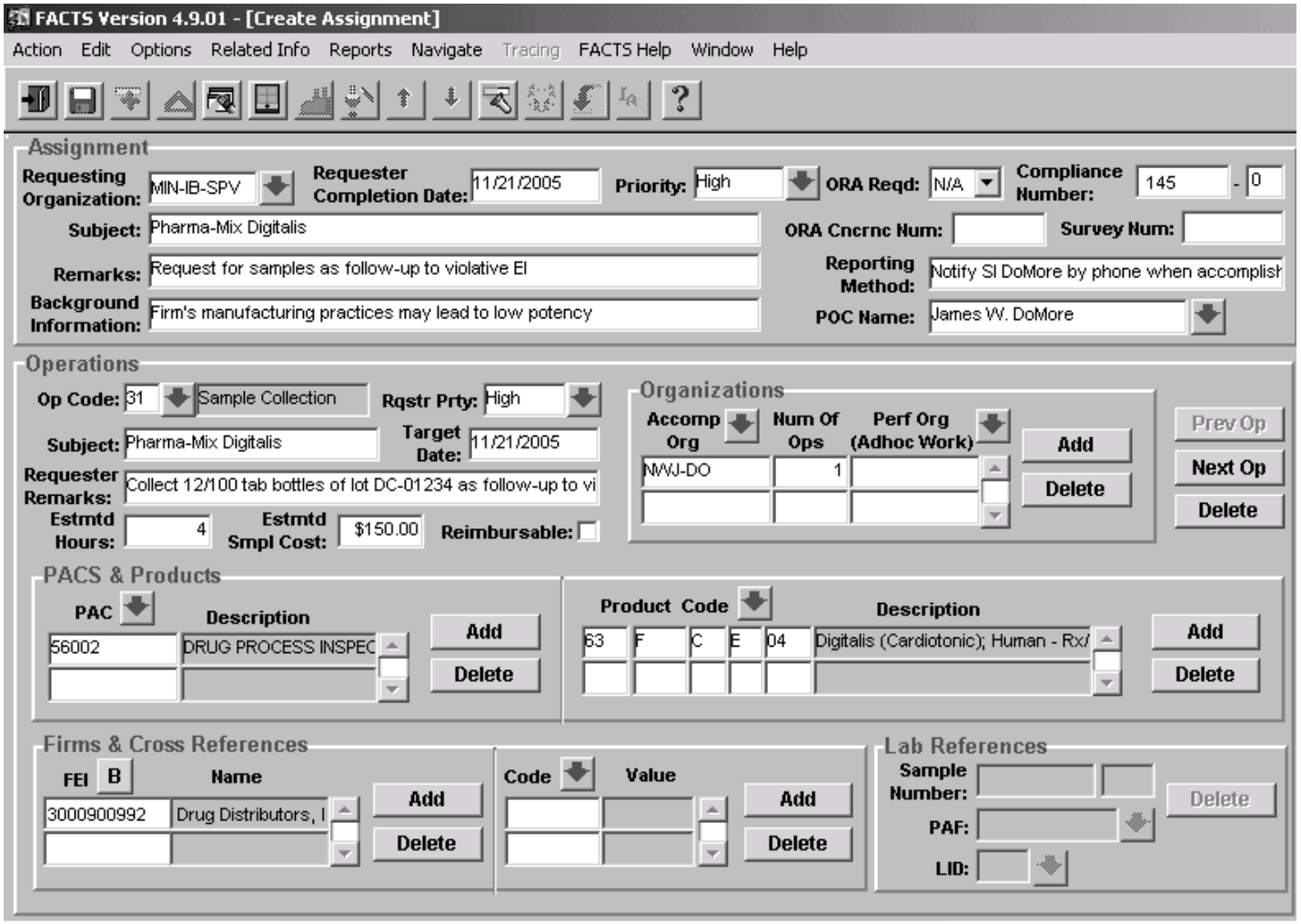


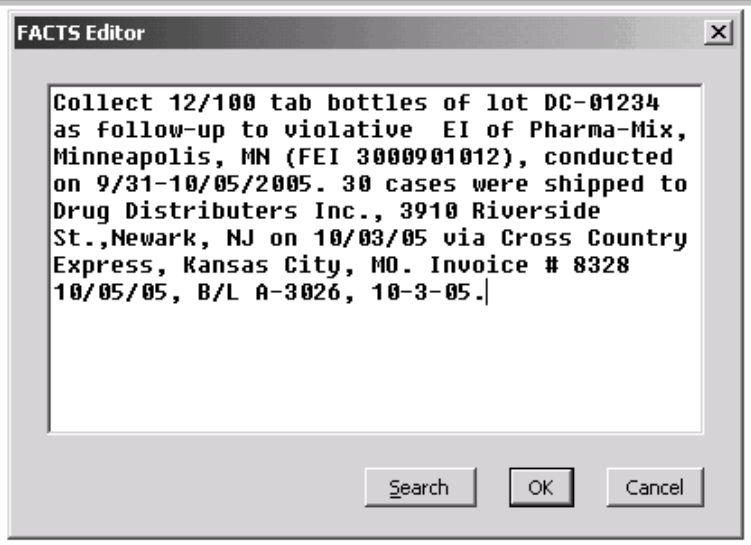
5-8 INSERTING DIGITAL PHOTOS INTO eNSpect (RESIZING USING MS WORD)





5-9 FACTS CREATE SAMPLE ASSIGNMENT SCREEN-





5-10 FORM FDA 482c NOTICE OF INSPECTION - REQUEST FOR RECORDS

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		1. DISTRICT OFFICE ADDRESS & PHONE NO.
TO	2. NAME AND TITLE OF INDIVIDUAL	3. DATE
	4. FIRM NAME	5. HOUR a.m. / p.m.
	6. NUMBER AND STREET	
	7. CITY AND STATE & ZIP CODE	8. PHONE # & AREA CODE

Notice of Inspection is hereby given pursuant to Section 704(a)(1) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374(a)(1)][1]. Written request is hereby given to access and/or copy the records described below, pursuant to the Federal Food, Drug and Cosmetic Act, Section 414(a) [21 U.S.C. 350c][2] and Title 21 Code of Federal Regulations, Section 1.361[3].

9. SIGNATURE *(Food and Drug Administration Employee(s))*	10. TYPE OR PRINT NAME AND TITLE *(FDA Employee(s))*

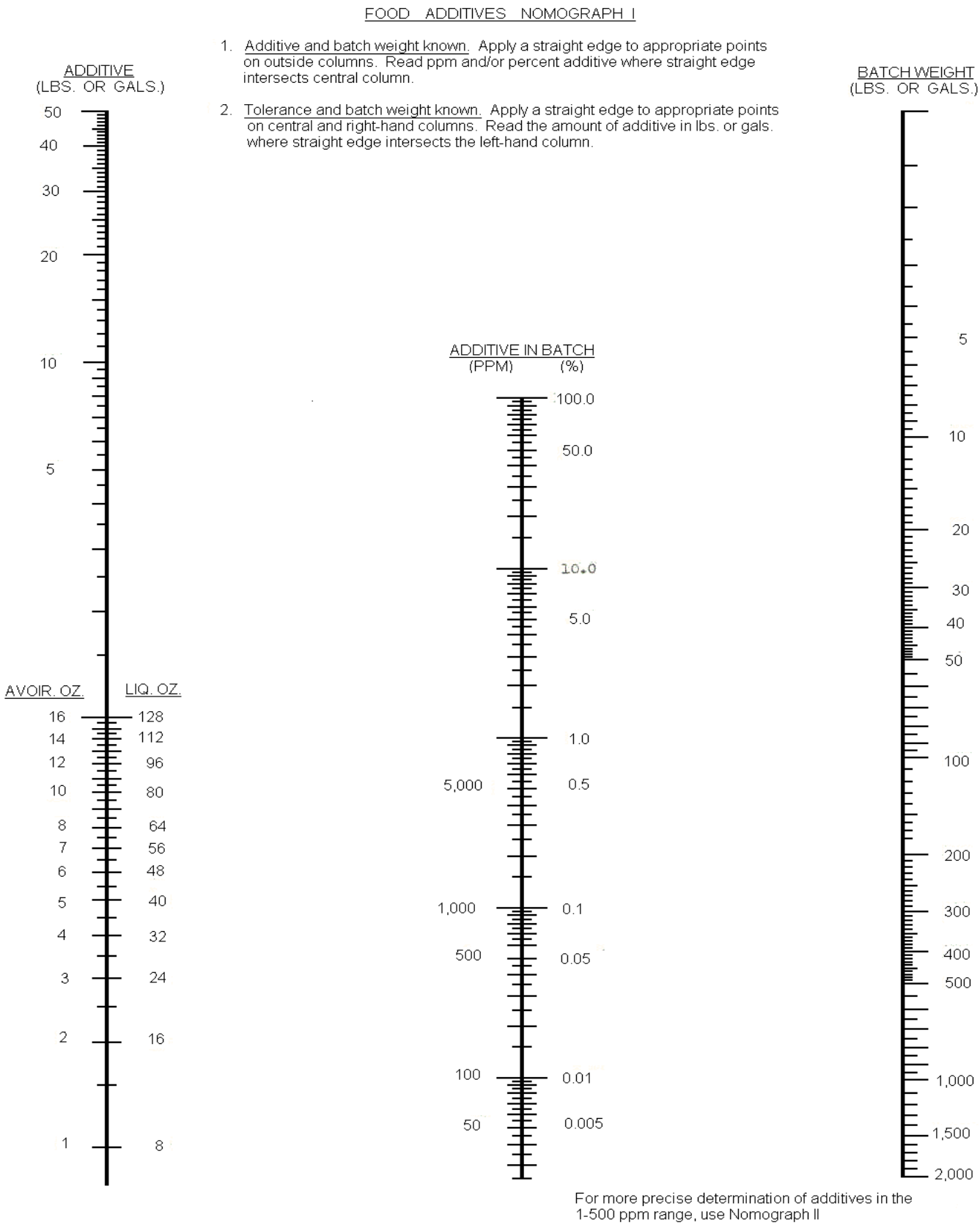
Applicable portions of Sections 704 and 414 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 374 and 350c) and Title 21 of the Code of Federal Regulations, are quoted below:

[1]Sec. 704.(a)(1) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers and labeling therein. In the case of any person (excluding farms and restaurants) who manufactures, processes, packs, transports, distributes, holds, or imports foods, the inspection shall extend to all records and other information described in section 414, when the standard for records inspection under paragraph (1) or (2) of section 414(a) applies, subject to the limitations established in section 414(d). In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs, nonprescription drugs intended for human use, or restricted devices are manufactured, processed, packed, or held, the inspection shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs, nonprescription drugs intended for human use, or restricted devices which are adulterated or misbranded within the meaning of this Act, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data (other than data as to qualifications of technical and professional personnel performing functions subject to this Act), and research data (other than data, relating to new drugs, antibiotic drugs and devices and, subject to reporting and inspection under regulations lawfully issued pursuant to section 505(i) or (k), section 519, or 520(g), and data relating to other drugs or devices which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(j). A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.

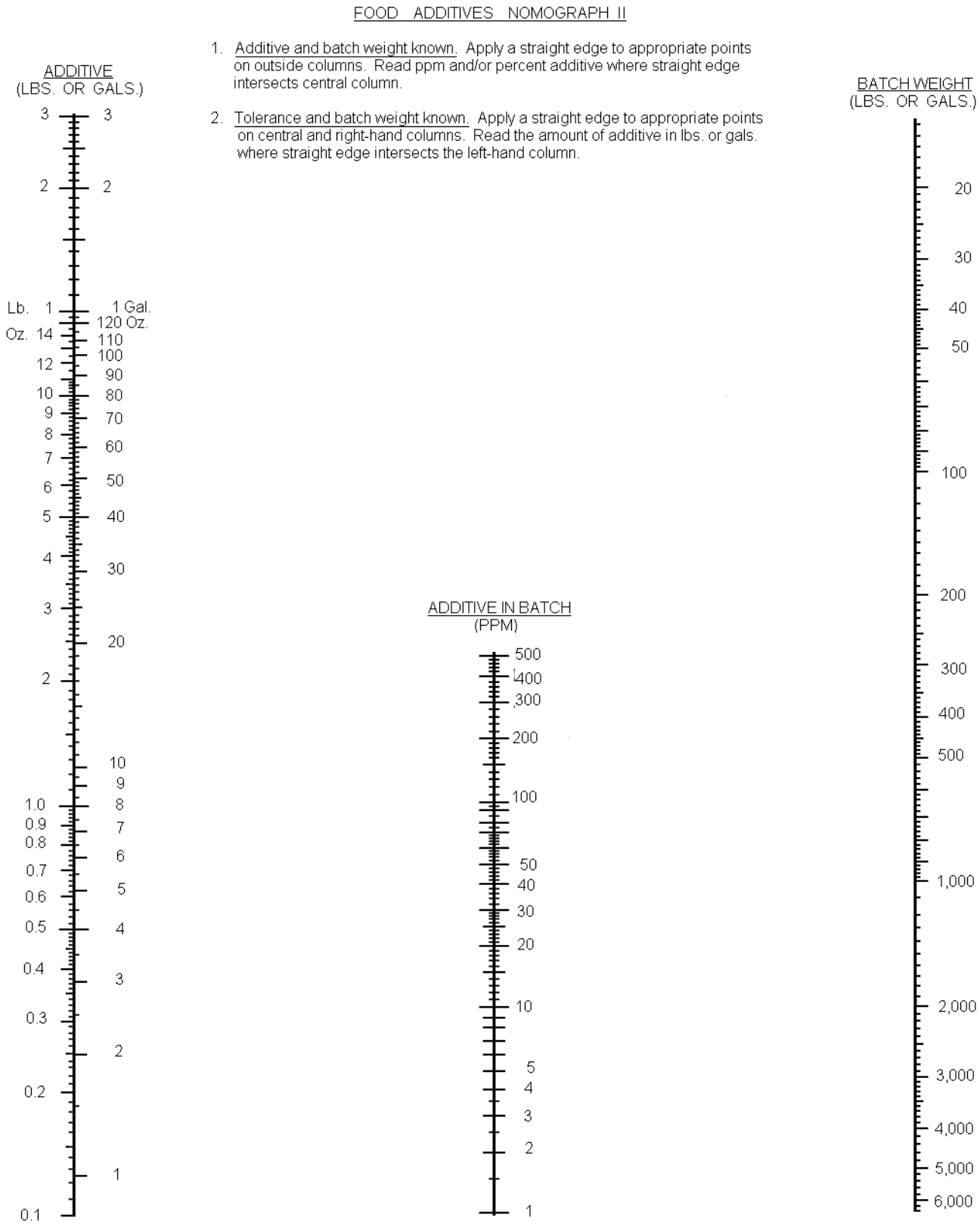
[2]Sec. 414(a) RECORDS INSPECTION. - (1) ADULTERATED FOOD. - If the Secretary has a reasonable belief that an article of food, and any other article of food that the Secretary reasonably believes is likely to be affected in a similar manner, is adulterated and presents a threat of serious adverse health consequences or death to humans or animals, each person (excluding farms and restaurants) who manufactures, processes, packs, distributes, receives, holds, or imports such article shall, at the request of an officer or employee duly designated by the Secretary, permit such officer or employee, upon presentation of appropriate credentials and a written notice to such person, at reasonable times and within reasonable limits and in a reasonable manner, to have access to and copy all records relating to such article, and to any other article of food that the Secretary reasonably believes is likely to be affected in a similar manner, that are needed to assist the Secretary in determining whether the food is adulterated and presents a threat of serious adverse health consequences or death to humans or animals. (2) Use of or exposure to food of concern. --If the Secretary 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 Secretary reasonably believes is likely to be affected in a similar manner, will cause serious adverse health consequences or death to humans or animals, each person (excluding farms and restaurants) who manufactures, processes, packs, distributes, receives, holds, or imports such article shall, at the request of an officer or employee duly designated by the Secretary, permit such officer or employee, upon presentation of appropriate credentials and a written notice to such person, at reasonable times and within reasonable limits and in a reasonable manner, to have access to and copy all records relating to such article and to any other article of food that the Secretary reasonably believes is likely to be affected in a similar manner, that are needed to assist the Secretary in determining whether there is a reasonable probability that the use of or exposure to the food will cause serious adverse health consequences or death to humans or animals. (3) Application.--The requirement under paragraphs (1) and (2) applies to all records relating to the manufacture, processing, packing, distribution, receipt, holding, or importation of such article maintained by or on behalf of such person in any format (including paper and electronic formats) and at any location.

[3]321 CF CFR 1.361 What are the record availability requirements? When FDA has a reasonable belief that an article of food is adulterated and presents a threat of serious adverse health consequences or death to humans or animals, any records and other information accessible to FDA under section 414 or 704(a) of the act (21 U.S.C. 350c and 374(a)) must be made readily available for inspection and photocopying or other means of reproduction. Such records and other information must be made available as soon as possible, not to exceed 24 hours from the time of receipt of the official request, from an officer or employee duly designated by the Secretary of Health and Human services who presents appropriate credentials and a written notice.

5-11 FOOD ADDITIVE NOMOGRAPH I



5-11 FOOD ADDITIVE NOMOGRAPH II



5-12 SUMMARY OF REGISTRATION AND LISTING HUMAN PHARMACEUTICALS

SUMMARY OF REGISTRATION AND LISTING REQUIREMENTS FOR THE MANUFACTURE OR DISTRIBUTION OF HUMAN PHARMACEUTICALS			
TYPE OF FIRM	**REGISTRATION STATUS**	**LISTING STATUS**	**FACTS CODE**
Manufacturer [including homeopathic & controlled drugs]	yes	yes	M
Contract Manufacturer	yes	yes	M
Own Label Distributor	no	yes	L
Wholesale Distributor (no manufacturing or distribution under own name and label)	no	no	W-*
Own Label Repacker	yes	yes	R
Own Label Relabeler [including recirculizer]	yes	yes	Y
Contract Relabeler	yes	yes	Y
Contract Testing Laboratory [dosage forms & active ingredient release]	yes	no	C
Contract Testing Lab [doing non-release tests]	no	no	C
Contract Sub-Manufacturer	yes	yes	M
IND Manufacturer [Clinical Drugs]	no	no	M
NDA and ANDA Manufacturer	yes	yes	M
Sponsor/Monitors/Clinical Investigator	no	no	4, 5, 6, 7
Contract Sterilizer	yes	yes	0
Fulfillment Packager [adding substantive labeling]	yes	yes	Y
Mail Order House [adding insubstantial labeling]	no	no	D
Printing House	no	no	None
Medical Gas Transfiller	yes	yes	MG
First Aid/Rescue Squad [transfilling for own use]	no	no	MG
Medical Gas Transfiller [operating out of a van]	yes	yes	MG
Contract Assembler	yes	no	M
Active Drug Substance Manufacturer	yes	yes	M
Excipient Drug Manufacturer	no	no	M
Manufacturer of Research Drugs	no	no	M
Drug Importer	no	no	A
Foreign Drug Manufacturer	yes	yes	M
Methadone Clinic	no	no	T
Retail Pharmacy	no	no	D
Salvage Operation	yes	no	X
Biopharmaceutical Clinical Facility	no	no	2
Outsourcing Facility	yes	no	OF

*Includes W, WA, WF, WR, and/or WZ

5-13 MEDICAL DEVICE REGISTRATION AND COMPLIANCE REQUIREMENTS

	Operation	Submit 510(k)	Register	List	COMPLY W/GMP	UDI Records Required
1.	Manufacture and distribute device	YES: 807.81(a)	YES 807.20(a)	YES 807.20(a)	YES	YES
2.	Contract manufacturer who commercially distributes device for specifications developer	NO: 807.81(a)	YES if domestic: 807.20(a)(2), YES if foreign 807.40(a)	YES if domestic 807.20(a)(2), YES if foreign 807.40(a)	YES	YES, IF THEY DISTIBUTE THE DEVICE UNDER THEIR NAME
3a.	Contract manufacturer who meets the definition of finished device manufacturer per 21 CFR 820.3(l).	NO	YES 807.20(a)	YES 807.20(a)	YES	YES, IF THEY DISTRIBUTE THE DEVICE UNDER THEIR NAME
3b.	Contract manufacturer who does not meet the definition of finished device manufacturer per 21 CFR 820.3(l) (e.g., component manufacturer or subassembler)	NO	NO 807.65(a)	NO, 807.65(a)	NO	NO
4.	Manufacturer modifies device or new intended use and distribute	NO: preamble no. 17 & 18 FR 942 FR 42526) YES: 807.81(a)(3) with signif. change in device or use	YES 807.20(a)	YES 807.20(a)	YES	YES
5.	Located in US and distribute US made device. No specification initiation (domestic distributor)	NO: 807:85(b)	NO: 510(g)(4) of act, 807.20(c)	NO 807.20(c)	NO	YES, IF THEY DISTRIBUTE THE DEVICE UNDER THEIR NAME
6.	Specification initiator and distribute only	YES: 807.81(a)	YES: 807.20(a)(1)	YES: 807.20(a)(1)	YES: .	YES
7.	Specification consultant only; no distribution	NO	NO:	NO	NO	NO
8	Relabeler or repacker: change labeling or packaging in manner other than adding own name	YES	YES: 807.20 (a)(3)	YES. 807.20(a)(3)	YES	YES
9.	Kit assembler using prelabeled & prepackaged devices only	NO: no change in device or existing labeling other than adding dist. name & address 807.81(a)(3)	YES: 807.20(a)	YES: 807.20(a)	YES	YES IF THEY DISTRIBUTE THE KIT UNDER THEIR NAME, REFER TO FDA's UDI KIT GUIDANCE
10.	Kit assembler changes intended use (801.4) of prepackaged/prelabeled devices	YES: 807.81(a)	YES: 807.20(a)	YES: 807.20(a)	YES:	YES
11.	Kit assembler changes prepackaged/prelabeled devices	FDA's Convenience Kits Interim Regulatory Guidance NO: if no significant change to labeling or device: otherwise YES: 807.81(a)(3)(i)	YES: 807.20(a)	YES: 807.20(a)	YES	YES
12.	Mfc of accessory who packages and labels for health purpose to end user	YES: 807.81(a)	YES: 807.20(a)(6)	YES: 807.20(a)(6)	YES	YES, IF THEY DSISTRIBUTE ACCESSORIES UNDER THEIR NAME
13.	Manuf. Components & dist. Only to finished device mfr.	NO: 807.81(a)	NO: 807.65(a)	NO	NO	NO

14.	Contract manufacturer of components/subassemblies that are not finished devices	NO	NO	NO	NO	NO
15.	Contract packager or labeler	NO	YES	YES	Yes	YES, IF THEY DISTRIBUTE THE DEVICE UNDER THEIR NAME
16.	Contract Sterilizer	NO	YES if domestic 807.20(a)(2), YES if foreign 807.40(a)	YES if domestic 807.20(a)(2), YES if foreign 807.40(a)	YES	NO
17.	Manufacture custom device (domestic or foreign)	Refer to FDA's Custom Device Exemption Guidance Document NO: 807.85(a)(1)&(2)	YES 807.20(a)	YES 807.20(a)	YES: also see 520(b); 520(f) of the FD&C Act	NO
18.	U.S. Establishment who manufactures for export only	NO	YES 807.20(a) and 807.25(g)(5)	YES 807.20(a) and 807.25(g)(5)	YES	NO
19.	Foreign manufacturers and all foreign establishments	YES: 807.81	YES, 807.40(a)	YES 807.40(a)	YES	YES
20.	Initial distributor/importer of device	YES: 807.81(a) or 807.85(b) unless 510(k) has been filed by foreign manufacturer or another init. Dist	YES: 807.20(a)(5)	NO:Must identify foreign manufacturer(s) or device(s) imported)	YES:.	Yes, IF THEY DISTRIBUTE THE DEVICE UNDER THEIR NAME
21.	Installer-mfr.'s agent	NO	NO	NO	YES:	NO
22.	Installer-user	NO	NO	NO	NO	NO
23.	Device being investigated under ide	Exempt: 812.1(a)	NO	NO: 807.40(c)	Exempt per 812.1(a), except for the requirements found in 820.10(c)	NO
24.	Mfr. Buys manufacturing rights for device (see no. 4)	NO: preamble 18 FR 8-23-77 only if same type of manuf. equip. is used and no signif. change to device	YES: 807.20(a)	YES 807.40(a)	YES	YES, IF THEY DISTRIBUTE THE DEVICE UNDER THEIR NAME
25.	Reprocessor of single use device	YES	YES: 807.20(a)(4)	YES: 807.20(a)(4)	YES	YES, IF THEY REDISTRIBUTE THE DEVICE UNDER THEIR NAME

5-14 eNSpect PROFILE - COMSTAT

PROFILING A FIRM'S CGMP/QS COMPLIANCE STATUS

Table 5-14.1 Quick Reference Guide
Table 5-14.2 Example of a Maintain Profiles Screen
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5-14.2 Purpose
5-14.3 Instructions
5-14.3.1 Pre-Inspection Preparation
5-14.3.2 Firm's Operations
5-14.3.3 Maintain Profiles Screen
5-14.3.4 Previous Inspection Profile
5-14.3.5 Firm information
5-14.3.6 Inspection Coverage of Profile Class Codes
5-14.3.7 Discontinue and Delete Buttons
5-14.3.8 CGMP Inspection and Other Toggle Buttons
5-14.3.9 Initial, In Review, and Final
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5-14.3.10.3 Unacceptable Status
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Table 5-14.6.1 Device, Biologic, Drug, and Veterinary Establishments TO Profile
Table 5-14.6.2 Establishment and Operations NOT to Profile.
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5-14.7 Profile Classes and Codes
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Table 5-14.7.1.1 Biologics
Table 5-14.7.1.2 Devices
Table 5-14.7.1.3 Drugs and Veterinary
Table 5-14.7.1.4 Special Veterinary

Table 5-14.1 Quick Reference Guide

Review Status	Profile Status	Data Entry Role	Remarks Field	Remarks *Status* Field	Purpose
Initial	Further Action Indicated	IB	Review and date Ex: "Referred to CB mm/dd/yy"		EI is potentially OAI
	Acceptable	IB	Usually no Remarks required.		EI is NAI or VAI.
In Review	Pending	CB	Recommended enforcement or alternative action; with date as well as review and date. Ex: "Recommend WL; Under review by [CB/Center]"		Enforcement or alternative action recommended.

Final	Other	IB/CB	Enter the action firm is operating under Ex: "Consent Decree (CD) for CGMP (Current Good Manufacturing Practices)/QS (Quality Systems) violations signed on mm/dd/yy." If the CD includes a sunset clause/date, add to Remarks. or "AIP invoked on mm/dd/yy."	When the firm is operating under CD/Injunction/AIP (Application Integrity Policy) and the CGMP/QS EI is: NAI or VAI, then "Acceptable (AC)"; or the inspection is OAI and further enforcement action is taken, then the Remarks Status is "Unacceptable (UN)."	Firm is operating under a CD or AIP, and a subsequent CGMP EI has occurred. Enforcement Action may involve medically necessary products or be process or product specific. In this case, such conditions should be reflected in Remarks field (see 3.10 & 3.11(2)).
	Acceptable	IB/CB	No outstanding OAI inspections, no compliance actions.		NAI and VAI inspections; or OAI inspections where no enforcement action was taken and/or was downgraded to VAI.
	Unacceptable	CB	Enter regulatory action taken and date. Ex. WL issued 1/1/18. UTL issued 3/10/18. Reg meeting held 4/10/18.		Only **after** an enforcement action occurred as a result of a CGMP/QSIT EI.

Table 5-14.2 Example of a Maintain Profiles Screen

5-14.1 Introduction

Firm profiles provide a snapshot of the firm's compliance status with CGMP or QS regulations. Profile status is monitored for domestic and foreign firms that manufacture, repack, label/relabel, sterilize, or test drug, medical device, or biological products.

5-14.2 Purpose

Firm profiles provide the compliance status as well as an inventory of product categories covered during a CGMP/QS inspection and are used to support:

- The Government Wide Quality Assurance Program (GWQAP).
- External users such as state and local regulatory authorities and foreign government agencies.
- Other FDA operations such as drug product approvals, export certificates and imports.

5-14.3 Instructions

5-14.3.1 Pre-Inspection Preparation

To obtain a comprehensive history of the firm you are going to inspect, go to ORADSS Domestic Reports folder named Establishment History Report and select EHR101 Firm Info and run the report entering the FEI you want reported. Make sure that a final status has been entered for all Profile Classes (PCs) for the previous inspection. If you find that one or more PCs have an initial status but not a final status, bring this to the attention of your supervisor and finalize prior entering any updates.

5-14.3.2 Firm's Operations

For profile purposes, the firm's operation type can be either as a single entity or in combination with other operations. Look at all the possibilities in the drop down menu before making a selection. Some selections allow for multiple operations. See below for examples:

a. Specification Developer Only versus Specification Developer Also.

When a firm is a specification developer and they do not manufacture any medical products onsite, select

profile class code, SPD, and the Operation Type, "Specification Developer Only."

When a firm is a specification developer and they do onsite manufacturing of medical products which are not the subject of the specifications developed, select SPD with the Operation Type "Specification Developer Also" **and** select the appropriate profile class of the products they manufacture with Operation Type "Manufacturer."

b. Veterinary Drugs Also versus Veterinary Drugs Only. When a firm manufactures both veterinary and human drugs, select the appropriate profile class code(s) that defines its operation then select the Operation Type Veterinary Drugs Also. When a firm manufactures veterinary drugs only, select the appropriate profile class code(s) that defines its operation then select the Operation Type Veterinary Drugs Only.

5-14.3.3 Maintain Profiles Screen

When entering profile information, it is important to access the Maintain Profiles screen properly as accessing a profile screen incorrectly will result in data quality errors.

The correct way for Field Offices and Centers to access the Profile screen is to use eNSpect, accessed from the eNSpect App link found on the Inside FDA's OII Applications page. From the menu toolbar, enter the FEI or eNSpect Operation and once the inspection record is selected, click the left-hand side Firm tab then select the Firm Profiling tab. You are now ready to enter/update the profile status.

5-14.3.4 Previous Inspection Profile

It is important that the profile for the previous inspection be complete with a final profile status for each PC before updating the profile for the current inspection. If this is not done, a banner will appear saying "Initial data already exists," and it will not be possible to close the current inspection in eNSpect on the Firm Profiling screen.

5-14.3.5 Firm Information

The Firm Overview, Additional Details, and the Firm Profiling screens should agree in firm name, address, and FEI number. For questions, contact the GWQAP staff gwqap@fda.hhs.gov.

5-14.3.6 Inspection Coverage of Profile Class Codes

When a CGMP/QS systems-based inspection is performed, coverage should reflect the overall state of control for the firm's operations. For this reason, the PCs should reflect all product classes produced by the firm as well as those covered during the inspection.

When a firm manufactures more than one commodity, e.g., drugs and devices, and the inspection covers only the drug systems, then only update the PCs that represent the drug commodity. See 5-14.7 for more information about profile classes and codes.

5-14.3.7 Discontinue and Delete Buttons

Proper use of the Discontinue and the Delete buttons*:

Discontinue button – The PCs should be discontinued if a firm goes out-of-business or no longer manufactures a drug, device, or biologic product.

Delete button - PCs and data entered in error can and should be deleted **prior** to clicking the save button and exiting the screen.

NOTE: If you save incorrect data before realizing it and you cannot delete it, contact the GWQAP Team for assistance. See 5-14.4 for Contact Information.

5-14.3.8 CGMP Inspection and Other Toggle Buttons

The CGMP Inspection toggle button is automatically activated when the Profile Required field is checked on the Maintain Inspection Results screen. The *Other* radio button should not be used for profiling purposes.

5-14.3.9 Initial, In Review, and Final

As reflected in Table 5-14.1 above, profile status should be entered as follows:

Initial: Normally entered by the Investigator. Potentially OAI inspections should be immediately entered as FAI and NAI/VAI as AC.

In Review: Pending should be entered by the Compliance Officer as soon as the record is received for review.

Final: AC should be entered by the Supervisor for NAI/VAI inspections; UN should be entered by the Compliance Officer for OAI inspections when a regulatory action has been taken.

NOTE: The Status Date automatically records the date that the information is entered or updated in Initial, In Review, and Final Profile Status. It is important to maintain the integrity of the profile information by not changing this date.

Foreign firms: The Divisions enter the initial status only and the appropriate Center enters the final profile class status.

For inspections covering CDER-regulated products the Office of Pharmaceutical Quality Operations (OPQO) will be the business unit entering the profile decision (Initial-Final) for domestic and foreign NAI and VAI inspections with the exception of for-cause assignments issued by CDER.

For inspection classifications of OAI and for NAI/VAI for-cause assignments issued by CDER, OPQO staff will be entering the Initial and in-Review status and CDER will enter the final profile decision.

5-14.3.10 Final Profile Status

It is important for the Field and Centers to understand that final profile status should be promptly entered when a final agency decision has been made. Profiles should not be held in Pending status if the Division or Center decides that the course of action is to not take enforcement action as defined by FMD-86, and, instead, re-inspect.

5-14.3.10.1 Other Status

Other should be entered as the final profile status for all profile class codes when a firm is operating under a consent decree (CD) or Application Integrity Policy (AIP). See Tables 5-14.1 & 5-14.2 above for more information.

5-14.3.10.2 Acceptable Status

AC should be entered as the final profile status when an inspection is classified as NAI or VAI and the firm is not operating under a CD or AIP. See Table 5-14.1 above for more information. If an OAI is not supported by an enforcement action, it is entered as AC as defined in Field Management Directive (FMD)-86.

5-14.3.10.3 Unacceptable Status

UN should be entered as the final profile status when there is an outstanding OAI inspection.

5-14.3.10.3.1 Continuation of Unacceptable Status

A UN status along with the regulatory action taken may be carried forward from one inspection to the next when the follow-up inspection reveals the firm had not addressed the violations identified in the original OAI inspection or an enforcement action. In this case, it is important that the Remarks field note this condition. See 5-14.3.11 Remarks field for more information.

5-14.3.10.3.2 Changing from Unacceptable to Acceptable Status

A UN status may be changed to AC when the agency's review of the firm's response to a warning letter reveals the firm's corrective actions adequately address the violations identified, a re-inspection for verification may or may not be warranted. The Remarks field must note the reason for the change.

5-14.3.11 Remark Status Field

The Remark Status field is used mainly to indicate the compliance status of a current inspection while the firm operates under a CD or AIP. See Tables 5-14.1 & 5-14.2 for more information and examples.

It may also be used to indicate an exception to the general compliance status. The profile status when under a CD will be "Others." The Remarks Status Field will show the current compliance inspection status (AC/UN). The Remarks Field will note that the firm is operating under a CD (include date and any information required concerning the current inspection.

5-14.3.12 Remarks Field

The Remarks field is a narrative field that is to be used as often as needed to:

1. Track the status of any potential or completed enforcement or alternative action with dates. This may include an explanation for a continuation of an UN final profile status from one inspection to the next when the follow up inspection reveals the firm's corrective actions were found inadequate. See Table 5-14.1 above or 5-14.4 below for more information

and accessing the OII/OBISM/DESS/ESB intranet site, respectively.
2. Indicate when a firm is operating under a CD or AIP with date. Note when there are specific conditions such as product(s) subject to the CD or AIP. This information must remain in Remarks for each PC until the CD/AIP is vacated or revoked.
3. Indicate the regulatory action and date regulatory action was issued.
4. Identify product(s) covered when using the catch all PCs MIS for devices, BMI for biologics and NEC for drugs; and
5. Indicate where a sterilization process(es) takes place such as onsite at the manufacturer, or offsite by a contract sterilizer. If offsite, include the name, address, and FEI of the contract sterilizer.

NOTE: After entering the information once, a copy and paste method can be used to update the Remarks field for each profile class involved as follows:

a. Highlight the narrative text by clicking in the Remarks field.
b. Select CTRL C to copy.
c. Select CTRL V to paste.

5-14.3.13 Out-of-Business Firm

When a profiled firm goes out of business, changes operations, or discontinues production of FDA regulated products, record the appropriate information in the eNSpect Application. From the Offline Field Client select the Firm Information tab followed by the Firm Profiling tab to discontinue each profile class code then select Save.

Navigate to the Assignment Details Page and select the **Convert to Investigation** followed by selecting the **OOB (Out of Business)** Washout Reason and confirm the selection. Synchronize to upload data to eNSpect Online.

From the Online Application select the assignment and Navigate to the Firm Overview tab. Select the Work Obligation as **N No** from the drop-down and select the **Save Assignment** button.

Once the Investigation is complete, the Out of Business data will get synched with the Firm Management Services and will update the firm's operational status to **Out of Business** and Work Obligation to **No**.

For assistance, contact the GWQAP Team. See 5-14.4 below for contact information.

5-14.3.14 Firm Merge

Before attempting to merge two or more firm records, always check to ensure all profile class codes have been finalized. Do not attempt to merge if the profile status is left in Initial or In Review. Merging firms where the profile classes are not finalized will cause problems that can only be resolved by GWQAP staff. See 5-14.4 below for contact information.

5-14.3.15 Troubleshooting

Troubleshooting information may be found at the GWQAP intranet site. See 5-14.4 for intranet site location.

5-14.4 Contact Information

To reach the Government Wide Quality Assurance Program select http://inside.fda.gov:9003/ORA/Offices/OPOP/ISM/DSS/ucm557080.htm. To contact the GWQAP Team email gwqap@fda.hhs.gov.

5-14.5 Data Quality Assurance Projects

Our GWQAP stakeholders, including the Department of Veterans Affairs (VA), the Defense Logistics Agency (DLA), as well as several Local, State, and Foreign Governments, use an external view of eNSpect profiles.

through the COMSTAT application to help them make procurement decisions for medical products. Since these stakeholders can view only the latest acceptable or unacceptable final profile status, profile classes **must** be finalized.

Each Division and Center is responsible for management of firm profiles specific to it by entering profile information and providing a profile status as soon as a final Agency decision is made. The GWQAP Team in the Division of Systems Solution/Enforcement Systems Branch (DSS/ESB) is responsible for monitoring the Divisions and Centers profile entries and communicating with the same on profile issues when profile information is incomplete, incorrect, or missing. To accomplish this, on a quarterly basis, an Online Reporting Analysis Decision Support System (ORADSS) program is run. Duplicate entries and non-finalized profile entries are addressed and a follow up is made with the Divisions and Centers when incomplete entries and/or errors are found. This data is maintained in an Excel program. It is the responsibility of the GWQAP Team to assure that

eNSpect and COMSTAT views are accurate, complete, and current.

Accessing and Running an ORADSS Report

1. From Inside. FDA select IT Applications located under Services.
2. Select OII Applications and click the ORADSS link.
3. Select Folders in the lower left corner.
4. Select the + Public Folders.
5. Select + Domestic Reports.
6. Select Firms.
7. Select FIR034_Profiles by Division.
8. A dialog box will appear to enter information
    a. From the top of the dialog box, select the appropriate Home District.
    b. Select GMP Insp Date (Start) by entering xx/xx/xxxx into the window that appears.
    c. Select GMP Insp Date (End) by entering xx/xx/xxxx.
    d. Select Enter to Run Query.
9. Saving the Report in Excel
    a. From the toolbar, select the down arrow of Export.
    b. Click Export Document as and select Excel.
    c. Excel will open with the imported data.
10. Removing Duplicate Entries in eNSpect
    a. Contact the GWQAP Team.

    Under this procedure:

    1. Profile Monitors are responsible for running quarterly reports from January 1- December 31.
    2. The GWQAP Team is responsible for conducting quarterly work group meetings and to follow-up with each Division to ensure profiles are up-to-date.

5-14.6 Establishment Profile Criteria

Table 5-14.6.1 Device, Biologic, Drug, and Veterinary Establishments TO Profile

Manufacturer	Makes a new or a changed product from one or more ingredients.
Remanufacturer	Processes, conditions, renovates, repackages, restores, or performs any other act to a finished device that significantly changes the device's performance or safety specifications or intended use.
Reprocessor	Performs remanufacturing operations on a single use device.
Packer/ Repacker	Packs a product or products into different containers without making any changes in the form of the product.
Labeler/Relabeler	An establishment which affixes the original labeling to a product or changes in any way the labeling on a product without affecting the product or its container.
Contract Sterilizers	Performs sterilization or irradiation of products or components of products regulated by FDA on a contract basis.
Control Testing Laboratories	Performs production quality control work related to products regulated by FDA on a contract basis.
Assemblers of Medical Device Kits	Responsible for assembling finished devices into medical device kits.
Specification Developer	Initiates or develops specifications for a device that is distributed under the establishment's own name but is manufactured by a second person.
HCT/P Establishment	Manufactures licensed/approved HCT/Ps that are regulated under the FD&C Act, PHS 351, 21 CFR 1271 and the drug (CGMP), medical device (QSR) or biological product regulations, i.e., “351 HCT/Ps”

Table 5-14.6.2 Establishment and Operations NOT to Profile

Blood Banks
Methadone Clinics
Manufacturers of "Research Use Only" Products
Pharmacies (including pharmacy compounders) and Retail firms
Distributors
Plasmapheresis Centers
Custom Device Manufacturers
Veterinary Medical Device Firms
X-ray Assemblers
Mammography Clinics
Manufacturers of General Purpose Articles (Devices)
Physicians Offices, Hospitals and Clinics
Laser Light Shows/Television and Microwave Oven Manufacturers

Sun tanning Establishments
Device Component Manufacturers
Clinical Investigators/Bioresearch Monitoring
Any Non-GMP Inspection
HCT/P establishments that manufacture products regulated solely under PHS 361 and 21 CFR 1271, i.e., "361 HCT/Ps"
HCT/P establishments that manufacture unlicensed/unapproved products that are regulated under the FD&C Act, PHS 351, 21 CFR 1271 and the drug (CGMP), medical device (QSR) or biological product regulations, i.e., "351 HCT/Ps"

5-14.6.3 Pre-Approval Inspections

Pharma product specific Pre-Approval and Post Approval Inspections should not be profiled unless the inspection is the initial inspection of a new profile class and the inspection results in an approval recommendation (VAI or NAI). Withhold recommendations for initial profile classes (the EI is classified as OAI) are not profiled, this assures the product cannot be marketed in the U.S. until a follow-up inspection verifies implementation of appropriate corrective actions or until corrections are substantially verified through other appropriate means.

Device Pre-Approval (PMA) inspections that cover the firm's quality management system (QMS) should be treated like any other device inspection. In all cases the initial profile status should be entered by the Investigator.

5-14.7 Profile Classes and Codes

The profile system is based upon product categories or classes and is not product specific. Select the most appropriate profile class(es) to describe the product(s) the firm manufactures or otherwise processes.

When describing devices, often more than one class is needed to describe the operations/assembly involved in the device. A rule of thumb is to think of the composition of the device and then select the profile classes that define the make-up of that device and its assembly. For example, a catheter and needle unit is profiled as MTL (metal fabrication and assembly) and PRF (plastic or rubber fabrication and assembly). A Cutter, orthopedic cast, 110 volt AC-DC, is profiled as MTL, PRF and ELE (electrical) For devices that have software and are operated by computer, codes COS (software) and COH (computer hardware) should be added.

SPD (specification developer) should be used if a firm only develops the design and specifications and has the device manufactured by someone else. Do not include other profile classes unless the firm also manufactures other medical products on-site.

When describing combination product (see IOM 5.12.1) multiple profile codes may be needed. (e.g., for a combination product CGMP inspection of a facility manufacturing a sterile- filled prefill syringe, use profile codes SVS-Sterile-filled small volume parenteral drugs and IDD-injectable delivery device (syringes, auto injectors/pens)).

Catch-all codes: MIS for devices, NEC and CRU for drugs, and BMI for biologics can be used when product does not fit into any product class identified by the list of PCs. When using these codes, identify the type of product in the Remarks field for that code. If the product is a sterile product, don't forget to include the appropriate sterilization.

5-14.7.1 Profile Class Codes

For more information, contact your Division Profile Monitor or the GWQAP team. See 5-14.4 for contact information.

Table 5-14.7.1.1 Biologics

BIOLOGICS	
Profile Class Code	**Definitions**
AEV	ANTITOXINS AND ANTIVENINS
AFP	ANIMAL DERIVED FRACTIONATION PRODUCTS
ALP	ALLERGENIC PRODUCTS
BBP	BLOOD AND BLOOD PRODUCTS UNLICENSED
BGR	BLOOD GROUPING REAGENTS
BMI	BIOLOGICAL PRODUCTS NOT OTHERWISE CLASSIFIED (Blood collection bags with anti-coagulant, plasma volume expanders, Limulus Amebocyte Lysate (LAL) test kit, etc.; Note specific product(s) in *Remarks* field)
CBS	COMPUTER BIOLOGICAL SOFTWARE
CGT	CELL AND GENE THERAPY PRODUCTS
HFP	HUMAN DERIVED FRACTIONATION PRODUCTS
LBI	LABORATORY, BIOLOGICAL TESTING

RBD	RECOMBINANT ANALOGUES OF BLOOD DERIVATIVE PRODUCTS
TIS	HUMAN TISSUE REGULATED BY FDA
VBP	VACCINE BULK PRODUCT
VFP	VACCINE FINISHED PRODUCT
VIV	IN VIVO DIAGNOSTICS
VTK	VIRAL MARKER TEST KIT

Table 5-14.7.1.2 Devices

DEVICES	
Profile Class Code	**Definitions**
AMP	ADDITIVE MANUFACTURING PROCESS (incl. 3D printing, additive manufacturing medical products)
CCR	CLINICAL CHEMISTRY REAGENTS (including diagnostic tapes, sticks, etc.)
COH	COMPUTER HARDWARE
COS	COMPUTER SOFTWARE (Devices only)
CSP	CHEMICAL STERILIZATION
CTD	CONTROL TESTING LABORATORIES "ALSO" (Device manufacturer that is also a contract testing lab.)
DKA	DEVICE KIT ASSEMBLER (Ex: lumbar puncture kit, anesthesiology kit, suture removal kit)
ELE	ELECTRICAL ASSEMBLY
FSP	FILTRATION STERILIZATION
GLA	GLASS OR CERAMIC FABRICATION AND ASSEMBLY
GSP	GAS (ETO, PROPYLENE OXIDE STERILIZATION)
HCP	HEMATOLOGY AND COAGULATION PRODUCTS
HSP	DRY HEAT STERILIZATION
HTD	HUMAN TISSUE DEVICES
IDD	INJECTABLE DELIVERY DEVICE (syringes, auto injectors/pens)
MED	MEDIA (including microbiological and tissue culture, growth media and accessories, and ingredients)
MIS	NOT ELSEWHERE CLASSIFIED (Note specific product(s) in *Remarks* field)
MSO	METERED SPRAY OTHER (incl. nasal sprays, sublingual sprays)
MTL	METAL FABRICATION AND ASSEMBLY
OID	ORALLY INHALED DELIVERY (incl. MDIs, DPIs, sprays)
OPT	OPTIC FABRICATION AND ASSEMBLY (Optical products or parts, e.g., eye glass lenses, intraocular lenses, contact lenses, lens portion of a laser, etc.)
PAT	PATCH (incl. conventional patches, micro needles)
PBM	PROCESSED BIOLOGIC MATERIAL (Only animal or plant material used as a device)
PRF	PLASTIC OR RUBBER FABRICATION AND ASSEMBLY
RIP	RADIOIMMUNOASSAY PRODUCTS
RSP	RADIATION STERILIZATION
SIP	SEROLOGICAL AND IMMUNOLOGICAL PRODUCTS (Including bacterial typing, rheumatoid factors, pregnancy kits, IVD other than VIRAL marker test kits, etc.)
SOL	DEVICE SOLUTIONS AND GELS (Including contact gels, dialysis solutions, dental pastes, adhesives, etc.)
SPD	SPECIFICATION DEVELOPERS (Note in *Remarks* field where finished product testing is conducted.)
SSP	STEAM STERILIZATION
TSP	FRACTIONAL TYNDALLIZATION STERILIZATION
TXT	TEXTILE FABRICATION AND ASSEMBLY
WOD	WOOD FABRICATION AND ASSEMBLY
WSP	WATER STERILIZATION

Table 5-14.7.1.3 Drugs and Veterinary

DRUGS	
Profile Class Code	**Definitions**
ADM	AEROSOL DISPENSED MEDICATION
CBI	RECOMBINANT/NON-RECOMBINANT PROTEIN DS OF BIOLOGIC ORIGIN
CEX	STARTING/INTERMEDIATE DERIVED FROM PLANT/ANIMAL EXTRACTION
CFN	NON-STERILE API BY FERMENTATION
CFS	STERILE API BY FERMENTATION
CHG	CAPSULES, PROMPT RELEASE
CRF	DRUG SUBSTANCE INTERMEDIATE (FERMENTATION)
CRU	DRUG SUBSTANCE INTERMEDIATE (CHEMICAL SYNTHESIS)

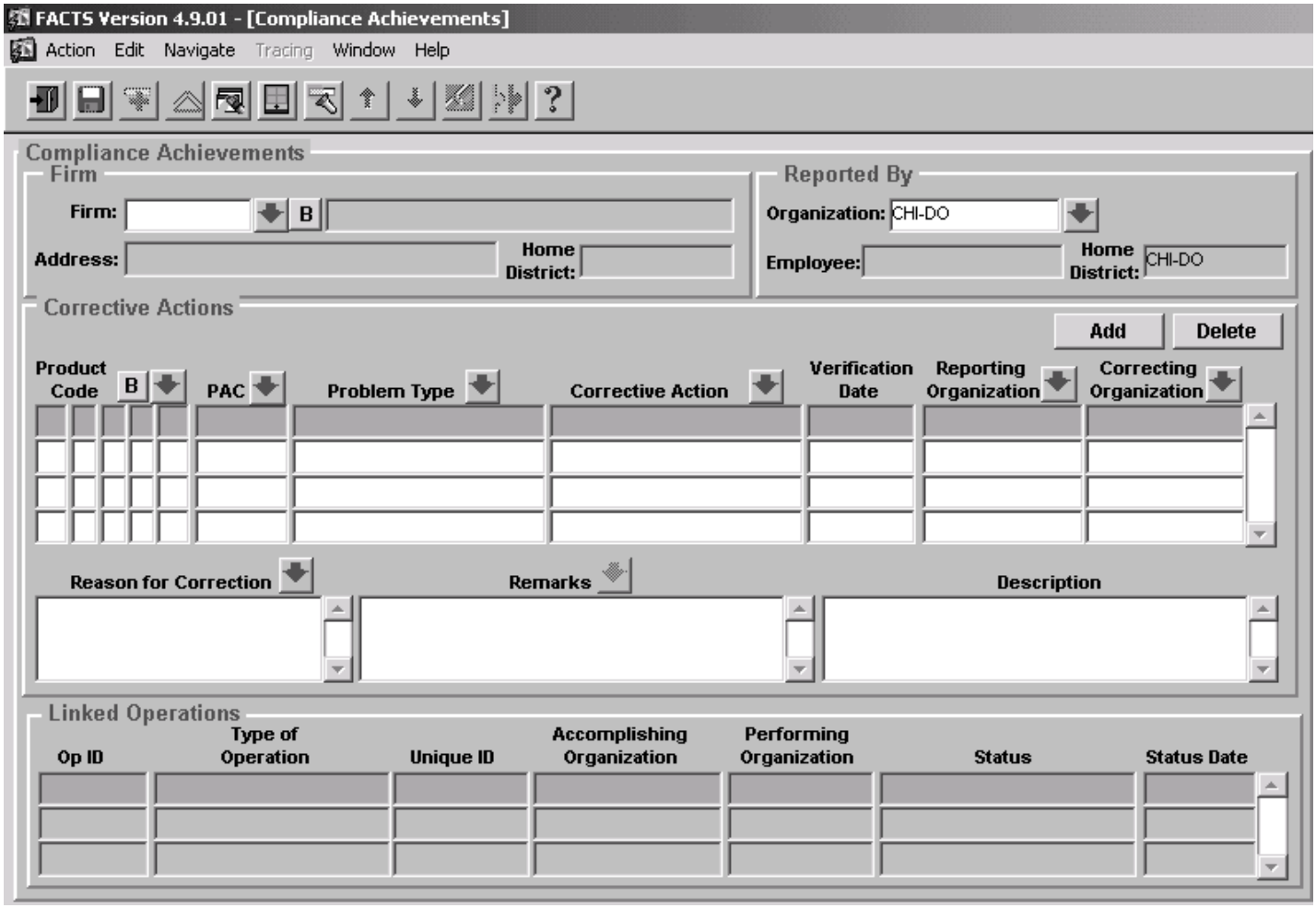
CRX	STERILE STARTING/INTERMEDIATE/NEC (not Plant/Animal)
CSG	CAPSULES, SOFT GELATIN
CSN	NON-STERILE API BY CHEMICAL SYNTHESIS
CSS	STERILE API BY CHEMICAL SYNTHESIS
CTR	CAPSULES, MODIFIED RELEASE
CXA	PURIFIED API DERIVED FROMPLANT/ANIMAL EXTRACTION
EXC	EXCIPIENT (also referred to as inactive ingredient)
GAS	MEDICAL GAS (includes liquid oxygen)
HMA	HOMEOPATHIC API/drug substance/tinctures
HMF	HOMEOPATHIC FINISHED DRUG PRODUCTS
LCP	LABORATORY, CHEMICAL/physical testing
LIQ	NON-STERILE LIQUID (other than suspensions & emulsions)
LMN	LABORATORY, MICROBIOLOGICAL-non-sterility testing
LMS	LABORATORY, MICROBIOLOGICAL-sterility testing
LVP	LARGE VOLUME PARENTERALS
PTC	PATCH (incl. conventional patches, no micro needles)
NEC	NOT ELSEWHERE CLASSIFIED FINISHED DRUG
OIN	OINTMENT, NON-STERILE (includes cream, jelly, paste)
PET	POSITRON EMISSION TOMOGRAPHY
POW	NON-STERILE POWDERS (Includes oral and topical)
SES	SUSPENSIONS AND EMULSIONS (NON-STERILE)
SLQ	STERILE LIQUID (other than suspensions & emulsions)
SON	STERILE OINTMENT
SPW	STERILE POWDER
SSE	STERILE SUSPENSIONS AND EMULSIONS (NON PARENTERALS)
SUP	SUPPOSITORIES
SVL	SMALL VOLUME PARENTERALS (Lyophilized)
SVS	STERILE-FILLED SMALL VOLUME PARENTERAL DRUGS
SVT	TERMINALLY STERILIZED SMALL VOLUME PARENTERALS
TCM	TABLETS, PROMPT RELEASE
TCT	TABLETS, DELAYED RELEASE
TDP	TRANSDERMAL PATCHES
TTR	TABLETS, EXTENDED RELEASE

NOTE: API - Active Pharmaceutical Ingredient is sometimes referred to as Drug Substance.

Table 5-14.7.1.4 Special Veterinary

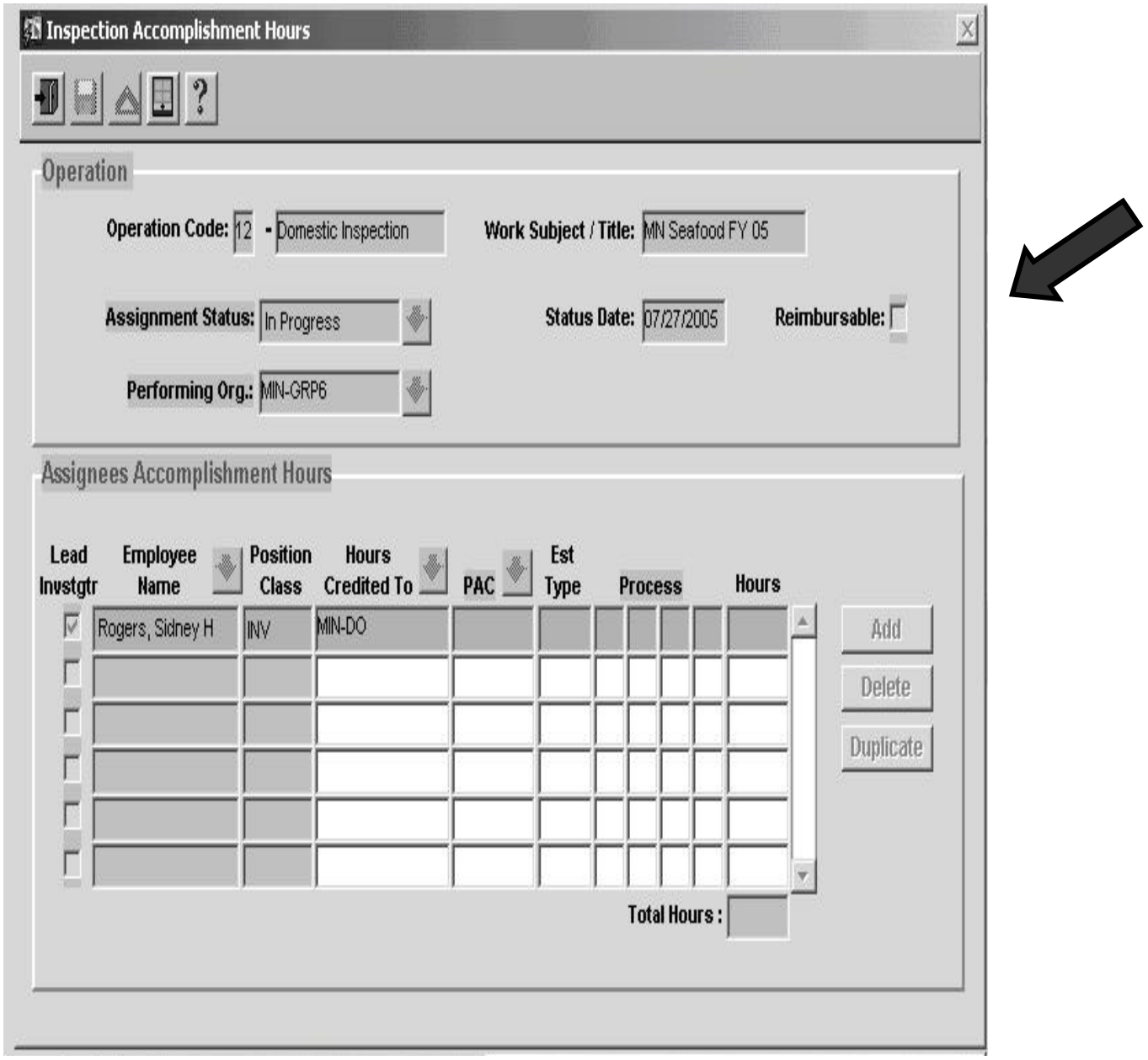
Profile Class Code	Definitions
IMN	IMPLANT NON-STERILE
IMS	IMPLANT STERILE
TAM	TYPE A MEDICATED ARTICLE

5-15 COMPLIANCE ACHIEVEMENT REPORT



5-16 FACTS REIMBURSABLE CHECK BOX

Screenshot showing location of Reimbursable check box:



5-17 FORM FDA 4056 – PRODUCE FARM INSPECTION OBSERVATIONS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

FDA

PRODUCE FARM INSPECTION OBSERVATIONS

NAME OF STATE AND DEPARTMENT *(if acting under commission with FDA)*	DISTRICT OFFICE ADDRESS

DISTRICT OFFICE PHONE NUMBER	DATE(S) OF INSPECTION *(mm/dd/yyyy)*	FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED *(First name, middle initial, last name and title of most responsible individual present)*

FARM NAME *(include business name, if different)*

FARM MAILING ADDRESS	FARM PHYSICAL LOCATION, IF DIFFERENT FROM MAILING ADDRESS *(e.g., location identifiers such as GPS coordinates)*

CROPS OBSERVED DURING INSPECTION

This form lists factual observations made by the FDA representative(s) during the inspection of the farm's operation.

This is not a final FDA determination of compliance, or non-compliance, with the Produce Safety Rule *(21 CFR Part 112)* or any other legal requirement.

This document lists observations made by the FDA representative(s) during the inspection of your operation. They are inspectional observations, and do not represent a final agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented or plan to implement corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to the FDA or state acting under commission at the address above. If you have any questions, please contact the FDA or state acting under commission at the phone number and address above.

Representatives of the regulatory agency may not examine every aspect of the farm's operation during an inspection, so a topic area left blank should not be interpreted to mean the farm is in compliance, or not in compliance, with requirements related to that topic area.

Inclusion of annotations regarding corrective actions does not signify any conclusion by the regulatory agency regarding the sufficiency of the actions.

FDA REPRESENTATIVE SIGNATURE	FDA REPRESENTATIVE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED *(mm/dd/yyyy)*

REPORTABLE OBSERVATIONS MADE DURING THE INSPECTION

☐ During an inspection of the operation (I) (we) did not observe any conditions and/or practices to be reported on this form.

☐ During an inspection of the operation (I) (we) observed the following conditions and/or practices as described below.

FARM NAME *(include business name, if different)*

DATE(S) OF INSPECTION *(mm/dd/yyyy)*	FEI NUMBER

For any observations noted, see Observation Descriptions beginning on page 4.	OBSERVATION	CORRECTIVE ACTION TAKEN
PERSONNEL QUALIFICATIONS AND TRAINING *(21 CFR PART 112, SUBPART C)*		
§§ 112.21 and 112.22: Qualifications and training for personnel who handle *(contact)* covered produce or food contact surfaces		
§ 112.23: Assignment or identification of supervisors		
§ 112.30: Record-keeping		
HEALTH AND HYGIENE *(21 CFR PART 112, SUBPART D)*		
§ 112.31: Measures to prevent ill or infected persons from contaminating covered produce with microorganisms of public health significance		
§ 112.32: Hygienic practices of personnel		
§ 112.33: Measures to prevent visitors from contaminating covered produce and food contact surfaces with microorganisms of public health significance		
AGRICULTURAL WATER *(21 CFR PART 112, SUBPART E)*		
§ 112.41: Quality of agricultural water		
§ 112.42: Inspecting and maintaining agricultural water systems		
§ 112.43: Assessing agricultural water used in growing produce other than sprouts		
§ 112.44: Water used as sprout irrigation water and for harvesting, packing, and holding produce		
§ 112.45: Measures taken for agricultural water to reduce the potential for contamination of covered produce and food contact surfaces		
§§ 112.46: Agricultural water treatment		
§ 112.50: Record-keeping		
BIOLOGICAL SOIL AMENDMENTS OF ANIMAL ORIGIN AND HUMAN WASTE *(21 CFR PART 112, SUBPART F)*		
§ 112.52: Handling, conveyance, and storage of biological soil amendments of animal origin		
§ 112.53: Use of human waste		
§§ 112.51, 112.54, 112.55, and 112.56: Determining status of biological soil amendment of animal origin; acceptable treatment processes; applicable microbial standards for such treatment processes; and, application requirements and minimum application intervals for biological soil amendments of animal origin		
§ 112.60: Record-keeping		
DOMESTICATED AND WILD ANIMALS *(21 CFR PART 112, SUBPART I)*		
§ 112.83: Measures related to grazing animals, working animals, or animal intrusion		
GROWING, HARVESTING, PACKING, AND HOLDING ACTIVITIES *(21 CFR PART 112, SUBPART K)*		
§ 112.111: Measures related to growing, harvesting, packing, or holding both covered and excluded produce		
§ 112.112: Measures to be taken immediately prior to and during harvest activities		
§ 112.113: Handling harvested covered produce		
§ 112.114: Disposition of dropped covered produce		
§ 112.115: Measures related to packaging covered produce		
§ 112.116: Measures related to food-packing *(including food-packaging)* material		

FARM NAME *(include business name, if different)*

DATE(S) OF INSPECTION *(mm/dd/yyyy)*	FEI NUMBER

For any observations noted, see Observation Descriptions beginning on page 4.	OBSERVATION	CORRECTIVE ACTION TAKEN
EQUIPMENT, TOOLS, BUILDINGS, AND SANITATION *(21 CFR PART 112, SUBPART L)*		
§ 112.123: Equipment and tools		
§ 112.124: Instruments and controls used to measure, regulate, or record		
§ 112.125: Equipment used in the transport of covered produce		
§ 112.126: Buildings		
§ 112.127: Domesticated animals in and around a fully-enclosed building		
§ 112.128: Pest control in buildings		
§ 112.129: Toilet facilities		
§ 112.130: Hand-washing facilities		
§ 112.131: Control and disposal of sewage		
§ 112.132: Control and disposal of trash, litter, and waste		
§ 112.133: Plumbing		
§ 112.134: Control of animal excreta and litter from domesticated animals		
§ 112.140: Record-keeping		
SPROUTS *(21 CFR PART 112, SUBPART M)*		
Check here if entity does not engage in growing, harvesting, packing, and/or holding of sprouts		
§ 112.142: Seeds or beans used to grow sprouts		
§ 112.143(a): Fully-enclosed buildings		
§ 112.143(b): Cleaning and sanitizing food-contact surfaces		
§§ 112.144(a), 112.145, and 112.146: Environmental monitoring for Listeria species or L. monocytogenes *(written environmental monitoring plan, collection and testing, corrective actions)*		
§§ 112.144(b) and (c), 112.147 and 112.148: Testing spent irrigation water or in-process sprouts for pathogens *(written sampling plan, collection and testing, corrective actions)*		
§ 112.150: Record-keeping		
ANALYTICAL METHODS *(21 CFR PART 112, SUBPART N)*		
§ 112.151 – 112.153: Analytical Methods		
RECORDS *(21 CFR PART 112, SUBPART O)*		
§ 112.161 - 112.167: General record-keeping		
OTHER OBSERVATIONS		
Other		

FARM NAME *(include business name, if different)*	
DATE(S) OF INSPECTION *(mm/dd/yyyy)*	FEI NUMBER
OBSERVATION DESCRIPTIONS AND/OR ADDITIONAL COMMENTS	

FARM NAME *(include business name, if different)*

DATE(S) OF INSPECTION *(mm/dd/yyyy)*	FEI NUMBER

OBSERVATION DESCRIPTIONS *(continued)*

Add Continuation Page

☐ If box is marked, see attached Produce Farm Inspection Observations Continuation Sheet(s).

The observations of conditions and practices listed on this form are reported:

1. Pursuant to Section 704(b) of the FEDERAL FOOD, DRUG, AND COSMETIC ACT, or
2. To assist firms inspected in complying with applicable laws and regulations.

Any reference to this report in labeling, advertising, or other sales promotion by any person is prohibited under Section 301(n) of the FEDERAL FOOD, DRUG AND COSMETIC ACT.

PRODUCE FARM INSPECTION OBSERVATIONS CONTINUATION SHEET

FARM NAME *(include business name, if different)*

DATE(S) OF INSPECTION *(mm/dd/yyyy)*	FEI NUMBER

OBSERVATION DESCRIPTIONS *(continued)*

Add Continuation Page

COMPLETION OF THE FORM FDA 4056Produce Farm Pre-Announcement

The OII Division of Produce Safety (DPS) should follow instructions in the Produce Safety Inspections Compliance Program Guidance Manual (CPGM) for inspection pre-announcement. Follow guidance in the Produce Safety Inspection Protocol for reporting in the Produce Farm Inspection Report (PFIR) when inspection pre-announcement does not occur.

Form FDA 4056:

General instructions – These instructions are updated for the revised FDA 4056, version (02/26). Form FDA 4056 is to be issued during the close-out meeting for all produce farm inspections, including when there are no written observations. The instructions below are specific to completion of the form. See 5.5.10 and 5.5.11 for instruction on other aspects of reporting observations.**Name of State and Department (if acting under commission with FDA**) – If the FDA 4056 is used by a state acting under FDA commission, the name of the state agency. For an FDA led inspection, place "N/A" in this section.

District Office Address –

- Domestic: the mailing address of the District Office where the farm is located. See Appendix E for boundary maps.
- Foreign: the mailing address for OII/DFFIGO (12420 Parklawn Dr, Rm 2037 HFC-130, Rockville, MD 20857).
- State under FDA commission: the state agency office mailing address.

District Office Phone Number - Area code and phone number of the District Office for the inspected location, or of the state agency, if applicable.

Date(s) of Inspection - Enter actual date(s) of inspection. If multiple consecutive days, dates can be represented as an inclusive date range. If there is insufficient space, enter the first and last dates of inspection as a date range followed by an asterisk: "[MM/DD/YYYY] – [MM/DD/YYYY] *". In the Under Observation Descriptions and/or Additional Comments , enter "*DATES OF INSPECTION" followed by the full listing of actual dates of inspection.

FEI Number – Enter the FDA Establishment Identifier as per the Official Establishment Inventory (OEI). States under FDA commission can enter either the FEI number (if known) or the farm's state ID number.

Name and Title of Individual to Whom Report is Issued (First name, middle initial, last name of most responsible individual present) - The legal name and full title of the person to whom the form is issued. If the person does not have a middle initial, enter "NMI" for no middle initial.

Farm Name (include business name, if different) - The full, legal name of the farm, including any abbreviations, quotation marks, dashes, commas, etc. If the farm uses another name for business purposes (i.e., a "dba"), include the other name also.

Farm Mailing Address – Address, city, state, and zip code at which the farm receives mail.

Farm Physical Location, If Different from Mailing Address (e.g., location Identifiers such as GPS coordinates) - Street address, city, state, and zip code where the farm is located. Do not use a P.O. Box unless P.O. Box is part of the address such as on a Rural Route. Include GPS coordinates of the main farm building, if available.

Crops Observed During Inspection - List the crops for which some element of growing, harvesting, packing, and/or holding were observed during the inspection. If the farm grows or handles other crops but those crops were not observed during the inspection, do not list them. Produce Safety Rule inspections should be conducted when covered activities on covered produce can be observed. As an exception, such as during an active outbreak response, enter "N/A" when no crops are observed.

FDA REPRESENTATIVE SIGNATURE

- eNSpect generated version: electronic signature of lead investigator.
- PDF version: electronic signature of lead investigator or state inspector.
- Paper version: signature in ink of each investigator and/or inspector.

NOTE: On the FDA 4056, the signature is captured on one page in the FDA Representative Signature block. .

The FDA 4056 should be completed and signed electronically in eNSpect prior to issuance by print or email. In circumstances where eNSpect cannot be used to complete the FDA 4056, complete the fillable PDF form. .

When it is not possible to complete an FDA 4056 using eNSpect, or the fillable PDF form, it is permissible to complete a hardcopy FDA 4056 in ink, printed from the PDF form. A copy of the signed FDA 4056 must be obtained for inclusion in the PFIR.

FDA REPRESENTATIVE(S) NAME AND TITLE - Name and title of all inspection team members (should match all members who signed the Form FDA 482(s), Notice of Inspection)

Date Issued – Date the inspection is completed and the form is issued.

Reportable Observations Made During the Inspection

One of the two boxes must be marked. The boxes indicate:

- ☐ During an inspection of the operation (I) (we) did not observe any conditions and/or practices to be reported on this form.
- ☐ During an inspection of the operation (I) (we) observed the following conditions and/or practices as described below.

When the first box is marked to indicate no reportable observations, the rest of the form will be left blank except for page headers, the Sprouts checkbox (if applicable; see Sprouts section in this document), , and any comments in Observations Descriptions and/or Additional Comments (e.g. full inspection date listing or full listing of team members).

Observation Column

When the second box above is marked, reportable observation(s) will be indicated in the table on pages 2-3 with Xs in the appropriate row of the Observation column. An X in a row of the Observation column can indicate one or more observations corresponding to the regulation section(s) in that row. However, an observation relating to more than one section of the regulation must only be marked in one row. Choose the row corresponding to the most appropriate regulation section. Use the Other row under Other Observations to indicate one or more observations that do not correspond to other table rows (e.g. those based on the FD&C Act or based on 21 CFR 117 requirements, if applicable). All observations indicated in the table are to have descriptions beginning in the Observation Descriptions and/or Additional Comments section.

NOTE: It is not an acceptable use of the form to only indicate areas of deficiency in the table without also including narrative description beginning in the Observation Descriptions and/or Additional Comments section.

Corrective Action Taken Column

Mark an X in the Corrective Action Taken column of the table on pages 2-3 only when all of the following apply:

1) The row is marked for an observation;
2) The corrective action status is either Corrected & Verified or Reported Corrected, Not Verified; and
3) The corrective action is for a current inspection observation (i.e. not for corrections to observations from prior inspections).

Sprouts

When an inspection covers sprouts in addition to covering other types of produce subject to the Produce Safety Rule, use the Sprouts (21 CFR 112, Subpart M) section of the table on pages 2 and 3 to indicate observations falling under Subpart M. Use the FDA 483 instead of the FDA 4056 for inspections that only cover sprouts. For all farms that do not engage in activities subject to Subpart M, check the box labeled "Check here if entity does not engage in growing, harvesting, packing, and/or holding of sprouts". If sprouts activities occur but were not inspected, enter in Observation Descriptions and/or Additional Comments: "Sprouts (21 CFR Part 112, Subpart M) were not covered during this inspection."

Observation Descriptions and/or Additional Comments

Previous sections of this instruction note instances where comments are to appear in this section beginning on page 4 of the form. Additionally, all amended FDA 4056s must state "AMENDMENT" in the this section followed by the amendment number, e.g. "AMENDMENT 1". Any additional amendments required for the same inspection will be identified with the next sequential number. See 5.5.10.9 for more information on correcting and amending the FDA 4056. On page 4, first list any comments and then begin observation descriptions.

Note: For each observation, provide the following information:

1) Observation number. Start with Observation 1, the most significant observation and continue with subsequent observations in descending order of significance.
2) The table row corresponding to the observation (from pages 2-3). Write out the regulatory citation number(s) and the text from that row, or if the observation corresponds to the Other row, write: "Other reportable observation made during the inspection."
3) The Long Description, or a one sentence summary of the deficiency from the regulation written in the second person. Long Descriptions are automatically generated from eNSpect. This is optional for state inspectors.
4) The specific description of the observation, beginning with the word "Specifically." Include enough detail for the farm and other readers to understand the specifics and the significance of the observation.
5) The corrective action status. If the corrective action status is Corrected & Verified; Reported Corrected, Not Verified; or Promised to Correct; include the words "Corrective Action:" followed by one of these three statuses. Otherwise, do not include corrective action information.

NOTE: It is best practice to verify the farm's completed corrective actions as long as the verification does not unreasonably extend the duration of the inspection. The corrective action statuses that can appear on the form indicate that corrections are fully implemented (Corrected & Verified; Reported Corrected, Not Verified) or that the farm has committed to corrective action but has not completed it by the close of the inspection (Promised to Correct). These three corrective action statuses are the only annotations permitted on form FDA 4056 (see 5.5.11.4, Annotation of the FDA 483 or FDA 4056). Do not provide further description of corrective actions on the form. Corrective action details should be documented in regulatory notes and described in the PFIR or inspection report summary, as appropriate. Corrective actions related to written observations from a previous inspection or to discussion items (current or previous inspection) do not appear on the form, but are to be described in regulatory notes and in the PFIR

(FDA and states) or the inspection report summary (states only). Consider whether items discussed with management during previous inspections need to be added as observations to the current FDA 4056, such as if no corrective action has been taken and conditions have worsened or present a risk to the product.

Example Observation Description:

Observation 1:
§ 112.151 - 112.153: Analytical Methods
You did not test the quality of water using a scientifically valid method.
Specifically, [specific description of the observation].
Corrective Action: Promised to Correct

Observation Descriptions (continued) Page 5, Observation Descriptions (continued) is the final page of the base form. In any instance where there are blank spaces on pages 4 and 5, write "N/A", "This section is intentionally left blank" or a similar statement.

If observation descriptions extend past the space provided on pages 4 and 5 of the base form, the process for adding pages depends on the format of the form.

System-generated form (eNSpect) – eNSpect Field Client will automatically generate as many additional Observation Description (continued) pages as needed to accommodate observation text. These pages will extend the number of pages in the base form. The eNSpect-generated form will not mark the box "If box is marked, see attached Produce Farm Inspection Observations Continuation Sheet(s)" because the additional pages are not considered continuation sheets. The total number of pages will be indicated in the form footer.

Fillable PDF form – page 5 of the form contains an "Add Continuation Page" button. Clicking this button adds the first page of the Produce Farm Inspection Observations Continuation Sheet and marks the corresponding box on page 5. Additional continuation sheet pages can be added by clicking on any "Add Continuation Page" button. The form automatically numbers continuation pages in the footer.

Hardcopy form – a paper form for completion with pen and ink would need to be created by printing either the non-fillable or fillable PDF version of the form. If printing the non-fillable pdf form, be sure to print as many copies of the Produce Farm Inspection Observations Continuation Sheet as needed to accommodate observations text. The continuation sheet box on page 5 will need to be marked. The continuation sheet pages will need current and total page numbers entered in the footer. It would also be possible to print the fillable PDF version of the form after generating the expected number of continuation sheet pages needed to accommodate observation description text.

5-18 – FORM FDA 483a

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF REVIEW OF YOUR FSVP RECORDS
#1	#2
	FEI NUMBER #3
Industry Information: www.fda.gov/oc/industry	

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
#4

FIRM NAME	STREET ADDRESS
#5	#6
CITY, STATE AND ZIP CODE	E-MAIL ADDRESS #7

This document lists observations made by the FDA representative(s) during the review of your Foreign Supplier Verification Program (FSVP). They are observations, and do not represent a final agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s), including by submitting this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

During a review of your Foreign Supplier Verification Program I (we) observed:

#8

ADD Continuation Page

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
	#9	#10	#11

FORM FDA 483a (2/16) **FSVP OBSERVATIONS** **Page 1 of 2**

PSC Publishing Services (301) 443-6740 EF

COMPLETION OF THE FORM FDA 483a

Presently there are three ways to generate an FDA 483a.

- eNSpect
- Electronic (non-eNSpect) version
- Handwritten hard copy

Where possible, you should be creating, issuing, and signing the Form FDA 483a via the eNSpect method. Many of the fields in the form are either partially or fully automated when using this method.

When using an electronic (non-eNSpect) or handwritten hard copy of the FDA 483a, the current version must be used.

The sections of the Form FDA 483a are identified below, with numbers corresponding to the preceding blank version of the form.

1 - District Office Address and Phone Number - Legibly print the home District address where the **firm** is physically located, regardless of program area or investigator duty station. Include the district office commercial telephone number and area code. If using eNSpect for the FDA 483a, select the home district of the firm.

For example, if a firm is located in Little Rock, Arkansas, then the district office would be Dallas District Office. See Appendix E for boundary maps.

For foreign inspections, the address to be used for this box will be provided as part of the assignment.

2 - Date(s) of Review of Your FSVP Records - Enter actual or inclusive date(s) of review.

3 - FEI Number - If the FDA Establishment Identifier is on the assignment, enter it here. If not readily available, leave blank.

4 - Name and Title of individual to whom report is issued - Enter legal first name, middle initial and last name, and full title of the person to whom the form is issued.

5 - Firm Name - Enter full, legal name of the firm, including any abbreviations, quotation marks, dashes, commas, etc.

6 - Street address, city, state, and Zip Code - Enter street address, city, state, and Zip Code. (Not P.O. Box unless P.O. Box is part of the address such as on a Rural Route).

7 – E-Mail Address – Enter the e-mail address for the firm.

8 - Observations – See IOM 5.5.11 for information about what observations are considered “reportable” and may be listed on the Form FDA 483a. Enter your reportable observations succinctly and clearly. Conditions listed should be significant and relate to an observed or potential problem with the facility, equipment, processes, controls, products, employee practices, or records. “Potential problems” should have a reasonable likelihood of occurring based upon observed conditions or events. Do not cite deviations from policy or guidance documents on your FDA 483a.

Where applicable, when formulating each FDA 483a observation, answer Who (using titles or initials when necessary), What, When, Where, Why, How Much and How Often? Challenge each observation by asking “So

What"? (regarding its significance).

As appropriate, FDA 483a observations should include relationship of observations to a given population, for example, "Two out of 50 records examined were * * *" or "4 out of 12 bags examined were ***." When appropriate, an FDA 483a observation may refer to inadequate situations as long as you provide supporting facts (examples) or explanation as to why the condition, practice or procedure observed is inadequate.

It is preferred not to identify individuals or firms by name (e.g., suppliers and consignees) within the FDA 483a. Where appropriate to support the FDA 483a observation, identify the individual(s) or firm(s) by substituting other non-specific identifying information as below. Document your evidence in your EIR, fully explaining the relationship(s).

f. The lot number for a component received from or shipped to firm "A".
g. The invoice number for a shipment from or to firm "A".
h. A patient #, record #. See IOM 5.2.3.3 item 7.
i. The study number for a particular Clinical Investigator site.
j. Other necessary but non-specific identifying information to show the observation's relationship to a particular firm and/or individual.

9 - Employee(s) signature

Everyone present under FDA inspectional authority at issuance signs the FDA 483a. However, absence of a team member at the conclusion of an inspection need not prevent issuance of the form (see IOM 5.1.2.5.1). If signing the FDA 483a digitally using eNSpect, the lead CSO's signature will appear on all pages of the FDA 483a and the remaining team members' signature will appear on the last page. When it is necessary to use pen to sign the form (e.g., when issuing a handwritten hard copy version), each person signs the first and last pages of the FDA 483a and initials each intervening page in the signature block.

When using eNSpect to sign the Form FDA 483a, the system will retain a copy of the digitally signed form automatically. If you do not use eNSpect to digitally sign the document, assure you retain a digitally signed copy. If using a pen to sign the form, make a photocopy or carbon copy of the signed form. An unsigned photocopy or printed duplicate is unacceptable to maintain with the division's files. See IOM 5.2.3.6.2.

10 - Employee(s) name and title

The names of everyone who participated in the inspection with the issuance of an FDA 482 should be listed on the FDA 483a, even if they are not available to sign the document.

11 - Date Issued - Enter the date the form is actually issued to the firm's management.

5-19 – Biosecurity

Routine Biosecurity Procedures for Visits to Facilities Housing or Transporting Domestic or Wild Animals

This section is FDA's guidance when you visit any type of facility where any domestic or wild animals are housed or transported. If a firm has more restrictive controls, follow those in addition to the controls cited below as long as they do not interfere with your assignment needs. The controls and procedures are intended to prevent you from becoming a vector or carrier of animal diseases, to prevent the spread of animal disease, and to set a good example for stockmen, growers, and industry servicemen. A number of chronic diseases, such as Johne's Disease, bovine virus diarrhea (BVD) and others exist in domestic animals which you can unknowingly spread. Any inspectional contact with herds of livestock (including poultry) or non-domesticated animals exposes you to potential claims of introducing or spreading disease. This could occur between sections of a single site, such as poultry houses, or between different sites or farms. The potential also exists for the introduction of disease from an animal processing plant, such as a slaughterhouse or renderer to a live animal facility. You can prevent this by following appropriate cleaning and disinfection steps between facilities. Generally, a break of 5 days or more between sites is sufficient to eliminate concern about transmission of infectious agents.

These precautions, biosecurity measures, are necessary in two types of situations. The first is when there is no known disease present and your actions are precautionary. This section primarily addresses those kinds of activities. The other situation involves known or suspected disease outbreaks or more notorious disease conditions such as salmonella in eggs, infectious Laryngotracheitis, foot and mouth disease, vesicular stomatitis, and blackhead which can be highly contagious and spread from one group of animals to another by movement of people and objects between infected and non-infected groups. In these cases, special precautions must be taken to make sure you are not an unknowing vector for the spread of disease.

Biosecurity on a produce farm is a set of preventive measures designed to protect the farm, including crops and livestock, from bacterial, fungal, and viral diseases and agricultural pests. When conducting a produce safety inspection, you should abide by the farm’s policies. During the pre-inspection call and prior to entering the growing area, you should ask if the farm has implemented biosecurity practices. You should follow these animal and phytosanitary practices and procedures requirements.

If you will only be inspecting an office or house away from areas where animals are housed or kept, clean and suitable street attire may be sufficient. Be aware if you visit any area of a facility where animals have been, you should always sanitize, clean, or change footwear and it may be necessary to change outerwear before visiting another animal site to prevent any possibility of transmission of disease.

Your vehicle may also transport infection if you drive through contaminated areas and may require frequent cleaning between sites.

Pre-Inspection Activities

When you know you are going to visit or inspect any animal production or holding facility, consider contacting the State Veterinarian and/or the Regional APHIS office to determine if there are any areas in the state under quarantine or special measures to control animal diseases. APHIS office locations can be found on their website. The State Veterinarian will be listed under Government Listings in your phone

book and is listed at this website. Milk Specialists frequently working with State counterparts in the Interstate Milk Shippers program should contact these sources at least quarterly for updates. Ask for any special controls or procedures they recommend. Follow any guidance they offer in addition to the precautions in this section. You should also consider pre-notification of the facility unless your assignment does not allow pre-notification. If you elect to pre-announce the inspection, in addition to the normal contact, ask to speak with the person at the facility responsible for their biosecurity measures and find out what they require of employees and visitors. If their requests do not interfere with your ability to do your job, follow their requests as we do when inspecting sterile manufacturing facilities.

Make sure your vehicle is clean and has been recently washed. Commercial car washes are adequate as long as you check to make sure any dirt, manure or other debris, which may be present from a previous site, has been removed. Some facilities may require additional disinfection of tires upon entry to the premises. Ensure tires and floor mats are clean. Consider designating places in your vehicle for storage of clean, unused supplies and dirty or used supplies.

In addition to your normal inspectional tools, obtain the following equipment and supplies from your program division:

- Laundered or disposable coveralls or smocks (coveralls are suggested because they give better coverage). If you are going to visit multiple facilities in one day or trip, obtain sufficient quantities so you can change into clean or unused clothing between each site.
- Disposable plastic gloves, rubber boots, which can be sanitized, and disposable shoe/boot covers. Rubber boots over which you place disposable shoe/boot covers are preferred.
- Reusable cloth or plastic laundry bag(s) for clothing to be laundered. (Disposable bags can be used.)
- Soap, water and disposable or freshly laundered individual hand (or paper) towels.
- Sanitizing solution(s) and equipment (brushes, bucket, tray, measuring devices, etc.) to permit you to properly sanitizing hands, boots, equipment, and your vehicle. Most disinfectants will require removing organic matter before use and good brushes are essential to remove dirt from boots and other objects.

Make sure any equipment you take with you has been thoroughly cleaned and sanitized as necessary. Clip boards, briefcases, flashlights, inspectional sampling tools, coolers, brushes, buckets, and other objects should be cleaned between uses as necessary and between visits to any suspected infected facilities. Disposable equipment should be used to the fullest extent possible.

Additional information for produce safety inspection staff to follow is in the Standardized Approach to Produce Farm Inspections document.

Maintain copies of any applicable Material Safety Data Sheets (MSDS) for disinfectants with you in your vehicle. If the firm's management requests information on the disinfectants you are using, they may read or copy these MSDS. Be familiar with the instructions and precautions concerning use of disinfectants. Any disinfectant should be effective against known or suspected microbiological agents.

In the event of a foreign animal disease, contact the USDA, APHIS Veterinary Services area Veterinarian in Charge for additional precautions and procedures to follow. (See 5.2.10.3)

General Inspection Procedures

Always begin each day with a clean vehicle free from any visible dirt or debris. During the day, take precautions to minimize contamination of your vehicle. If your vehicle becomes obviously dirty with adhering mud or manure, clean it before visiting another animal facility. When you arrive at a facility where animals are located, check to see if there are designated parking spots or pads for visitors. If so, park your vehicle there unless directed otherwise by the firm. If there is no guidance, park well away from all areas housing animals. When you arrive, inquire about or reconfirm any biosecurity measures the firm employs. Confirm your actions are suitable and follow expectations of the facility when this does not interfere with your inspection ability. Follow steps requested by the firm to remove contamination from vehicles, which may include troughs or pools of disinfectants for tires or other control measures. Avoid driving through manure, mud, or wastewater at these sites.

In general, entry to animal housing or feeding areas, corrals, calf pens, hospital pens or special treatment facilities should be avoided unless the assignment requires their inspection or there are specific reasons requiring entry. If you must visit the feeding area occupied by livestock or birds, first determine if any groups are infected with disease. Arrange to visit the known non-disease areas first. Do not handle any animals unless official duty requires such contact. Before leaving the area where you parked your car, put on protective clothing as described and proceed with the purpose of your visit; sanitizing hands (and gloves if worn) and boots as necessary during the visit or inspection.

General procedures:

- Wear rubber boots or other suitable footwear, which you disinfect upon arriving at the site and prior to departure. It is preferable to also place disposable foot coverings over your footwear, regardless of the type, after you have disinfected them. If the firm has footbaths, use them. Boots and footwear should be disinfected with any of the agents identified at the end of this subsection using a good brush. Clean and disinfect the brush(es) and bucket you use for these activities.
- Wash your hands with soap and water. If you are visiting a facility where a known animal disease is present or the firm's biosecurity protocol requires, wear disposable gloves.
- Wear disposable or freshly laundered coveralls, when appropriate. Some facilities may provide disposable coveralls and require visitors to shower in and shower out at their facilities. If requested by the firm and facilities are provided, you should follow those requests.
- Wear appropriate head coverings, as necessary. If you wear a head covering, clean and disinfect between facilities or use disposable head coverings.
- Minimize any materials you carry with you such as notebooks, flashlights, etc. to what is required. Consider keeping these things in clean plastic bags or containers between uses. Disinfect any of these types of items as best you can between visits to facilities or between different animal-housing areas.
- If you are visiting production units with animals of multiple ages, always try to work from the youngest to the oldest.
- Avoid direct contact with livestock or wild animals, bodily fluids or animal byproducts when visiting facilities.
- Milk Specialists, Milk Safety Branch and State Training Team staff frequently working with State counterparts in the Interstate Milk Shippers program shall follow any biosecurity measures the firm employs, any biosecurity measures the State employs, and as a minimum shall follow the coded memoranda issued by HFP Milk Safety Branch on this subject.

Upon completing your assignment in a given animal area, return to the same area where you donned protective clothing. Remove disposable shoe/boot covers and gloves, if applicable, and place them in a disposable paper or plastic bag. Clean and sanitize boots/footwear. Remove the protective clothing, if applicable, by peeling it off inside out. (This keeps the surfaces exposed to contamination on the inside.) Unless the firm's biosecurity plan prohibits removal of waste from their premises, all waste should be disposed of by the investigator as follows: Place all disposable items in a disposable, nonporous bag for appropriate disposal according to State and/or local regulations. Place reusable coveralls or other reusable protective clothing in a separate bag for disposition at the office.

Follow guidance on biosecurity provided in the applicable Compliance Program or "Guide to the Inspection of "***" in addition to precautions in this Section.

Repeat these procedures for each separate location visited or inspected.

Purchase commercially available solutions for disinfecting objects or consult with your servicing laboratory. Commercial products such as Nolvosan, Efersan, One Stroke Environ or Virkon-S may be used as long as they are registered by EPA for the intended purpose. Lye or chlorine based cleaners and disinfectants may also be used.

The following formula for household bleach may be used. Mix 3/4 cup (6 oz) of liquid bleach (5.25%) in one gallon of water (128 oz). This solution will be approximately 1:20 dilution. Formulations of household bleach, which are more concentrated than 5.25% are commercially available. Dilute accordingly to these directions. A more concentrated 1:10 solution (1-oz bleach to 9-oz water) may be used with decreased contact time required. Dilutions should be prepared fresh daily and protected from light.

You should read the label and be familiar with directions and precautions, such as removing any organic matter from objects to be disinfected, for any disinfectant you use. In the absence of directions or for chlorine solutions you prepare: 1. Remove visible dirt from the object (boots, tools, tires, etc.). 2. Wipe, brush or scrub surfaces with the solution and keep wet for 2 minutes. 3. Allow to air dry or dry with previously sterilized toweling.

Special Situation Precautions

If you are required to inspect or visit a facility known or suspected to be involved in a contagious animal disease an outbreak or otherwise identified as having diseased animals, contact the Center for Veterinary Medicine and/or Center for Food Safety and Applied Nutrition for additional precautions which may be necessary before you visit these sites. Your activities may be limited to visiting a single site in a day, taking extra-ordinary decontamination steps, ensuring you do not visit or inspect another facility for 5 or more days following the visit to the contaminated site or other steps. APHIS may have special restrictions or precautions for you to follow. The State Veterinarian may also request you follow additional requirements. During inspections of poultry operations where salmonella contamination is known or suspected, you should make sure you contact HFP directly for specific procedures to follow. Additional decontamination steps will be required.

Standard Operating Biosecurity Procedures for Egg Farm Inspections/ commercial Poultry Operations

Classification of Farms

Program divisions should categorize inspections according to risk with farms providing out-door access being considered the highest risk to HPAI. Large farms (those with ≥ 50,000 layers should be inspected first, followed by small farms (those with between 3,000-49,999 layers) and farms with outdoor access (regardless of the number of birds at the farm) should be inspected last. For example, if a program division is assigned 15 inspections as part of an Egg Assignment, and 5 of those firms provide outdoor access, the 10 farms that do not provide outdoor access should be inspected first and the 5 with outdoor access should be inspected last. Of the first 10 of these inspections the largest farms (from a number of layers at the farm perspective) should be inspected first and then in descending order as the number of layers decreases (a farm with 1 million layers would be inspected before a farm with 750,000 layers, even though both are classified as large farms).

Biosecurity Practices

These practices should be followed on every egg farm inspection. It is the responsibility of the lead investigator to brief his/her inspectional team on these practices prior to arrival at the farm.

Pre-Inspection Measures

1. Contact the State Veterinarian to check for quarantines. No egg inspections should be initiated without first contacting the state veterinary office and checking for quarantines. Investigators should ask if there is any type of quarantine and follow that up with a question specifically about HPAI-related quarantines. If quarantines are in place, investigators should ask how long they are expected to continue. If the state veterinarian or official designated by the state indicates that inspections should not continue, those instructions should be followed, and no inspections should be conducted until state clearance is given. If an extended quarantine is expected (longer than 2 weeks), the program division should organize a follow up meeting to include the program division, State Veterinary Office or designated state official, ORA-OFFO, CFSAN-OFS, and CFSAN-OC (see contacts at the end of this document). The purpose of these meetings will be to establish a channel of communication between FDA and the State to ensure state concerns are addressed while ensuring FDA's inspectional obligations are met.
2. Following clearance from the state veterinarian's office, the lead investigator should conduct a cross reference check of the inspection location against the HPAI Current Avian Influenza findings on the USDA/APHIS web page. The Current Avian Influenza findings can be found at the following web address: https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/nvap/NVAP-Reference-Guide/Poultry/Avian-Influenza
3. During the cross check, investigators should check the state and county from the USDA/APHIS webpage against the location of the farm to be inspected. If the farm is in the same county as a confirmed HPAI occurrence, the program division should cancel the inspection and set up a follow up meeting to include the program division, OII OCE, HFP-OCE and HFP-OMFS (see contacts at the end of this document). During this meeting, the following information will be considered: the confirmation date of the occurrence (how far removed from the time HPAI was detected to when the current inspection is scheduled), the relative locations of the HPAI infected site and the farm to be inspected (the infected, buffer, and surveillance zone criteria established by APHIS will be considered), and other

pertinent information. After all pertinent information is considered, a decision will be made to either cancel the inspection or reschedule it for a more appropriate time.

4. The mandatory minimum wait time between different farms is 72 hrs. However, many farms have increased the wait period to longer than 72 hrs. in response to lessons learned from the 2015 HPAI outbreak. If the wait time established by the producer is longer than 72 hrs., that specified wait time should be adhered to. In situations where the farm to be inspected includes outdoor access for the birds (this information should be established during the pre-inspection call) the minimum wait time between farms increases to 1 week. Contact with specific bird populations could also result into mandatory one week minimum wait times. Bird populations should be categorized into two broad categories. Population 1 includes birds that are under a biosecurity plan as specified in 21 CFR 110 118.4(b)(1) through (5) (this populations most often will refer to only those birds at commercial farms, i.e., those to be inspected). Population 2 includes all other birds, including but not limited to backyard flocks, duck or geese or other bird populations at municipal parks, avian species at zoological gardens, chicks, or ducklings at feed stores, etc. If an investigator only has contact with Population 1 AND if the farm to be inspected has an established wait time of less than 1 week, that time requirement should be followed. If an investigator has contact with Population 2, they MUST wait 1 week before conducting an inspection.
5. When possible, program divisions should send separate inspectional teams on egg farm inspections such that the time between separate farm visits for any one inspectional team is maximized. For example, rather than sending Inspectional Team A to conduct inspections at Farm 1, Farm 2 and Farm 3, every attempt should be made to instead send Inspectional Team A to conduct the inspection at Farm 1, Inspectional Team B to conduct the inspection at Farm 2 and Inspectional Team C to conduct the inspection at Farm 3. The goal being to increase the length of time that any of the three inspectional teams have to visit the next farm up for inspection.
6. Vehicles to be used during inspections should be washed a maximum of 24 hours before and after each egg inspection. Given that HPAI is highly susceptible to detergents, high temperatures and desiccation, cars washes where hand held nozzles are available should be used when possible. Initially, a cycle should be conducted where a high-pressure rinse is used to remove all organic matter (e.g., mud, dirt and debris) with specific care taken to address the wheel wells, tires, vehicle undercarriage, and vehicle body. This should be followed by a cycle where a scrub brush with a detergent is used on the whole vehicle including the wheel wells, tires, and vehicle body. Subsequently, a high-pressure rinse that includes the wheel wells, tires, vehicle undercarriage and vehicle body should be completed. The interior of the vehicle should then be vacuumed thoroughly to remove organic matter and floor mats sprayed with a disinfectant aerosol spray. The vehicle should then be allowed to dry thoroughly in a sunny area (as opposed to a shaded garage). After the vehicle has dried, disinfectant should be applied to the wheel wells, tires, and undercarriage (See item #11 below for appropriate disinfectant selection). The vehicle body does not have to be disinfected.

When necessary or during inclement weather, drive-through car washes may be substituted for manual car washes provided that the cycle includes an undercarriage wash, application of a detergent and a

high-pressure rinse. The interior should still be vacuumed and disinfected following the car wash. After the vehicle dries, the tires, wheel wells and undercarriage should be disinfected as described above.

During-Inspection Measures

- Follow the farm's own biosecurity program to the extent that it does not interfere with investigators conducting the inspection.
- Do not enter or inspect houses where birds are known to have disease, including but not limited to, SE.
- FDA personnel participating in the inspection cannot be bird owners. Ownership of birds disqualifies that investigator from participation in all egg farm inspections.
- Always change all Personal Protective Equipment (PPE) between houses. PPE includes disposable body coverings, boot covers, hair bonnets, sterile gloves, respirators, eye, and hearing (in areas where loud machinery is in use) protection. The use of disposable PPE and respirators is preferred to eliminate the need for disinfection between poultry houses. In situations where permanent eyewear is worn it must be cleaned and disinfected between each poultry house.
- Investigators should wash hands thoroughly before donning gloves for entry into the house. Where available, use soap and water; if not available, use hand sanitizing gels. It is the responsibility of the team lead to ensure that all members of the team are adhering to protocol. This should be done at both the clean and dirty areas established at the farm, prior to entry into any poultry house.

Selection of disinfectants:

- Ethanol should be used to disinfect the lids of evaporated milk cans, scissors and can openers used during sampling within a poultry house.
- Phenolic or quaternary ammonium-based sanitizers should be used on wheel wells, tires, and vehicle under carriage. The vehicle body should not be disinfected, as the detergent from the car wash is sufficient and some sanitizing compounds can damage the vehicles finish.
- Lysol or equivalent based aerosol spray should be used on floor mats and soles of shoes.
- Purell or equivalent hand gel should be used for hand disinfection.

In situations where reusable respirators are used, they must be cleaned and disinfected in accordance with manufacturer's recommendations. Selection of the appropriate disinfectant is critical; for questions or assistance with disinfectant selection please contact HFP/ OLOAS (see contacts at the end of this document).

- No item which has been in a layer house may be brought into a different house without a complete cleaning and disinfection or replacement with a new one. This includes all items, e.g., pens, supply tubs, scissors. Replacement of items is more effective than disinfection and lessens the workload on site; therefore, all efforts should be made to replace items rather than transfer between houses.
- Plan carefully prior to inspections and pack inspection kits on a per house basis so as to eliminate the need to share equipment between houses. Aside from permanent eyewear and "egg pad" tablets, there should not be a need to share equipment/items between houses.

- Use disposable cameras, when possible. Otherwise, digital cameras are to be placed within plastic bags prior to entry into the house.
- Double bag all garbage; specifically, one bag is to be left at the vehicle and the other taken into the house to be inspected. When the garbage is removed, it is placed into the bag left at the vehicle, so as to assure that the bag which went into the layer house never touches the vehicle interior.
- Houses should be inspected from the cleanest areas to the dirtiest areas and from the youngest to oldest birds.
- Do not wear jewelry in poultry houses.
- Where possible, wear clothing that has not been on another egg farm and ensure the clothing is laundered. If possible, use the hot water cycle to launder clothing that will be used during an egg inspection.
- If possible, park the car at the beginning of the driveway or outside the farm and carry all of their equipment onto the farm. Investigators should coordinate with farm management to determine the best parking spot for the vehicle.
- Eyeglasses should be cleaned and disinfected with disposable decontamination wipes.

Items listed below represent either direct or indirect contact with Population 2 as described in the pre-inspection measures above. A minimum of 1 week, preferably longer, prior to participating in an FDA egg farm inspection, all investigators involved in the inspections should:

- Not come in contact with bird feeders or bird baths for a minimum of 1 week prior to participating in an egg farm inspection.
- Stay away from family members, friends or acquaintances that are pet bird owners or have backyard poultry flocks of any type.
- Not visit fairs where poultry or birds are shown or exhibited.
- Not visit live bird markets of any type, or gatherings where live birds may be present.
- Not visit flea markets, trade shows, or swap meets where live poultry or birds of any type may be present.
- Not visit zoos, theme or amusement parks where live birds maybe present.
- Not visit known nesting grounds or resting place for wild birds, such as natural preserves or refuges, known breeding grounds or bird sanctuaries.
- Not attend birthday parties or functions where a petting zoo that includes poultry is part of the event, e.g., baby chicks, pet ducks or geese, are present.
- Not come in contact with birds, such as ducks or geese, at municipal, state or other types of parks. e.g., where ducks, geese or pigeons and other birds are local inhabitants and people congregate to feed them.
- Not visit an ocean side town where you may come in contact with shorebirds, e.g., gulls.
- Not visit feed stores or other retail establishments where live poultry may be sold, e.g., baby chicks, turkey poults, ducklings, etc.
- Not go hunting for wild fowl or handle wild fowl. If you have family members or friends who hunt fowl, do not come in contact with them for a least the week prior to the inspection.

- Not meet with other known bird owners either as part of your work (e.g., meeting another producer at a location away from their farm) or meet with other known bird owners in your social circle.

Post-Inspection Measures

- Wash the vehicle used during the inspection as specified in item #5 in the pre-inspection procedures of this directive.
- Clean and disinfect the sampling kit(s), e.g., tubs, scissors, can openers
- Clean and disinfect respirators in accordance with manufacturer's recommendations.

Contacts

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5-20 – Film Photography

General Considerations

If you are using a film-based camera (e.g., 35mm), follow applicable guidance in IOM section 5.6.7 regarding documentation of digital photographs in addition to the specific guidance below. Regardless of the technology used, you must create a trail, starting with the taking of the photo, confirming its original accuracy and establishing a record describing the chain of custody. To do this, you must make sure each photograph is described in your regulatory notes in sufficient detail to assure positive correlation of the photo with your inspection findings. One way you can do this is to photograph a card with your name, program division address and phone number as the first frame or picture on a roll of film. This will help identify the film and assist in tracking if it is lost or becomes separated from its identification envelope during processing or storage. Proper procedures will also allow the agency to provide evidence confirming the authenticity of the photographs in the event you are not able to testify personally.

Cameras

Film Prints Identification and Preparation

Identify each print used as an exhibit in the EIR on the margin with exhibit number, firm name, date taken or inclusive dates of inspection, and your initials. Do not place any identifying marks on the picture area of the print. Mount the photo(s) on letter size paper; a narrative description may be placed on the mounting paper next to the print if insufficient area is available in the photo margin. If borderless prints are created, place identification along the back bottom edge of the print and mount the print so the identification can be read without removing the print from the mounting paper.

All film prints mounted on paper and used as exhibits must be scanned utilizing appropriate hardware and labeled for submission in eNSpect. See SOP ORA-OO.004 Using eNSpect to Create, Store, and Preserve Electronic Records Associated with an Establishment Inspection Report. Store the original negatives according to the section below.

Film Negative Identification

Identify the edge of at least two negative strips, with the same information as for prints using a 3/16" strip of pressure sensitive tape. Place all negatives in an FDA-525 or similar envelope. Complete blocks 2, 3, 5, 7, and 12 and seal with an Official Seal, FDA-415a. If negatives are not part of a DOC Sample, enter firm name in the Sample Number block.

Do not scan the FDA 525 or envelopes containing the negatives and upload in eNSpect as exhibits. The actual photographs included and described in the EIR are the official exhibit and are maintained in the eNSpect system. The officially sealed negatives should be included with the unlabeled hard copy exhibits and attachments filed in accordance with applicable procedures. The following statement should be included section 5.11.4.3.16 - Additional Information, “The

officially sealed negatives of the photographs taken during the inspection are filed with the unlabeled exhibits and attachments."

Video cameras

Videotape Identification and Preparation

Unused videotapes should generally be used to capture the video and, for subsequent copies of the original recording. Handle and protect the original video record just as if it were a photograph (see IOM 5.6.7). If the video is planned to be used as an exhibit to an inspection, where possible employ technology to digitize the video in its entirety for identification and upload into eNSpect. Where this technology is unavailable, upload a document in place of the video in eNSpect explaining the circumstances and indicating the video is available in the firm's establishment file.

Identify the original video recording with a label with the firm name, date taken, and your initials. Seal the original copy of the video tape in an FDA-525 or similar envelope. If using a form FDA 525, complete blocks 2, 3, 5, 7, and 12. If you use a larger envelope, identify the envelope with your name, title, home program division, date, firm name, firm address (include zip code), and description of the contents of the envelope. Using either method, label the outside in large bold letters "STORE AWAY AND PROTECT FROM MAGNETIC FIELDS" and seal with an Official Seal, FDA-415a. Submit any officially sealed tapes with the unlabeled hardcopy exhibits in accordance with applicable procedures. The following statement should be included section 5.11.4.3.16 - Additional Information, "The officially sealed videotape(s).

5-2 – Pesticide Inspections/Investigations

Pesticide Inspections

The objective of a Pesticide Inspection is to determine the likelihood of excessive residues of significant pesticides in or on products in consumer channels, and to develop sources of information for uncovering improper use of pesticide chemicals.

Typically, many Pesticide inspections whether for use, misuse, drift, and similar pesticide applications are completed at the state level by agencies working with the Environmental Protection Agency (EPA) on the FRodenticide Act (FIFRA)". Coordination with FDA State Liaisons and Emergency Response Coordinators is recommended.

This requires directing coverage to two major areas:

- Pesticide practices in the production and processing of many raw agricultural products and crops. Application of pesticide chemicals in establishments storing and processing raw agricultural products and crops.

Coverage of raw agricultural products will generally be on a growing-area basis.

Problem areas include:

1. Improper use of pesticides around animals and in raw agricultural crop/products - gross misuse of sprays and dips in animal husbandry may result in pesticide residues in foods, as misuse or misapplication of pesticides on raw agricultural crops/products may also result in pesticide residues in foods.
2. Use of contaminated animal feeds - waste and spent materials from processing operations may contain heavy concentrations of pesticide residues, which were present in the original commodity. See Compliance Policy Guide 575.100.
3. Past pesticide usage - past pesticide practices on growing fields. Past use of persistent pesticides may result in excessive residues in the current food crop. You may need to check on pesticide usage for several years prior to an incident to ensure you gather enough information. Some pesticides last for many years in the environment.

Current Practices

Cooperative Activities - important sources of information relative to evaluating the "Pesticide Environment" include:

1. Coordination of your inspection with your supervisor and the appropriate FDA state liaisons and or the divisional emergency management coordinators (ERC) is one of the starting point for this type of inspection/investigation. They will identify the appropriate state, local or regional agency responsible for pesticide use and applications within the jurisdiction, when available.
2. At the start of the growing season, spray schedules recommended for each crop by county agents, state experiment stations, large pesticide dealers, farmers cooperatives, et al should be obtained.
2. Visits to agricultural advisors may provide information relative to heavy infestation of insect pests and fungal infections on specific crops in specific areas.
3. Daily radio broadcasts in most agricultural areas may provide information on spray schedules, insect pests, harvesting and shipping locations, etc.
4. Field employees of fruit and vegetable canning and freezing plants usually recommend spray schedules, pesticides, and harvesting schedules for products produced by contract growers.
5. United States Weather Bureau Offices and their reports will provide data on weather conditions, which may affect insect growth and their development, size of fruit or leaf growth, and dissipation of pesticide chemicals.
6. USDA Market News Service daily price quotations, and weekly quotations in trade magazines provide information regarding harvesting schedules since market prices are indicators of how quickly a crop will be

harvested in a given area. Growers who have the opportunity to obtain high prices may harvest their crops without regard to recommended pre-harvest intervals.

7. State Colleges of Agriculture seminars or short courses on food and vegetable production may alert you to significant departures from usual agricultural practices. Prior approval to attend such meetings should be secured from your supervisor.
8. Pesticide suppliers and distributors may provide information on spray practices, schedules, and the name and address of growers, etc.

NOTE: The U.S. Department of Agriculture has a Pesticide Data Program (PDP), which provides data on pesticide use and residue detection. This program helps form the basis for conducting realistic dietary risk assessments and evaluating pesticide tolerances. Coordination of this program is multi-departmental, involving USDA, EPA, and FDA, covered by a MOU (Federal Cooperative Agreements Manual). As a part of this program USDA collects data on agricultural chemical usage, and factors influencing chemical use, and collects pesticide residue data through cooperation with nine participating states. USDA provides this data to EPA, FDA, and the public. Several USDA publications are listed below as reference material.

Reference materials - the following reference materials provide background and data necessary or helpful in evaluating current practices. This material should be available at the program division office.

1. Pesticide Chemicals - Regulations under the Federal Food, Drug and Cosmetic Act on tolerances for pesticides in food administered by the Environmental Protection Agency (EPA).
2. EPA's Pesticide Regulations - Tolerances for Raw Agriculture Products. (See 40 CFR 180)
3. EPA's Rebuttable Presumption Against Registration (RPAR) List.
4. Pesticide Index. - By William J. Wiswesser. A publication containing information on trade names, composition and uses of commercial pesticide formulations.
5. The Daily Summary or Weekly Summary. News releases and reports from USDA.
6. USDA's Weekly Summary Shipments-Unloads.
7. Agricultural Economic Report No. 717 Pesticide and Fertilizer Use and Trends in U.S. Agriculture (May 1995)
8. Annual Pesticide Data Summary
9. Reports from USDA's Crop Reporting Board.
10. USDA's Pesticide Assessment Reports.

Growers

Preliminary investigation of growing areas at the start of the season will provide data necessary for program division work planning including production schedules, types and acreage of crops, pesticides used and the names and addresses of growers and shippers. The Produce Safety Network (PSN) can be of assistance in obtaining some of this information.

Growing Dates - The significant growing dates relative to pesticide usage are as follows:

1. Planting date,
2. Date of full bloom, and
3. Date of edible parts formation.

Harvest Dates - The dates of the anticipated harvest season will provide planning information relative to pre-harvest application and shipping.

Acreage - This will provide volume information for work planning.

PESTICIDE APPLICATION

Ascertain the actual pesticide application pattern for each crop. Look for objective evidence to document actual grower practice. Check the grower's supply of pesticide chemicals, look for used pesticide containers, visit his source of supply, etc. Check spraying and dusting practices. Establish if pesticide chemicals are used in such a manner that excessive residues might result.

The following information provides a basis for evaluating pesticide usage:

1. Pesticide Chemical Applied - List the common name if there is no doubt as to the chemical identity of the pesticide. Include labeling indications and instructions.
2. Method of Application - Describe the method of application i.e., ground rig, airplane, greenhouse aerosol, hand, etc.
3. Formulation - Describe the formulation i.e., wettable powder, emulsifiable concentrate, dust, granules, aerosol, etc. Express as pounds of active ingredient per gallon or percent wettable powder.
4. Number of Applications and Dates.
5. Rate of Last Application - Calculate the amount of active ingredient per acre.
6. Pre-Harvest Interval (PHI) - Calculate the number of days between the day of the last application of pesticide and the harvest date or anticipated harvest date. Compare to the PHI.
7. Visible residue on grower's crop.
8. Summary of Usage - Determine the USDA Summary Limitations and evaluate the responsible usage.

PESTICIDE MISUSE/DRIFT/SOIL CONTAMINATION

Pesticide residues, which exceed established tolerances, action levels, or "regulatory analytical limits", may be caused by pesticide misuse which can include:

1. Excessive application of a chemical on a permitted crop.
2. Failure to follow labeled time intervals between the last pesticide application and harvest.
3. Use of a non-approved pesticide on a crop.
4. Failure to wash a crop when pesticide labeling requires it (e.g., for certain EBDC's).

Other conditions, which may cause illegal residues, include spray drift and soil contamination.

Drift may be documented by determining which crops and pesticides have been grown/used in fields adjacent to those sampled. Determine direction of prevailing winds and wind condition on the day of spraying. Selective sampling will aid in determining if drift occurred. Compliance Samples collected to document pesticide drift should be Flagged as a Pesticide Sample and noted in the Remarks section of the CR as "Drift Sample - Maintain as Individual Subs".

Soil contamination by compounds, which are relatively stable in the environment, may cause systemic uptake of the compounds by growing crops. Follow-up investigations to violative samples may, in some limited cases, include soil samples as an attempt to determine the source of the contaminant. Do not routinely collect soil samples.

Packers and Shippers

Follow the same general procedure as in IOM 5.4.12.3. Observe and report the following:

1. Treatment Before Shipping - This may include stripping of leaves, washing, vacuum cooling, application of post-harvest preservative chemicals, use of cartons with mold-inhibiting chemicals, waxes, colors, fumigation, etc.
2. Identification of Growers' Lots - Determine procedure or methods used to maintain the identity of each grower's lot. Provide the code and key if any.
3. Labeling - Quote labeling or brand names.
4. Responsibility - Determine whether the packer or shipper knows what sprays have been used on the products shipped.

Pesticide Suppliers

Pesticide suppliers should be visited routinely during growing-area coverage. They may provide valuable information about pesticides being used on various crops in the growing area. Some suppliers may suggest spray schedules or advise growers about pesticide usage.

Determine what representations were made by the manufacturer of pesticide chemicals for which there is only a temporary tolerance or experimental permit. Get copies of any correspondence relating to sale and use of these products. Obtain names of growers to whom sales are made if such sale was not for use on acreage assigned under the experimental permit. Collect Official Samples of any crops treated with the pesticide.

Pesticide Applicators

Pesticide applicators may provide valuable information about pesticides being used on various crops in the growing area. Interview several pesticide applicators, particularly those using airborne equipment. Determine the pesticide chemicals, their formulation, and on what crops they are currently being applied. Determine who supplies the pesticides and how they are prepared to assure proper concentration. If state law requires the applicator to keep a record of each spray application, request permission to review such records. Determine what steps are taken to assure drift on adjoining crops does not result in violative residues. Where there is likelihood of drift, collect Selective Samples from adjoining fields.

Sample Collections

See IOM Sample Schedule Chart 3 - Pesticides.

5-22 – Standards of Identity for Food

The FD&C Act (Section 401 [21 U.S.C 341]) requires the Secretary of the Department of Health and Human Services to promulgate reasonable definitions and standards of identity (SOI) for food to promote honesty and fair dealing in the interest of consumers. When a SOI becomes effective, it establishes the common or usual name for the article, defines the article and fixes its standard of identity. It is then the official specification for the food. The food industry actively participates in the development of a SOI and supplies much of the data upon which the regulation is based. There are currently more 250 SOIs and these may be found in 21 CFR Chapter 1, Subchapter B, Parts 131-169. Additional information on FDA's standards of identity for food can be found here: Standards of Identity for Food | FDA.

The food standards (FS) inspection is made to obtain data for use, together with information from other sources in developing a food standard. Food standard inspections are also made to determine a firm's compliance with food standards regulations, when manufacturing a standardized food.

Conducting a food standards inspection

These inspection assignments usually originate from HFP. When an inspection is planned for the purpose of collecting data to support a proposed food standard regulation, the program division may elect to advise the firm, if HFP has not already done so. If the firm selected does not choose to cooperate, it may be necessary to visit additional plants to obtain the desired information. Selection of additional firms should be done in consultation with the HFP.

Some firms often contend their entire process and formulas are "trade secrets". Attempt to persuade management the term "trade secret" should only be used to cover the process and/or quantitative-qualitative formulation which is truly unique to the firm. In instances where the firm is reluctant to release any of the information requested, point out FDA will, within the limits of the Freedom of Information Act, make every effort to preserve the confidentiality of the composition, make-up, and production levels of the product using codes, which cannot be traced back to the firm. Include as much of the compositional and processing information as you can in the body of the report, without violating the firm's confidence.

FS establishment inspection reports

FS EIR's may be used as exhibits at public hearings and are subject to review by any interested party.

Three copies of the report are prepared. The original and one copy will be submitted to CFSAN, and one copy kept for the establishment file. Sign the original and duplicates of the first and last pages of each report sent to the Center.

Divide the report into three sections. To relate the sections of the report to each other and to any assignments, and to assure any parts of the reports made public will not be identified as to the name of the firm or individuals therein, each program division will set up a master list of numbers. One number will be assigned to each establishment covered, e.g., "BLT FS-3". For each FS inspection, place the assigned number next to the firm name on the EI record. All other pages of the report shall be identified only by this number, the name of the commodity, and date. Example: "EIR Frozen Fish Sticks 10-3-87 BLT FS-3". This indicates a FS EI of frozen fish sticks conducted by Baltimore OHAFO Division 2E on 10-3-87 in a plant designated as #3.

Where a producer may be reluctant to release any of the information requested, point out the FDA will, within the limits of the FOIA, make every effort to preserve the confidentiality of the composition, make-up, and production levels of his product using codes, which cannot be traced back to the firm.

Body of the EIR

Prepare the body of the report following the narrative outline as for any other food EIR except for the restrictions below.

The body of the FS report should also contain information regarding the approximate annual value and volume as well as the percent of interstate business for each product covered. This is necessary because the coversheet, which contains this information, identifies the firm, and will not be made public. Processes and the listing of raw materials used by the firm, which are not restricted by the term "trade secret" should be included. Any opinions, recommendations, or other information obtained or offered by individuals interviewed should be reported. Any suggestions made by individuals interviewed regarding what should be placed in the Standards for the products covered should be included. All individuals interviewed, firm name, etc. should have an identifying code assigned.

The body of the report should not include names and titles of individuals, (including USDA, USDI, or other inspectors), trade secret information, labeling, trade names, formulas, sample numbers, firm name, or location of plant (other than by state or region), shipments, or other distribution information, legal status, or regulatory history. This information will be placed in the "Special Information" section of the report.

Special information section

This is a separate attachment to the EIR which lists the names and titles of individuals (including other government inspectors) and firms with a reference code for each. The EIR should refer only to "Mr. A.," "Mr. B.," "Firm X," "Firm Y", etc. Do not use the firm or individual's actual initials in the body of the report. Include all information excluded from the body of the report and mount all labels obtained during the EI Labels may be quoted in the body of the report, but do not identify the firm. List the "Special Information Sheet" in the FACTS endorsement section as an enclosure.

Supplemental Reports - If, because of an additional visit or visits to the same firm on the same project, it is necessary to prepare another EIR, flag the report with the same number as assigned to the original report. For example, mark the EI Record "BLT FS-3 Supplemental Report", and the remaining pages, "EIR Frozen Fish Sticks 10-25-87 BLT FS-3 Supplemental Report."

Violative inspections

When an inspection made in connection with the Food Standards project shows insanitary or other conditions which are not germane to the assignment or in the program division's opinion suggests regulatory action, an appropriate narrative of the violative conditions should be prepared as a regulatory addendum.

5-23 – RECONCILIATION EXAMINATIONS

Conduct reconciliation examinations only for cause or as directed by your assignment or supervisor.

Examinations are conducted on raw materials used in the manufacture of foods or cosmetics, or finished products received by the firm for further distribution. Preference should be given to products of foreign origin. Where possible, these examinations should be performed on products as they are received by the firm.

Consult the establishment file for any information on special conditions in the facility that may affect selection of personal protective equipment. Consult your supervisor for any recommendations on personal protective equipment. Have available all necessary personal protective equipment to conduct the activity.

As Part of an Import Field Examination and Entry Review - See IOM 6.3.1 and 6.4.4. For imported food and cosmetics, a reconciliation examination should be conducted:

1. Per Part A during all routine import field exams. You should only report time under the Counter Terrorism PAC at the direction of your supervisor or if there is a for cause assignment.
2. In instances where review of entry information raises suspicion (resulting in a detailed reconciliation exam per Part B.

A detailed reconciliation exam should be conducted when there are anomalies in entry declaration information. These may include new, unusual, or unfamiliar commodities, manufacturers, importers; suspicious trans-shipments; or credibility issues such as those between the product and declared country of origin.

If anomalies are found, entry documents should be requested and reviewed for discrepancies between the information declared through electronic filer submissions and that found in entry documents. Entry documents may include invoices, bills of lading, export certifications, and other relevant documents obtained from the importer, filer, or manufacturer/processor of the product. Fields in which discrepancies are found that may raise concern include country of origin, manufacturer, product description, product code, and quantity.

Avoid duplication of examination of the same foreign manufacturer unless a prior reconciliation examination disclosed an unexplained discrepancy.

Follow guidance below for domestic and import reconciliation exams.

RECONCILIATION EXAMINATION GUIDANCE PART A

Reconciliation examinations are performed to ensure that:

- The product is what it purports to be
- There are not unexplained differences in the quantity of product ordered, shipped, and received, and
- There are no signs of tampering or counterfeiting.

Before initiating the exam make a general assessment of the appearance of the lot. Look for packaging that: appears to have been opened and resealed; appears wet, stained, punctured, or powdered. Also, be alert to abnormal chemical odors. If any of these conditions are detected stop the exam and contact your supervisor for guidance. If the lot appears normal proceed with the examination. To the extent possible the exam should be performed in a well-ventilated, well-lit area.

Determine, to the extent possible, whether:

- The actual goods in a lot are the same as those that are declared in the shipping documents.
- There is consistency in the manufacturer declared on the product labeling, bulk product packaging, and shipping documents; and
- There is no (unexplainable) inconsistency in actual quantity of goods in the lot, and the quantity ordered and declared in the shipping documents.

If no unexplained inconsistencies are detected, no further action is indicated.

If unexplainable inconsistencies are detected, document the occurrence, including photographs of the labeling and packaging, and an accurate count of the lot. Contact your supervisor, who should, in the case of imported products, contact the U.S. Customs and Border Protection for appropriate action. If the examination discloses evidence that inaccurate product identification data was submitted to the OASIS entry screening system, the program division should evaluate the need for follow-up with a compliance filer evaluation and consider providing the information to the U.S. Customs and Border Protection for appropriate action.

In addition, if unexplained inconsistencies are detected, follow part B of this guidance while conducting a detailed reconciliation exam.

RECONCILIATION EXAMINATION GUIDANCE PART B

Open the shipping packaging of a quantity of product approximating the square root of the number of shipping cartons/packages in the lot and examine the contents. Look for the following:

- Product identity on the package that does not match the identity declared on the shipping documents
- Mixed product sizes within a carton or within the lot;
- Product sizes that do not match the sizes declared on the shipping documents
- Differences in product configuration or package type (e.g. plastic containers mixed with glass jars or aluminum or steel cans)
- Easily apparent variations in weight
- Product labels that display crude, unprofessional, or inconsistent styles of print, color, or use of language
- Unusual placement of labels (e.g., off-center)
- Variations in lot coding ink color, appearance of embossing, or format (e.g., two line vs. three line, use of letters, numbers and symbols). unusually excessive use of a single code in a very large lot
- Differences between the actual can codes in the lot and those listed on the shipping documents
- The existence of a tamper-evident notice on the labeling when the packaging does not contain a tamper-evident feature
- Product that is beyond its expiration date
- Inconsistencies in expiration dates within a lot

If no unexplainable discrepancies are noted select at least 1 package at random from the entire shipment and examine their contents. For those products that the contents are visible through the package it is not necessary to open the package. For other products, open the package and examine and field destroy the contents. Look for the following:

- Differences between the product and that which is declared on the label
- Color differences in the product between containers of the same lot
- Style differences in the product between containers of the same lot or between the actual product and the label and document declaration (e.g., sliced vs. whole, colorless noodles vs. egg noodles)
- Readily detectable abnormal odors (e.g., strong decomposition, bitter almond, petroleum odor, garlic, chlorine, sulfur). Note: specific sensory examination is not expected.

Verification that the product is consistent with the product ordered may require that you obtain information from the owner of the goods, importer, filer, or custom house broker. Review of the following types of documentation may be necessary to accomplish the above instructions, to the extent that they are available: authentic label supplied by the owner of the goods, importer, filer, or custom house broker; purchase order; invoice; shipping records (bill of lading, weigh bill, manifest). Depending on the findings of the exam and record review, you may wish to request that the importer assist in an evaluation of the authenticity of the product, based on the importer's experience with the product.

Every effort should be made to document any discrepancies through use of photographs, and additional records that may be available from the filer, importer, owner, or customs house broker.

SPECIAL SAFETY PRECAUTIONS

See IOM Chapter 10 - Safety.

When performing an establishment inspection or reconciliation examination, follow these instructions:

1. If there are no signs of tampering or counterfeiting, use level I protection, which consists of: work gloves; coveralls; work boots; and in a dusty situation, a dust mask.
2. If there are signs of tampering or counterfeiting, use level II protection and consult your supervisor for any additional safety precautions needed. Level II protection consists of: work gloves worn over surgical gloves; full face respirator with appropriate cartridges; disposable coveralls; and work boots.

Consult with an Industrial Hygienist if you are unsure what protective equipment should be used during sampling.