

CHAPTER 5 - ESTABLISHMENT INSPECTIONS

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SUBCHAPTER 5.1 - INSPECTION INFORMATION

5.1.1 - AUTHORITY TO ENTER AND INSPECT

See IOM 2.2 for discussion of statutory authority.

It is your obligation to fulfill the following requirements because failure to do so may prevent use of evidence and information obtained during the inspection.

There may be occasions where you may be accompanied on your inspection or investigation by other officials. These officials 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 person if officials without inspection authority wish to accompany you during your inspection/investigation. You should document in your EIR when other non-FDA officials accompany you during your inspection, and whether they entered under their own authority or the responsible individual at the firm gave permission (identify, by name and title, the responsible individual giving permission). See IOM 5.2.2 and 5.11.4.3.3.

5.1.1.1 - FDA Investigator's Responsibility

Your authority to enter and inspect establishments is predicated upon specific obligations to the firm as described below. It is your responsibility to conduct all inspections at reasonable times and within reasonable limits and in a reasonable manner. Proceed with diplomacy, tact and persuasiveness.

During inspections or investigations, when you have evidence of conditions whereby there is a reasonable probability the associated products will cause imminent and serious adverse health consequences or death, you should notify your supervisor immediately to consider a Risk Control Review (RCR) evaluation.

5.1.1.2 - Credentials

Display your credentials to the top management official be it the owner, operator, or agent in charge. See IOM 5.2.2.

NOTE: Although management may examine your credentials and record the number and your name, do not permit your credentials to be photocopied. Federal Law ([Title 18, U.S.C. 701](#)) prohibits photographing, counterfeiting, or misuse of official credentials. Do not permit a firm to take your fingerprints, contact your SCSO for more information.

5.1.1.3 - Written Notice

After showing the firm's representative your credentials, issue the original, properly executed, and signed FDA 482, Notice of Inspection, to the top management official. Keep a copy for submission with your report. A notice of inspection is not required to be issued during foreign inspections; however, credentials should be presented to the top management official.

5.1.1.4 - Written Observations

Upon completing the inspection and before leaving the premises, provide the highest management official available your inspectional findings on an FDA 483 - Inspectional Observations or an FDA 4056, Produce Farm Inspection Observations, for produce safety inspections. See Section [704\(b\) of the FD&C Act](#) [21 U.S.C. 374 (b)] and IOM 5.2.3 and 5.2.7.

5.1.1.5 - Receipts

Upon completion of the inspection, furnish the top management official the original of the FDA-484 - Receipt for Samples describing any samples obtained during the inspection. See IOM 5.2.4.

5.1.1.6 - Written Demand for Records

In low-acid canned food and acidified food EI's, an FDA 482a - Demand for Records (exhibit 5-2) is required under [21 CFR 108.35\(h\)](#) and [21 CFR 108.25\(g\)](#) to obtain records required by [21 CFR 113](#) and [114](#).

5.1.1.7 - Written Requests for Information

There are several methods of requesting records. These may include a request for information under LACF or AF inspections, and FDA 482d Request for FSVP Records, 703 written requests, and requests for records under the BT Act (IOM 5.4.1.3).

5.1.1.7.1 – LACF / AF Food Inspections

In low-acid canned foods and acidified foods EI's, an FDA 482b, Request for Information (exhibit 5-3), is required under [21 CFR 108.35\(c\)\(3\)\(ii\)](#) and [21 CFR 108.25\(c\)\(3\)\(ii\)](#) to obtain information concerning processes and procedures required under [21 CFR 113](#) and [114](#).

5.1.1.7.2 – Requests for Records under Section 703 of the FD&C Act

Per [CPG Sec. 160.300](#), Requests for Records under [Section 703](#) [21 U.S.C. 373], evidence obtained in response to a specific written request under Section 703 cannot be used in a criminal prosecution of the person from whom obtained. With Supervisory approval, in certain circumstances, you may decide to issue a 703 written

request when the importance of the evidence is crucial to protecting the public health.

Procedure: All 703 written requests must comply with IOM 4.4.7.2.2. Consider obtaining the evidence from other sources before using the 703 written request. In the case of foods and feeds, if there is a risk or threat of serious adverse health consequences, the division program division should invoke the BT Act records access authority. All BT Act records requests must comply with IOM 5.4.1.3.

5.1.1.8 - Business Premises

Authority to inspect firms operating at a business location is described in IOM 5.1.1 and requires issuing management an FDA 482, Notice of Inspection, and presenting your credentials. A warrant for inspection is not necessary unless a refusal or partial refusal is encountered or anticipated.

5.1.1.9 - 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:

Owner Agreeable - The owner or operator is fully agreeable and offers no resistance or objection whatsoever. Clearly document in the EIR that you are inspecting a residence and the owner was agreeable. or;

Physically Separated - The actual business operations to be inspected are physically separated from the living quarters by doors or other building construction. These would provide a distinct division of the premises into two physical areas, one for living quarters and the other for business operations, and you do not enter the living area.

In both the latter cases, proceed as any other inspection with the appropriate presentation of credentials and issuance of a Notice of Inspection. For safety precautions, it is recommended that two credentialed FDA employees are present when conducting inspections in a residence.

5.1.1.10 - Facilities where Electronic Products are Used or Held

[Section 537\(a\) of the FD&C Act](#) provides the FDA with the authority to inspect the facilities of manufacturers in certain circumstances. The electronic product radiation control provisions were originally enacted as the Radiation Control for Health and Safety Act of 1968 (P.L. 90-602)

It is lawful for FDA personnel to enter the facilities of an electronic product distributor, dealer, assembler or user for the purpose of testing an electronic product for radiation safety when the entry is voluntarily permitted. Congress has not specifically prohibited FDA from conducting such voluntary examinations and such examinations would clearly agree with the congressional declaration of purpose expressed in section 532(a) of the RCH&S Act.

Under the Medical Device Authority, electronic products utilized in human and/or veterinary medicine, e.g., x-ray, laser, ultra-sound, diathermy, etc. can be considered prescription devices. In these cases the authority of [Section 704 of the FD&C Act](#) [21 U.S.C. 374] can be used to obtain entry to inspect the user facility. If the Medical Device Authority is utilized, credentials must be displayed and a FDA 482, Notice of Inspection, must be issued.

5.1.1.11 - Multiple Occupancy Inspections

You are required per [FD&C Act 704\(a\)\(1\)](#) [21 U.S.C. 374(a)(1)] to issue a Notice of Inspection, FDA 482, to each firm inspected. When firms have operations located in different sites or buildings, you should use judgment to determine when multiple FDA 482 forms need to be issued. For sites located a distance apart, it is preferable to issue a FDA 482 to the most responsible person at each site. One rule of thumb which can be used is if the sites or buildings are within walking distance, your original Notice of Inspection can be considered sufficient to cover both. During your initial interview with management, after you issue the FDA 482, make sure you clearly indicate the facility and sites you intend to inspect. The Act requires the issuance of a Notice of Inspection, but does not prohibit issuing multiple notices if management so requests. As with all of our work, good judgment, and knowledge of the OEI and the FD&C Act are necessary in deciding what legally must be done.

5.1.1.12 - Authority for Examinations and Investigations

[Section 702\(a\) of the FD&C Act](#) [21 U.S.C. 372 (a)] authorizes examinations and investigations for the purpose of enforcing the Act.

5.1.1.13 - Authority to Implement Section 702(e)(5) of the FD&C Act

[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 authority in 702(e) to make arrests, to execute and serve arrest warrants, to carry firearms, or 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 the ACRA.

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 (i.e., the profits) obtained as a result of counterfeiting.

5.1.1.13.1 - 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 thing which you have reasonable grounds to believe is designed or used in making a counterfeit drug.

NOTE: You and your supervisor must be constantly aware of the potential dangers involved in confiscating property from individuals. Special care should be taken to ensure your safety. 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.

5.1.1.13.2 - 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 the drug to be confiscated is a counterfeit and it is a drug which "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 Program Division Director from the Office of Enforcement and Import Operations (OEIO), in conjunction with the Center for Drug Evaluation and Research or the Center for Veterinary Medicine.
2. When engaged in counterfeit investigations, you should proceed as follows upon encountering items to be confiscated.
 - a. Evaluate safety needs and check the 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.
 - 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.

5.1.1.13.3 - FOLLOW UP GUIDANCE

After items are confiscated, certain actions must be taken to bring confiscated items under the control of the court. Proceed as follows:

1. After an item is confiscated, immediately notify your supervisor.
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. Office of Medical Products and Tobacco Program Operations (OMPTO) should be advised of any action utilizing this authority.

5.1.1.13.4 - 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.

5.1.1.14 - Products Imported Under the Provisions of Section 801(d)(3) of the FD&C Act

The FDA Export Reform and Enhancement Act of 1996 (PL 104-134 and 104-180) amended the FD&C Act by adding [Section 801\(d\)\(3\)](#) ("Import for 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 has to satisfy in order to import a product under this Section. See IOM 6.2.3.4.

5.1.1.14.1 - REQUIREMENTS FOR BIOTERRORISM ACT

These requirements include:

1. A statement confirming the intent to further process such article or incorporate such article into a product to be exported,
2. The identification of all entities in the chain of possession of the imported article,
3. A certificate of analysis "as necessary to identify the article" (unless the article is a device), and
4. Executing a bond providing for liquidated damages in the event of default, in accordance with U.S. Customs. This bond remains in effect until the final product is exported and destroyed.

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 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 Prohibited Acts under [Section 301\(w\)](#).

Filers making entry under the Import for Export provisions must either identify entry submissions with the OASIS Affirmation of Compliance "IFE" (Import for Export), or 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 forward all written documentation to the home program division of the initial owner or consignee for incorporation into the appropriate Establishment File.

5.1.1.14.2 - INSPECTIONAL PREPARATION

Before conducting an Establishment Inspection, contact your program division's designated individual with access to OASIS/ORADSS Reports to obtain a printout of any import entries made by the establishment under the Import for Export provisions through OASIS. In addition, check the program division factory file for copies of any Import for Export documents forwarded from the import program division where entry was filed. During the inspection examine the firm's records to determine the disposition of any items identified at time of entry as intended for incorporation into products for export. Document any instances in which such products were introduced into domestic commerce or cannot be accounted for (see IOM 6.2.3.4.3).

5.1.2 - INSPECTIONAL APPROACH

An establishment inspection is a careful, critical, official examination of a facility to determine its compliance with the laws and regulations administered by FDA. Inspections may be used to collect evidence to document violations and to support regulatory action, when appropriate, or they may be directed to obtaining specific information on new technologies, good commercial practices, or data for establishing food standards or other regulations. In order to facilitate on-the-job training, multiple points of view, and perspectives of firms being inspected whenever practical, those with assignment authority, should consider assigning 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 (e.g. full scope, limited scope; Level I, II or III; and full or abbreviated) used to conduct an inspection is defined by the compliance program, assignment, and/or your supervisor.

The inspectional approach used is according to the following definitions:

Comprehensive Inspection -directs coverage to everything in the firm subject to FDA jurisdiction to determine the firm's compliance status; or

Directed Inspection -directs coverage to specific areas to the depth described in the program, assignment, or as instructed by your supervisor.

See IOM Chapter S for information on safety, use of protective gear, trash disposal, dealing with potential hazards and other safety issues.

See special report requirements in IOM Subchapter 1.7.3 when objectionable conditions which may be of public health significance implicate establishments in other division(s).

5.1.2.1 - Depth of Inspection

The degree and depth of attention given various operations in a firm depends upon information desired, or upon the violations suspected or likely to be encountered. In determining the amount of attention to be given in specific cases, consider the:

1. Current Compliance Program,
2. Nature of the assignment,
3. General knowledge of the industry and its problems,
4. Firm history, and
5. Conditions found as the inspection progresses.

5.1.2.2 - 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 plant, raw materials, manual and automated processes, sources of contamination, manufacturing flow, method of data collection including computer terminals, are some of the areas 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 obvious potential problem areas such as: general house-keeping, state of operation for processes and processing equipment, and people dependent operations. Visual inspections of areas used for failure investigation, product sampling and testing, product reworks, return goods, and

product quarantine areas should be inspected for obvious potential product problems.

Depending on the product being inspected, some of the general inspectional equipment an investigator should have available, may include, eye and ear protection, boots and protective clothing. Some specialized equipment may include radiation or ethylene oxide (EO) monitoring devices, magnifiers, and timing devices as needed. For some domestic and foreign plant 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 S.

5.1.2.3 - Signing Non-FDA Documents

Occasionally a firm will request you sign various documents including:

1. 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,
2. Form letters concerning access to confidential information the firm does not want released,
3. A training form acknowledging that you were briefed on the personnel gowning procedures,
4. Information/data you request during the inspection be put into writing, etc.

If you receive such a request, inform the firm you are not authorized to sign such documents, letters, requests, waivers, etc., but will report the firm's request in your EIR. 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 4.3.4.3 and 4.5.4.6. Obviously, the key issue is you are not authorized to waive, without supervisory approval, any of FDA's rights to inspect, sample, photograph, copy, etc. or to sign any interstate shipping record document which could infer the firm could not be prosecuted under the Act.

5.1.2.4 - Technical Assistance

If you determine 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 ORA components or Center scientists and engineers. If specialized skills are necessary and are not available locally or through your Division, contact the Division of Domestic Human and Animal Food Operations (DDHAFO) for CFSAN and CVM (food) products or Office of Medical Products and Tobacco Program Operations (OMPTO) for CBER, CDER, CDRH, CTP and CVM medical products. See FMD-142 and IOM 1.9.2.2.1 for additional information.

5.1.2.5 - Team Inspections

The use of teams to conduct inspections may be beneficial. Very often individuals well versed in an analytical or inspectional technique or technology can provide assistance and advice. For combination product inspections, teams may be needed to bring appropriate program expertise to the inspection. (See IOM 5.12.1)

When inspection teams are involved in an inspection, one investigator will be designated as the team leader by the inspecting Division or by DDHAFO or OMPTO if a headquarters directed special inspection is involved. The team leader is in charge of the inspection and bears the overall responsibility for the inspection and the EIR. A team may consist of multiple investigators, laboratory personnel and other FDA employees, and your supervisor/coach, who may participate as part of the ORA Quality Assurance program.

5.1.2.5.1 - TEAM MEMBER RESPONSIBILITIES

Each team member is responsible for preparing those portions of the report pertaining to his/her activities. Team members shall identify their portion of the report, so they can later identify that portion as the part he/she performed and reported. Since reports should be written in the first person, one system might be to head each portion with a statement "The following operation(s) was/were observed and reported by Investigator _____", who can then report in the first person.

All team members must sign the EIR. Only those team members present at issuance sign the FDA-483 of FDA 4056. The issuance of the FDA-483 should not be delayed, in the absence of a team member's signature. See IOM 5.2.3 for instructions for signing an FDA 4056 and a multi-page FDA 483.

5.1.2.5.2 - TEAM LEADER RESPONSIBILITIES

The Team Leader shall be responsible for:

1. Issuing unused notebooks for taking regulatory notes during the EI or investigation to headquarters personnel on the team. He/she is also responsible for instructions on their use, if necessary, and when the report is finished, for obtaining the headquarters individual's signature on the original EIR and completed and properly identified regulatory notes and submitting them to the supervisor for filing. See IOM 2.1.3.
2. Directing the overall inspection to accomplish the objectives of the assignment including;
 - a. Planning the inspection,
 - b. Scheduling and coordinating team members' pre-inspection preparations,
 - c. Determining, to the extent possible, the firm will be open and operating,
 - d. Calling to pre-announce an inspection if required
 - e. Planning for needs of visiting scientists if applicable. When the team leader is not familiar with all the

- processes or technology involved in the inspection, provide for primary coverage of selected areas by other team members,
- f. Determining an orderly, efficient, and effective approach and sequence to be used and discussing the inspection plan with the team,
 - g. Modifying the inspection plan as necessary during the EI, to permit following leads, documenting evidence, etc.,
 - h. Setting team policy on how communications with the firm are to be handled,
 - i. Discussing personal conduct in dealing with headquarters personnel as necessary,
 - j. Assuring an early understanding by team members of their roles in note taking and reporting,
 - k. Assuring communications are open among team members, especially if the team is allowed to separate and work independently,
 - l. Reviewing inspection progress at least daily, discussing remaining objectives with the team members, and setting objectives for the following day,
 - m. Continually assessing the progress of the inspection to evaluate how the inspectional approach is working and to keep the division supervisor advised of the inspection's progress,
 - n. Providing guidance and direction to team members as necessary,
 - o. Advising each team member of reporting responsibilities and dates when drafts are to be provided,
 - p. Following up promptly on any delays or failures to report as required, and
 - q. Assisting the supervisor with further follow up, as indicated.
3. 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 actually taking part in the EI;
 4. Completing and/or correcting the computer-generated coversheet;
 5. Preparing the Summary of Findings;
 6. Completing all headings of an administrative nature in the narrative report;
 7. Compiling and submitting the complete final report; and
 8. Resolving any disputes or differences of opinion among the team members, including items, which may be listed on the FDA 483 or FDA 4056.

5.1.2.6 - Post-Inspectional Contacts

If the firm contacts the Investigator after the inspection regarding the inspection or follow-up, the Investigator should refer the request to his or her supervisor or to Compliance Branch if a regulatory action is contemplated. The Investigator should not respond to the firm regarding the adequacy of the firm's response to inspectional observations or any follow-up planned.

After the inspection is concluded, if the Investigator finds that a document or other required information is missing,

the Investigator should discuss the needed information and how to proceed with their supervisor.

5.1.3 - INSPECTION OF FOREIGN FIRMS

Inspectional requirements apply to all inspections, including foreign inspections. However, there are some exceptions. For instance, the FDA 482 is not issued, 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.

5.1.3.1 – Review of Foreign-Language Document

When reviewing documents in a foreign language, do not use any web and mobile applications translation tools that have not been authorized by FDA for this particular purpose. Use of these tools may result in unauthorized disclosure of non-public information.

If, based on the information you are reviewing, 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, you may do so. Ensure that, if all your searches were read together, the combination of searches would not result in any unauthorized disclosure.”

5.1.4 - INSPECTIONAL PRECAUTIONS

Our concern over microbiological contamination emphasizes the need for you to 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 sanitation 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, conducting environmental investigations at poultry layer facilities, conducting dairy farm inspections or audits of state activities, investigating drug residue reports or working in the veterinary bioresearch area or conducting produce safety inspections. See IOM 5.2.10 for information outlining precautions for you to follow.

Exercise caution in all activities in the firm. Follow the firm's sanitation program for employees and wash and sanitize hands, shoes, vehicles and equipment as indicated. Restrict unnecessary movement between various areas in plants 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 pharmaceutical or device firms), follow the sterile program required of the firm's employees. In general, it is unnecessary to enter sterile rooms except in the most extraordinary circumstances. These areas are usually constructed to provide visual monitoring. Take no unsterile items with you (note-

book, pencils, etc.). In this type of situation, you can enter 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 for microbiological examination. See IOM 4.3.6.

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 firm's using chemicals, pesticides, etc., ask to review the Material Safety Data Sheets (MSDS) for the products involved to determine what, if any, safety precautions you must take. This could include the use of respirators or other safety equipment.

5.1.4.1 - Clothing

Wear clean coveralls or other protective clothing for each inspection 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 pens, pencils,, 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.

Clean protective clothing should be either individually wrapped or placed in clean plastic bags and taped to protect from contamination. If the package has been sterilized, 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 IOM 5.2.10.1 for protective clothing and equipment necessary when visiting livestock or poultry producing areas.

5.1.4.2 - PHS Recommendations - Basic Sanitary Practices

FDA personnel are not required by law to have health certificates, take physical exams or submit to requirements, which ensures their compliance with sanitary procedures in the performance of their official duties. However, it is critical you adhere to basic sanitation practices. See S.8.1 - General Preventive and Protective Measures and <https://fda.sharepoint.com/sites/insideFDA-EmployeeResources/SitePages/Occupational-Health-Services.aspx,S.17.2> - Immunizations, and S.17.3 - Physical Examinations.

[The Food Code 2017](#) is available electronically from the FDA CFSAN web page under Federal/State Programs-Retail Food Safety References. Printed copies may be ordered from the [National Technical Information Service](#) website.

5.1.4.3 - Representatives Invited by the Firm to View the Inspection

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

Regardless of whom the firm invites to observe the progress of an inspection, the presence of outside representatives should not disrupt the inspectional process. You should continue to conduct the inspection in a reasonable fashion. The presence of these individuals should have no impact on the manner in which 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 inspection is recorded via videotaping, other photography, and/or audio recordings. Where applicable, refer to IOM 5.3.5 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 privileged information provided to him/her during the inspection, it is the firm's responsibility to protect privileged/confidential information observed or recorded by those individuals invited by the firm.

5.1.5 - GENERAL PROCEDURES & TECHNIQUES

The procedures and techniques applicable to specific inspections and investigations for foods, drugs, devices, tobacco products, cosmetics, radiological health, or other FDA operations are found in part in the IOM (inspectional and investigational policy/procedure), and the Compliance Program Guidance Manual (program specific instructions).

Some procedures and techniques which may be applicable to overlapping areas or operations are as follows:

5.1.5.1 - 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 below 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 generally 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 utilize the firm's candling equipment. Various other light sources for candling are also available including overhead projectors. Exercise care when using overhead projectors and protect the glass surface and the lens from scratches and damage. All candling is best accomplished when light outside the item being candled is masked so 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.

5.1.5.2 - 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 management's attention. See also IOM 5.2.3.2 regarding labeling for blood and blood products.

If 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 PMA supplement, it is essential the label and labeling be collected.

5.1.5.3 - Field Exams

A field examination is an on-site examination of a domestic product (or a foreign product in domestic channels of trade) sufficient in itself to determine if the product is in compliance 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, e.g., 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 "Guides to Inspection of ****" and Compliance Programs. The Sample Schedules in Chapter 4 also provide guidance on lot examinations for special situations.

SUBCHAPTER 5.2 - INSPECTION PROCEDURES

5.2.1 - PRE-INSPECTIONAL ACTIVITIES

Prior to the start of any inspection or investigation, you should conduct a number of activities. These will differ based on whether this is an inspection or an investigation. Review establishments history, e.g. previous EIRs, complaints, registration listing, recalls. The purpose of this review is to determine the location of the establishment and obtain an overview of the establishment's operations and products as well as an understanding of their compliance history. Consumer complaint review will also determine if there are any complaints with open assignments, or with the status "Surveillance information for next EI" that need to be closed. You should also review the establishment factory jacket to determine if there were any prior safety issues noted, e.g. documented Investigator safety incidents or whether any specific personal protective equipment is needed prior to the start of the inspection. If there has been a past personal safety incident, you should discuss with your supervisor and develop a Situational Plan prior to the start of the inspection. See IOM 5.2.1.4 – Personal Safety Plan.

Prior to initiating any inspection, you should become familiar with the reporting requirements for the specific assignment, as well as the requirements of IOM Subchapter 5.10.

If the inspection or investigation is a directed assignment from a Center, ORA headquarters or another program division, read the assignment and attached materials to assure you understand the assignment. If the inspection or investigation is being conducted in part or solely as a recall follow-up or complaint, refer to Chapter 7 (Recalls) or Chapter 8 (Investigations) of the IOM for additional guidance.

You should review the eNSpect assignment to determine if the Personal Safety Alert Indicator is set to yes for this specific firm. The reason for the Personal Safety Alert should be listed in the Endorsement for the previous inspection and should be accompanied by a memo to the Establishment File Jacket. See IOM 5.2.1.3 eNSpect Personal Safety Alert.

You should also review the applicable Compliance Program Guidance Manual(s) prior to the start of your inspection or investigation. Division of Domestic Human and Animal

Food Operations (DDHAFO) The Centers have issued numerous guidance documents for industry. These documents are normally posted to the appropriate Center's Internet web site.

Subchapters 5.4-5.9 of the IOM contain additional, program specific pre-inspectional activities, which you should follow.

Imported products cross all program areas and our regulation of them does not stop at the border. Determine if there are any "import for export" follow-up assignments and be prepared to cover them during your inspection. See IOM 6.2.3.4 for guidance. Please be alert to imported products whenever you make 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.

5.2.1.1 - Pre-Announcements

Pre-announcements are mandatory for all medical device surveillance inspections in accordance with the criteria and instructions below and some BIMO inspections. Routine produce safety inspections should be pre-announced, unless otherwise directed. In some other program areas, pre-announcements may be made at the discretion of the program division. If you are going to visit facilities where livestock (including poultry) or wild animals are housed or processed, review IOM 5.2.10. In general, it may be inappropriate to pre-announce inspections of food establishments, blood banks, source plasma establishments and some BIMO inspections, but this too is subject to program division discretion.

If a program division believes pre-announcing an inspection of an establishment will facilitate the inspection process, then the procedures below for doing pre-announcements for medical device inspections should be followed. ORA's primary purpose for pre-announcing is to assure the appropriate records and personnel will be available during the inspection. It is not to make an appointment for the inspection. It should not 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).

In the case of drug inspections, if efforts to schedule a pre-announced inspection are met with unreasonable delays by the establishment, including requesting 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)]. FDA will make reasonable accommodations for 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 be reasonable.

The Program division may use this data in the future when considering whether this establishment should be eligible for pre-announced inspections.

The Produce Safety Network (PSN) should follow the pre-announcement instructions provided in the Produce Safety Inspections assignment.

The following is the general outline for pre-announcement of medical device inspections. You are advising the establishment's management of the date and time you will be arriving at the establishment to conduct the inspection. The establishment has no authority to negotiate this. If you, as the investigator, feel the need to accommodate the establishment's request, be sure there are sound reasons for doing so and report them in your inspection report.

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.

5.2.1.1.1 - 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 Criteria for Consideration) The program division does not have the discretion to decide the types of medical device 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 5 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 5 calendar days from the original date. Inspections may be conducted sooner than 5 calendar days if requested by or acceptable to the establishment and if this date is acceptable to the investigator/team.

To participate in the pre-announcement portion of the program, establishments are expected to meet the commitment to have appropriate records and personnel available during the inspection.

Pre-announced inspections will not limit an investigator's authority to conduct the inspection. Inspections will be as thorough as necessary.

5.2.1.1.2 - CRITERIA FOR CONSIDERATION

Determine whether an establishment requires or qualifies for a pre-announced inspection (see section 5.2.1.1 Pre-Announcement). Examples include:

1. Pre-market inspections (PMA, 510(k))
2. Foreign inspections
3. Instructed by Compliance Program, assignment or directive
4. Quality System Surveillance Inspections
5. During Health Emergency Crisis; e.g.: epidemic, pandemic

5.2.1.1.3 - PROCEDURES

Procedures:

1. The investigator designated to conduct the inspection will 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. The program division should use good judgment as to what is a reasonable time frame to await the return call.
2. Changes in dates should be kept to a minimum. If a change is made, a new date should be provided as soon as possible, which will facilitate the inspection and accommodate the investigator's schedule. The establishment should 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, specific records/personnel will be requested at the time the inspection is pre-announced.
5. The notification should be as specific as reasonably possible and specify the date for the start of the inspection.
6. Produce Safety Inspections should follow any additional instructions provided in the Produce Safety Inspection assignment.

Include in your EIR whether or not the inspection was pre-announced and include information on any difficulties experienced in notification or accessing records or personnel, which should have been available as a result of pre-announcing the inspection. For medical device establishment inspections, if not pre-announced, describe briefly in the EIR why not. If an establishment should become ineligible for pre-announcement, the endorsement of the EIR should include this statement. This information will be necessary for making a determination regarding future pre-announced inspections of the establishment. In addition, it is advisable to inform the establishment during the current and subsequent inspections of the action(s), which may have caused them to be ineligible for pre-announcement.

Subchapters 5.4-5.9 of the IOM contain additional, program specific pre-inspectional activities, which you should follow.

5.2.1.2 - Personal Safety

ORA considers the safety of investigators, inspectors and all those who meet with regulated industry to be of the utmost importance. Personal safety concerns are defined as those factors FDA employees should maintain awareness of which potentially affect their safety during an inspection, such a threatening situation; or where specific personal protective safety equipment is warranted; or where a particular inspection may be medically contraindicated for specific FDA personnel. When these conditions are noted during an inspection, the investigator should discuss the situation with their supervisor and ensure that the Personal Safety Alert is checked in FACTS/ eNSpect and a Memo to the File is generated – see IOM 5.2.1.3. For information concerning personal protective equipment, see IOM Subchapter 1.5.

Physical resistance to FDA inspections and threats to, or assaults on, FDA employees engaged in their work are extremely rare. However, there will be times you are confronted by unfriendly or hostile persons. ORA has offered various conflict resolution training courses to assist and prepare you for how to diffuse a situation. In most instances, conducting your activities with tact, honesty, diplomacy, and persuasiveness will be enough to diffuse the situation. 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 5.2.5.4 for Hostile and Uncooperative Interviewees.

Safety is the responsibility of all FDA employees, including you, your supervisor and other Agency management. When you receive an assignment, it is important to evaluate the assignment not only in accordance with IOM Section 5.2.1, but also with respect to your personal safety. If you determine there is the possibility of a threat to your personal safety, consult with your supervisor. You and your supervisor should consider developing a Situational Plan in preparation for the inspection.

5.2.1.2.1 - PREPARATION

Below are some 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.

1. Does the assignment involve working with other Federal Agencies such as U.S. Marshals, Federal Bureau of Investigations, and U.S. Customs in executing search warrants, seizures, etc.?
2. Does the assignment involve working with or contacting FDA's Office of Criminal Investigations (OCI)?
3. Does the assignment involve a firm where there is a suspicion and/or knowledge of questionable or illegal activities?
4. Does the assignment involve a suspected tampering and/or a visit to an individual's residence?

5. What is the past history from a personal safety standpoint with the prior interactions with representatives of this firm? Have the FDA's state counterparts or other Federal and/or local agencies indicated a concern for personal safety? What does the firm's establishment file indicate about personal safety over the past inspections?
6. What is the location of the firm or the operation? Is it in an area which may be unsafe? Have the inspected firm or any of its employees been uncooperative with government officials?
7. Is the firm known to the Agency? Has the Agency any additional information which would assist in your evaluation?

If these questions and/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 5.2.1.4 – Personal Safety Plan.

Due to the unlimited variability of potential safety situations, it is not feasible to prescribe in the IOM what to do in every instance. The decision of what to do in each individual circumstance rests with the investigator and their program division management. 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, the experience of your program division management combined with the various training courses on conflict resolution may also be consulted. Program divisions should notify OMPTO or OHAFO to inform headquarters of any potential safety concern, 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: orahqcsosafety@fda.hhs.gov.

5.2.1.2.2 - PHYSICAL RESISTANCE/THREATS/ ASSAULTS

If you receive physical resistance or threats, or if you sense the real possibility of an assault, disengage from the confrontation, get to safety, and call your supervisor immediately. Make careful and exact notes later of who said what to whom, who did what, and whether someone tried or succeeded in threatening, assaulting or taking information or equipment or samples from you. Be careful in any descriptions you give or write of such events, just as you are in recording other evidence that may result in a court case. Your safety is more important to the United States than the inspection or the sample collection. FDA will work with law enforcement government officials, e.g., the Federal Protective Service (FPS), FDA's Office of Criminal Investigations' (OCI) Special Agents, local police, or United States Marshals to assist an inspection team if there is a reasonable fear of danger to the investigator.

If you are assaulted (either physically or put in fear by threats of physical violence), your supervisor can summon local police, the Federal Protective Service (1-877-437-7411), United States Marshals, FBI or contact OCI headquarters for assistance (301-294-4030). While OCI does not normally provide physical security in these cases, they will assist in threat evaluation based on specific facts and available criminal databases. OCI can also make contacts with local police and federal agencies based on previous established liaisons. 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. Be careful in any descriptions you give or write of such events, just as you are in recording other evidence that may result in a court case. Make sure that any inspected facility where weapons are observed, or where threats or assaults occur, is identified on that facility's Endorsement page of the inspection report for that facility and to your supervisor, so that Investigators or Agents who follow you into that facility will be alert to those possibilities. Your supervisor would also be responsible for checking the Personal Safety Alert box in FACTS and for beginning the notification process to alert other Federal or State agencies that also inspect the facility of the possible danger. For more information see IOM 5.2.1.3 Personal Safety Alert. For specific safety guidance related to inspections and interviews, see IOM 5.2.5.4.2 Hostile and Uncooperative Interviewees.

In addition, in any instance where you have perceived a threat to your personal safety during an inspection, investigation or sample collection, you should exit the situation immediately and report it to your supervisor. Potential threats may include geographic locations, concern about entering into a residence to conduct official business, or animals that are not caged or contained. You should then write a memorandum of the event in a factual manner including information pertaining to the who, what, when, where, and how of the event. Be careful in any descriptions you give or write of such events, just as you are in recording other evidence that may result in a court case. This memo will be filed in the official establishment file jacket and copies be sent to any and all resident posts and import program division offices who may interact with this firm. The memo will be filed on the opposite side of the folder from all other documents and will be a printed on eye-catching color paper in order for the document to be visible to the next Investigator. The memo should be retained and maintained within the division. A copy of the Memo documenting the personal safety situation should also be sent to the headquarter component via orahqcsosafety@fda.hhs.gov.

5.2.1.3 – eNSpect Personal Safety Alert

In eNSpect, the person creating an assignment may add an "Active Personal Safety Alert" (PSA) on the "Firm" page. This field is editable any time after the assignment is created. The "Personal Safety Alert" tab on the "Firm Details" page in Management Services (FMS) should be checked for the existence of a PSA when assignments are

created and before inspections are conducted. Only the FACTS Supervisor Role will allow for updating the Maintain Firms screen. This personal safety alert may be selected when there is a potential hazard identified:

1. Where a previous threat/assault or physical resistance occurred
2. Where specific personal protective equipment is needed (respirators, etc.)
3. Where there are specific medical considerations for a population of investigators (e.g. the firm manufactures a drug hazardous to women of child-bearing years or those with allergies to peanuts, penicillin, or other products.)

In any example listed where there is a Personal Safety Alert, the specific safety alert should be documented both in the Endorsement and in a Memo to the File. The memo should be flagged "MEMO TO FILE - PERSONAL SAFETY ALERT" and should provide the factual information to support why the investigator should be alerted to the safety issue. Be careful in any descriptions you give or write of such events, just as you are in recording other factual evidence that may result in a court case. The memo should be filed in the official establishment file jacket and copies sent to any and all Resident Posts and import program divisions who may interact with the firm. The memo will be filed on the opposite side of the folder from all other documents and will be a printed on eye-catching color paper in order for the document to be visible to the next Investigator. The memo should be retained and maintained at the Program division office. A copy of the Memo documenting the personal safety situation should also be sent to orahqcsosafety@fda.hhs.gov. The supervisor and/or other program division management will be responsible for evaluating any corrective actions taken by the firm or individual to remove or stop the potentially dangerous situation or condition. Follow-up inspections at the facility should continue to document whether or not the safety situation continues exists. If the situation has been resolved (new management, dismissal of an employee, cessation of penicillin in a facility, etc.) the Personal Safety Alert should be removed from FACTS by the supervisor.

5.2.1.4 – Personal Safety Plan

A Personal Safety Plan is an investigative tool developed to assist in managing and preparing for a potentially dangerous situation. Program division's should develop a Personal Safety Plan when the conditions surrounding the specific inspection, investigation or sample collection indicate a plan is needed. The plan allows all those involved to carefully evaluate the specific inspection in order to prepare for a successful conclusion. Utilizing Personal Safety concepts prior to a potentially dangerous situation is part of the training programs of many other Federal Agencies. The plan should document what specific roles and responsibilities are needed to conduct the inspection/investigation or sample collection. The plan should also answer the questions: Who, What, Why, When and Where concerning the potential danger.

There are seven principles to a Personal Safety Plan. These are:

1. **Summary of Potential Hazards:** This section of the personal safety plan includes all of the potential hazards, in a detailed description, that prompted the need for a personal safety plan. Be sure to answer the questions: Who, What, Where, When, and Why. Also include any specific hazards that require personal protective equipment or situations at the facility that may cause allergic reactions for investigators or analysts. Include in the section information from past inspection reports, discussions with previous FDA, State or local investigators, as well as any environmental or plant/facility specific information that would negatively impact a successful personal safety plan when initiated.
2. **Sources of Information:** This section of the personal safety plan includes all the sources from which your potential hazards were collected. For instance, document which FDA investigator or State inspector supplied factual statements; state the documents or databases from which you obtained information to assist in your hazard summary. This section is important, as it documents factual evidence, similar to all of your other FDA factual inspection gathering information.
3. **Response Alternatives:** This section will be the most important part of your plan because it includes all of the details of what will be done to mitigate the hazards. In this section, provide a list of factual, practical responses or options to consider. This will also allow your supervisor to see all the possible ways to handle the situation. The response plan should also outline all of the tools that you possess to assist you in handling the situation carefully, including training, experience, and other procedures you have at your disposal. Roles and responsibilities of all involved in the plan should be identified including those intended to be on-site, and those who will be off-site, and participating in the plan.
4. **Communication:** provide all information about how communication will occur between on-site and off-site participants; between those present on-site, and any emergency, law enforcement or medical responders. Also consider types of communication, e.g. code words for emergencies.
5. **Transportation:** Provide information in the plan as to how travel to the facility will happen. Is there a coordination point? Do you intend to use Government marked or unmarked cars? Who will ride in each car? 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:** Include in this section all equipment needed to initiate this plan. Is personal protective equipment needed? Is there any special sampling equipment or other equipment needed? Include in this section, equipment such as communication tools, FDA forms, etc. Assure that the equipment needed is in full functioning mode.

7. Emergency Exit Strategy: Describe in this section what the exit strategy will be in the event of an emergency. Consider emergency strategies for safety (issues), as well as any medical emergency. How will the emergency be communicated on-site and off-site? How do you exit the facility and return to your vehicle? Is there a scheduled meeting point to assure all are safe? The goal is to have no one left behind. Remember to contact your supervisor when you return to safety.

Once the plan has been completed, a debriefing of the situation should occur with all who were involved in the plan development. Evaluate what went well, what needed improvement, what would be done differently the next time. Evaluate whether the plan was successful and document lessons learned for the next time.

The Personal Safety Plan should be developed by the investigator, supervisor, other investigators who may be familiar with the facility, compliance officer, if needed, and any other individuals (Program Division or HQ experts, etc.) who may be able to assist in the depth, scope, and specifics of the firm in question. The decision of who should be involved in the development and approval of the plan is left to the program division's discretion.

Program division management and all involved in writing the personal safety plan should meet when necessary in order to assure a well-developed and understood personal safety plan. You and your supervisor should maintain contact during the execution of the personal safety plan. The supervisor should contact the employee during these personal safety situations at a predetermined frequency outlined in your plan. A debriefing session should be held following the execution of the plan. Discussions should include what actions worked well and where there are areas of improvement.

For foreign inspections where a Personal Safety Plan is warranted, headquarters 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.

The Personal Safety Plan should be placed in the official establishment file jacket separate from any EIRs in the same location as any Personal Safety Alert memos. A copy of completed and executed Personal Safety Plans must be sent to orahqcsosafety@fda.hhs.gov in order to maintain a reference library of all Personal Safety Plans.

5.2.2 - NOTICE OF INSPECTION

Upon arrival at the firm locate the owner, operator or agent in charge of the establishment. This should be the top Management Official on site. Be certain of this individual's status. Introduce yourself by name, title and organization. Show your credentials to this person and present a properly signed, completed original of the FDA 482, Notice of Inspection or FDA 482d Request for FSVP Records. The

FDA-482 or FDA 482d should have the address of the home district of the firm. *

If additional Agency personnel accompany you during the inspection, they must show their credentials to the top Management Official upon arrival at the site. A new FDA 482, Notice of Inspection or FDA 482d Request for FSVP Records must be issued. Submit a copy of the FDA 482(s) or FDA 482d with your EIR. 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. Non-FDA officials and those who do not hold FDA credentials do not sign the FDA 482 or FDA 482d. See IOM 5.1.1 and 5.11.4.3.3.

For multiple occupancy inspections in drug establishments, refer to IOM 5.1.1.11. Inspections of multiple firms, which are separate legal entities, should be reported under separate EIRs.

If faced with a refusal, or partial refusal of inspection, proceed as outlined in IOM 5.2.5.4.

Any time an FDA 482 is issued, also issue an FDA 484 (at the conclusion of the inspection), Receipt for Samples, if you collect any samples at the firm. See IOM 5.2.4. See IOM 4.1.1.1 and 4.1.1.2 for instructions for issuance of the FDA 482 in certain sampling situations.

If you have concerns of when to or when not to issue the FDA 482, discuss with your supervisor.

*: For all firms within the State of Arizona, the Home District is Denver District. Home District boundaries are identified in Appendix E.

5.2.2.1 - 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 (i.e., a week or longer) before you can return to the firm to complete the inspection, be sure management is aware of the delay and discuss with your supervisor whether or not you need to issue another FDA 482 or FDA 482d.

5.2.2.2 - Inspection of Vehicles

If vehicles are present which are owned or leased by the firm being inspected and it is necessary to inspect the

vehicles, the inspection of these is covered by the FDA 482, Notice of Inspection, you issued to the firm.

If vehicles (trucks, trailers, RR 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:

1. Issue the FDA 482 to the driver of the vehicle.
2. If the driver is not present and if, after a diligent search, he 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 RR 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.

5.2.2.3 - 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 authority 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 inspections under these situations, obtain a copy of the injunction or other court order bearing the filing stamp and all relevant signatures. Prior to starting the inspection study, the order thoroughly for any special instructions of the court. Your supervisor will assist you in determining the depth of the inspection necessary to cover all of the court requirements.

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, modified to read, "Notice of Inspection is hereby given under authority of injunction (provide here the injunction number and/or other identification) against 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 that person.

"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 the pertinent section(s) or portion of the order to the person refusing so there will be 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 5.2.5 for 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.

5.2.2.4 - Conducting Regulatory Inspections When the Agency is Contemplating Taking, or is Taking, Criminal Action

You should not issue a Notice of Inspection if the agency is contemplating taking, or is taking, criminal action against a firm without first discussing the matter with your supervisor. Program division management will obtain advice from the Office of Chief Counsel and will allow or not allow, the inspection to proceed based on any considerations related to the criminal investigation. Decisions to inspect under such circumstances should be based on considerations of whether or not the request is consistent with FDA's responsibility to assure articles 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 these considerations are documented. In no circumstance should an inspection be conducted *solely* to obtain evidence to support a possible criminal case.

Inspections conducted in accord with this 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 United States Constitution prohibits searches without a warrant supported by probable cause. One exception to the warrant requirement includes the inspection of industries long subject to close supervision and inspection, which are conducted under a statute dispenses with the need for a probable cause warrant. 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 Federal Food, Drug, and Cosmetic 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 2.2.1.1. 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. As long as 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 make it more likely a court would find the use of statutory authority to be pretextual and render the evidence obtained to be inadmissible. Concerns related to the conduct of an inspection while a criminal investigation is being considered or pursued should be discussed with the Office of Chief Counsel.

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 the Office of Criminal Investigations (OCI) is conducting a criminal investigation of a firm which is subject to regulatory inspection. OCI may determine it is not in the interest of the agency to disclose to other components of FDA the existence of its investigation, as long as OCI is not involved in the agency decision to conduct a regulatory inspection. However, OCI and other components of FDA may also share information as set out below.

5.2.2.5 - When Evidence of a Criminal Violation is Discovered in the Course of a Regulatory Inspection

There may also be occasions where you are conducting a regulatory inspection at a facility, and, in the course of 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. The program division should refer the 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 assure articles are being produced in conformity with the Food, Drug, and Cosmetic Act. Additional inspections may be warranted. Such inspections should be planned and documented in accordance with the preceding section, "Conducting Regulatory Inspections When the Agency is Contemplating Taking, or is Taking, Criminal Action."

5.2.2.6 - Use of Evidence Gathered in the Course of a Criminal Investigation

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

Information and evidence gathered in the course of 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 in the course of 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.

5.2.2.7 - Use of Evidence Voluntarily Provided to the Agency

Criminal and regulatory investigators may share information and evidence voluntarily provided to 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.

5.2.2.8 - 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 Office of Criminal Investigations Headquarters staff to discuss issues related to the timing of administrative, civil, and criminal actions. The Office of Criminal Investigations and other components of FDA may share information subject to the reservations set out earlier.

5.2.2.9 - 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 Department of Justice attorney or the Office of Chief Counsel attorney assigned to the grand jury case. See IOM 2.2.7.3 for additional information on Grand Jury proceedings.

5.2.3 - REPORTS OF OBSERVATIONS

The FDA 483, Inspectional Observations (see Exhibit 5-5) and the FDA 4056 Produce Farm Inspection Observations (See Exhibit 5-18) is intended for use in notifying 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 5.2.3.2) which were observed during the inspection. These observations are made when in the investigator's "**judgment**", conditions or practices observed, indicate that any food, drug, device, or cosmetic have been adulterated or are being prepared, packed, or held under conditions whereby they may become adulterated or rendered injurious to health. The issuance of written inspectional observations is mandated by law and ORA policy.

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

All FDA-483s and FDA 4056s should adhere to the following general principles:

1. Observations which are listed should be significant and correlate to regulated products or processes being inspected.
2. Observations of questionable significance should not be listed on the FDA-483 and FDA 4056, but will be discussed with the firm's management so that they understand how uncorrected problems could become a violation. This discussion will be detailed in the EIR.

All FDA-483s and FDA 4056s should have the following characteristics to be useful and credible documents:

1. Each observation should be clear and specific.
2. Each should be significant. Length is not necessarily synonymous with significance.
3. Observations should not be repetitious.
4. The observations should be ranked in order of significance.
5. All copies of the FDA-483 and FDA 4056 should be legible.

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 and FDA 4056.

Investigators and analysts should make every reasonable effort to discuss all observations with the management of the establishment as they are observed, or on a daily basis, to minimize surprises, errors, and misunderstandings when the FDA 483 or FDA 4056 is issued. This discussion should include those observations, which may be written on the FDA 483 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. Investigators are encouraged to verify the establishment's completed corrective actions as long as the verification does not unreasonably extend the duration of the inspection.

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 5.2.3.4 - 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 for food inspections. 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 document review reveals observations on a different day than the documents were collected or in other circumstances. When these instances occur immediately prior to the conclusion of the inspection the lack of a daily discussion of observations does not preclude listing of significant observations which were not previously discussed on the FDA 483 or the FDA 4056.

eNSpect

eNSpect is an automated FDA 483, FDA 4056 and EIR reporting system. Use eNSpect to generate the FDA 483 or FDA 4056 where applicable cite modules exist. eNSpect should not be used to create an FDA 483 or during an inspection of a firm involving multiple commodity areas when FDA 483 cites do not exist for ALL of the commodity areas for which observations need to be included on the FDA 483. You should be able to write the entire FDA 483 and FDA 4056 using eNSpect.

Use eNSpect for all EIRs whether or not your FDA 483 or FDA 4056 was generated using eNSpect and when no FDA 483 was issued. See IOM 5.11.4.

5.2.3.1 - 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 at a later time to issue and discuss your inspectional observations. In this case, you should advise the firm’s management your inspection has not been completed and you will return to issue the FDA 483 and discuss inspectional findings. There should be no unreasonable or unwarranted delays in issuing and discussing the FDA 483. During the inspection, do 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.

5.2.3.1.1 - INDIVIDUAL HEADINGS

District Office Address and Phone Number - Legibly print 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.

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.

See IOM 1.6.5.1 – Professional Stature for situations where firms express a concern during routine enforcement activities where an FDA 483 was not issued, or the activity is not an inspection.

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.

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

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).

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

FEI Number - If the FDA Establishment Identifier 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, cannery, wholesale warehouse, drug repacker, salvage warehouse, etc.

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, and FDA 4056 even if they are not available to sign the FDA 483, FDA 483a, and FDA 4056. Each member of an inspection team should sign the FDA 483, FDA 483a, and FDA 4056. However, absence of a team member at the conclusion of an inspection need not prevent issuance of the FDA 483, FDA 483a, or FDA 4056. See IOM 5.1.2.5.1. If you use an electronically generated FDA 483, FDA 483a, or FDA 4056, assure you have a copy for the program division files -- an unsigned photocopy or printed duplicate is unacceptable. See IOM 5.2.3.6.2.

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. 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 – first inspection of the farm
- Routine – normal surveillance inspection
- Follow-up – follow-up to a violative inspection
- For-cause – inspection to follow-up on a specific issue, such as an outbreak or positive sample
- Other (please specify) – inspection that doesn’t meet one of the other categories (will be 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 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.

5.2.3.1.2 - SIGNATURE POLICY

Everyone present under FDA inspectional authority at issuance signs the first and last pages of the FDA 483 and initials each intervening page in the 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 will appear on all pages of the FDA 483 and the remaining team members' signature will appear on the last page.

On the FDA 4056, the signature is captured on one page in the FDA Representative Signature block. Everyone present under FDA inspectional authority during the inspection should be listed in the Representative(s) Name and Title box.

The FDA 4056 should be completed and signed electronically in eNSpect prior to printing and issuance. In circumstances where eNSpect cannot be used to complete the FDA 4056, complete the fillable PDF form. Only the lead FDA representative is to electronically sign the PDF FDA 4056.

If electronic signature in eNSpect or the fillable PDF FDA 4056 is not possible, print the FDA 4056 and all FDA representatives present at the close-out of the inspection are to sign in ink.

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. Everyone present under FDA inspectional authority are to sign the document in ink. A copy of the signed FDA 4056 must be obtained for inclusion in the Produce Farm Inspection Report (PFIR), which is the equivalent of an EIR for produce farm inspections.

See IOM 5.2.3.6 -Distribution of the FDA 483 and FDA 4056.

5.2.3.1.3 - DATE ISSUED

Enter the date the form is actually issued to the firm's management.

5.2.3.1.4 - OBSERVATIONS

Where applicable, when formulating each FDA 483, FDA 483a, and FDA 4056 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)

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, FDA 483a, and 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, and FDA 4056 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 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).

1. The lot number for a component received from or shipped to firm "A".
2. The invoice number for a shipment from or to firm "A".
3. A patient #, record #. See IOM 5.2.3.3 item 7.
4. The study number for a particular Clinical Investigator site.
5. Other necessary but non-specific identifying information to show the observation's relationship to a particular firm and/or individual.

Presently there are three ways to generate an FDA 483, FDA 483a, and FDA 4056.

1. eNSpect
2. Traditional hard copy
3. Electronic (non-eNSpect) version

When using a traditional hard copy FDA 483 or electronic (non-eNSpect) version of the FDA 483, the current version of the 483 must be used. As of the printing of the current IOM, the current version of the FDA 483 is dated 9/08.

5.2.3.1.5 - MEDICAL DEVICE INSPECTIONS

The following language should be inserted on the FDA 483 in addition to 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 any and all violations of the quality system requirements."

5.2.3.1.6 - CORRECTION OF FDA 483, FDA 483a, and FDA 4056 ERRORS

These procedures do not pertain to adverse conditions noted and then corrected during the inspection.

Observations of this type stand and should remain on the FDA 483, FDA 483a, and FDA 4056.

The Inspectional Observations (FDA 483), Request for FSVP Records (FDA 483a) and Produce Farm Inspection Observations (FDA 4056) is of critical importance to both the Agency and regulated industry. Individual FDA 483s, FDA 483a, or FDA 4056 may become public through publishing in industry trade press, FOI inquiries, Headquarters postings and other means. Therefore, complete and accurate documentation of corrections to this official document is critical.

5.2.3.1.6.1 - Errors Discovered Prior to Leaving the Establishment

Non-eNSpect, FDA 483s, FDA 483a, and FDA 4056s:

1. 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.
2. 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 the establishment has no such equipment or refuses to provide you with a copy of the original corrected FDA 483, FDA 483a, or FDA 4056 then make the corrections, initial the changes and retain a copy of the corrected FDA 483, FDA 483a, or FDA 4056 for your Division's official establishment file.

eNSpect FDA 483s:

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

1. Changes made to correct errors in the text of the observation will show on the face of the final printed FDA 483. Changed Text deletions will remain visible as strike through and correction made. For example, "lot 1234 5678" – (select text, right click, select font and select strike-through) or from "lot 1234" to "lots 1234 and 5678" and bold the changes "lots 1234 and 5678"
2. If an entire observation is removed or the underlying citation is changed, incidental text will be used to add the statement "An observation concerning *** was removed [or the underlying citation was changed] based on discussions with management."
3. Addition of a new observation or changes to the observation.

5.2.3.1.6.2 - 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.

1. Non-eNSpect, FDA 483s, FDA 483a, FDA 4056s: Discuss any errors with your supervisor. If necessary, a revised FDA 483, FDA 483a, or FDA 4056 will be prepared.
2. eNSpect FDA 483s, FDA 483a, and FDA 4056s: Discuss any errors with your supervisor. Make all corrections/deletions in eNSpect per 5.2.3.1.6.1.
3. Issuing FDA 483s, FDA 483a, or FDA 4056s: Personally deliver the amended FDA 483, FDA 483a, or FDA 4056 to the firm for discussion. If personal delivery is not practical, mail the amendment to the firm with a full explanation cover letter. Include a copy of the original FDA 483, FDA 483a, or FDA 4056, 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 your discussion in your EIR.

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 the original FDA 483, FDA 483a, or FDA 4056 was issued.

FDA 483s, FDA 483a, and FDA 4056s should be issued in eNSpect unless there are no commodity specific cites in eNSpect, technical difficulties, or certain multiple commodity situations (See IOM 5.2.3) Other options are:

1. Electronic (non-eNSpect) version of the FDA-483, FDA 483a, or FDA 4056.
2. Handwritten FDA 483, FDA 483a, or FDA 4056.

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

5.2.3.2 - Reportable Observations

You should cite factual observations of significant deviations from the [FD&C Act](#) [21 U.S.C. 301], [PHS Act](#), [21 CFR](#), and other acts where FDA has enforcement authority unless these cites require concurrence or are specifically prohibited – see IOM 5.2.3.3 Non-Reportable Observations. Examples of these observations generally fall into two categories.

5.2.3.2.1 – Adulteration Observations

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]. Include specific factual observations of:

1. Foods, drugs, devices, or cosmetics consisting in whole or in part of filthy, putrid, or decomposed substances.
 2. Undesirable conditions or practices, bearing on filth or decomposition, which may reasonably result in the food, drug, device, or cosmetic becoming contaminated with filth.
 3. Insanitary conditions or practices which may reasonably render the food, drug, device, or cosmetic injurious to health.
 4. Careless handling of rodenticides or pesticides.
 5. Results of field tests (organoleptic examination of fish, crackout of nuts, etc.) if the results revealed adulteration.
 6. 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.
 7. Observations of faulty can closures and/or deviations from recommended processing times and temperatures.
 8. Deviations from the animal proteins prohibited in ruminant feeds requirements ([21 CFR 589.2000](#)).
 9. Results of analytical laboratory findings which reveal adulteration.
- 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].
 8. 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]}
 9. 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)]}
 10. Observations of non-conformity to the Unique Device Identification (UDI) requirements of 21 CFR 801 Subpart B and 21 CFR 830.
 11. 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.
 12. In general, observations indicating noncompliance with medical device pre-market notification requirements and pre-market approval requirement under FD&C Act sections 510(k) and 515 [21 U.S.C. 360 (k) and 360e] respectively, should be included with the prior confirmation of CDRH and/or CBER

5.2.3.2.2 - 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 CPs and other agency directives. In some cases, you may cite labeling deviations as directed below. This list is not all inclusive.

1. 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].
 2. Observations, forming the basis for product non-acceptance under the Government Wide Quality Assurance Program (GWQAP). See IOM 5.2.3.5.
 3. Deviations from blood and blood products labeling requirements as specified in [21 CFR 606.121](#) and [21 CFR 640](#).
 4. 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)].
 5. Deviations from the applicable labeling regulations for human cells, tissue, and cellular and tissue-based products (HCT/PS) as specified in [21 CFR 1271](#) and [CP 7341.002](#).
 6. 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.
 7. Observations indicating non-conformity with the post marketing adverse drug experience reporting
13. [21 CFR PART 200.10](#) does allow reporting observations noted at a contract facility to the contracting facility. Before doing this, check with your supervisor to determine if this is appropriate.
 14. 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.
 15. Deviations from the applicable labeling requirements for outsourcing facilities as specified in Section 503(B)(a)(10) of the FD&C Act.
 16. Observations at animal food facilities that are not subject to animal food regulations (e.g., 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. See [Compliance Program 7371.000: COMPREHENSIVE ANIMAL FOOD INSPECTION](#) for more details.

5.2.3.3 - Non-Reportable Observations

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. See IOM 5.2.7 involving discussions with management at which time opinions may be discussed.

Do not quote Regulations (e.g., specific CFR sections) when listing items.

Do not report observations pertaining to:

1. Label and labeling content, except per IOM 5.2.3.2.2, 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

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 5.2.3.4. These actions should be reported in the EIR.

Use eNSpect to document in the “Summary” and “General Discussion with Management” section Non-Reportable Observations, which you discussed with management. These objection-able conditions fall into three basic categories:

1. Observations of significant deviations from specific Laws and/or regulations, non-reportable items 1-9 above.
2. Observations of deviations from specific Laws and/or regulations, which 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 which in your judgment deviate from official published guidance, not regulations, but warrant discussion with management.

The reporting of observations for an FDA 483 or FDA 483a in these 3 categories is 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 5.4.1.5.2 is not reportable.

Category 2 or 3: You should always report these two categories of observations which were discussed with management under the “General Discussion with Management” heading in the EIR as specified by IOM

5.11.4.3.15. You have options in choosing how observations in category 2 are reported. You may select the appropriate cite in eNSpect, enter the “specifically” text regarding the observation, and discussion with management, set it to “Do not print”, save, and it will be automatically entered into the eNSpect when it is generated.

The second option which is also true for category 3 (i.e., there are no eNSpect cites for official guidance, only regulations) is the observation/s discussed with management may be entered directly into the eNSpect EIR under the “General Discussion with Management.”

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. ... Observations, which you discussed with management. These objection-able conditions fall into three basic categories: 1. Observations of significant deviations from specific Laws and/or regulations, non-reportable items 1-9 above. 2. Observations of deviations from specific Laws and/or regulations, which 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 which in your judgement deviate from official published guidance, not regulations, but warrant discussion with management.

5.2.3.4 - Annotation of the FDA 483 and 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 program at some point prior to the final discussion with management. Determine from management whether they wish to have their FDA 483 observations annotated. It 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. The annotations are 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 5.2.3 for discussions of FDA 483 observations with management.

If the establishment has promised and/or completed a corrective action to an FDA 483 observation prior to the completion of the inspection, the FDA 483 should be annotated with one or more of the following comments, as appropriate:

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

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" means "to confirm; to establish the truth or accuracy". In this case, you must do 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, as a whole should not be annotated on the FDA 483 or FDA 4056. If firm does not wish to annotate and FDA 483, then 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 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 xxx date" or "within xxxx 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.

5.2.3.5 - Government Wide Quality Assurance Program (GWQAP)

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, which result in non-acceptance. There must be a clear differentiation on the FDA 483 between these two types of deficiencies.

Enter the FD&C type deficiencies (GMP deviations, etc.) first on the FDA 483. If there are deficiencies in contract provisions, draw a line across the sheet and add a heading "The Following Additional Contract Non-Conformances Were Observed." Enter each deficiency, which forms a basis for non-acceptance, followed by the reference to the applicable contract requirement or specification.

5.2.3.6 - FDA 483, FDA 483a, and FDA 4056

The FDA 483, FDA 483a and FDA 4056 should be issued to the most responsible person available at the close of the inspection.

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.

Per 5.2.3.1., FDA 483s should be issued at the conclusion of the inspection and prior to leaving the premises.

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

1. Physical paper copy. Be sure printed versions of the signed FDA 483s, FDA 483a, and FDA 4056s are legible.
2. Electronically by email as a PDF attachment (on site prior to leaving the premises).
3. Electronic Media transfer to the firm (e.g., USB, CD/DVD...). Follow all IT security policies and procedures when using electronic media, including FDA policy with portable media devices available here http://inside.fda.gov:9003/it/ITAcquisitions/lro_nKeyRollout/default.htm and IOM 5.3.8.3.1 - ELECTRONIC RECORDS and IOM 5.3.8.3.3.1 - IDENTIFYING AND SECURING ELECTRONIC STORAGE MEDIA

If the FDA 483, FDA 483a or FDA 4056 is issued electronically, document your method of issuance and FDA-483 discussions with management in your regulatory notes per IOM 5.2.7 – Discussions with Management.

5.2.3.6.1 – Non-eNSpect generated FDA 483, FDA 483a, and FDA 4056

Before leaving the premises at the end of the EI, print and present the issued FDA 483, FDA 483a, or FDA 4056 to the most responsible individual Upload into eNSpect one

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

5.2.3.6.2 – eNSpect generated FDA 483, FDA 483a, and FDA 4056

Before leaving the premises at the end of the EI, present the printed signed FDA 483, FDA 483a, or FDA 4056 to the most responsible person available.

5.2.4 - RECEIPT - FACTORY SAMPLES

You must issue an FDA 484, Receipt for Samples, if you collect any physical sample during an inspection. At the end of the EI and prior to leaving the premises, issue the original FDA 484 to the same individual who received the FDA 482. (See IOM 4.2.5) If this person 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. Do not comment on type of examination expected or promise a report of analysis.

5.2.4.1 - Items Requiring Receipt

Issue an FDA 484 for any item of food, drug, device, or cosmetic actually 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 4.4.10.3.44.

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

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

5.2.4.2 - Items Not Requiring Receipt

Do not issue an FDA 484 for:

1. 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 5.2.3.2),
2. Labels and labeling, including promotional material,
3. Photographs taken during the inspection, or
4. 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 5.3.8.5 for procedures when a firm requests a receipt for records copied during an inspection or investigation.

5.2.5 - INSPECTION REFUSAL

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

For a refusal experienced during an inspection conducted under section 704 of the FD&C Act, 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 presented your credentials and given the responsible individual a properly prepared and signed Notice of Inspection, FDA 482 for domestic inspections.

Inspection refusals may take several forms. All refusals to permit inspection must be reported in your EIR under the "Refusals" heading.

In the case of drug inspections, inspection refusals, as well as delaying, denying, or limiting your ability to conduct the inspection, may cause a drug to be deemed adulterated under Section 501(j) of the FD&C Act [21 U.S.C. 351(j)]. See subsection 5.5.5.8 in Subchapter 5.5 (Drugs) for further guidance on responding to these situations.

For foreign food inspections, section 807(b) of the FD&C Act (21 U.S.C. 384c(b)), authorizes 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."

5.2.5.1 - Refusal to Permit Inspection

When you are faced with a refusal of entry, call the responsible individual's attention to the applicable sections of the Act (e.g., sections 301(f) and 704 of the FD&C 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. If entry is still refused, leave the completed Form FDA 482, leave the premises and contact your supervisor immediately for instructions.

Note: CPG Sec. 130.100 Inspectional Authority; Refusal to Permit Inspection

In the case of drug inspections, if the person refuses entry or delays, denies, or limits your ability to conduct the inspection, also call the person's attention to Section 501(j) of the FD&C Act [21 U.S.C. 351(j)] (an adulterated drug could lead to further prohibited acts under 301(a), (b), (c) [21 U.S.C. 331(a), (b), (c)]). See subsection 5.5.5.8

in Subchapter 5.5 (Drugs) for further guidance on responding to these situations.

For international inspections, a refusal to permit inspection may result in a recommendation for regulatory action (e.g., Import Alert, cancellation of Food Facility Registration). 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

5.2.5.2 - Refusal to Permit Access to or Copying of Records

If management objects to the manner of the inspection or 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 copying of any record 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 PHS Act. If management still refuses, proceed with the inspection until finished.

In the case of drug 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 could lead to prohibited acts under 301(a), (b), (c) [21 U.S.C. 331(a), (b), (c)]).

Furthermore, if during a drug 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 subsection 5.5.5.8 in Subchapter 5.5 (Drugs) for further guidance on responding to these situations.

It is not an inspection “refusal” when management refuses to provide information e.g., formulation, lists of shipments and manufacturing codes, unless it is 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.

5.2.5.3 - Refusal after Serving Warrant

If you have been refused entry, obtained a warrant, tried to serve or execute it and are refused entry under the warrant, inform the person, 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), leave the premises and promptly telephone the facts to your supervisor.

If you have served the warrant and during the inspection you encounter partial refusal or resistance in obtaining

access to anything FDA is authorized to inspect by the warrant, inform the firm 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, leave the premises and promptly telephone the facts to your supervisor.

5.2.5.4 - Hostile and Uncooperative Interviewees

More often than not, investigations or inspections are conducted in a reasonable atmosphere. Nonetheless, there will be times you are confronted by unfriendly or hostile persons.

Your activities must always be conducted with tact, honesty, diplomacy, and persuasiveness. Even though you must at times adopt a firm posture, 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 previously distasteful 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. Often the mere fact you patiently listen while individuals share their views will make them receptive to your quest.

5.2.5.4.1 - INDICATORS

Normally you have no way to predict the nature of the individuals you meet. However, there are often indicators, which can alert you, such as:

1. Establishment inspection reports, endorsements or memorandums 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 may reveal instances where uncooperative individuals and problem situations were encountered.
3. The nature of the assignment, program or information requested may indicate some degree of caution is needed.
4. A firm located in an area with a reputation for unfriendliness to law enforcement personnel should alert you some employees of the firm may be less than cooperative during the investigation.

If you find yourself in a situation which, in your judgment, indicates violence is imminent, stop the operation and make an exit as soon as possible. Immediately report the facts to your supervisor.

5.2.5.4.2 - SAFETY PRECAUTIONS

The FDA recognizes there are situations where it is advisable to take precautions for your personal safety. In

those, consult your supervisor. Some procedures, which may be utilized to minimize the danger, include:

1. Inspections or investigations carried out by a team of two or more persons.
2. Consider whether or not the use of an unmarked government car would be more beneficial to assist you in your inspection in lieu of a marked government car.
3. Request additional information from your State and/or Local Agencies who also regulate and inspect the facilities in question. In many instances, your State counterparts may have more information regarding the facility. This may be especially helpful for those firms that FDA has not yet inspected but were inspected by your State counterparts.
4. Each inspection team should be assigned one FDA cell phone or alternate communication device. While we recognize that some Investigators carry a personal cell phone, FDA strongly suggests that your personal cell phone not be utilized to contact the firm or firm's management. In some instances, such uses in the past have resulted in later inappropriate contacts from the firm to the individual FDA Investigator.
5. Request assistance from local law enforcement agencies prior to or during investigations. This assistance may include information about the facility you are to inspect, assistance with communication devices, or police protection, if the police jurisdiction allows for such an action.
6. In potentially hazardous investigations such as methadone or schedule II Class Drugs, two investigators may be used and personnel from the U.S. Drug Enforcement Administration, State, or local law enforcement agencies may be requested to accompany you.

5.2.5.4.3 - PROCEDURES WHEN THREATENED OR ASSAULTED

In instances when you are actually assaulted or threatened, you should immediately notify your supervisor. Your supervisor can summon local police, United States Marshals, or contact OCI headquarters for assistance (301-294-4030). OCI can make contacts with local police and federal agencies based on previous liaison. Also, the program division should notify orahqcsosafety@fda.hhs.gov.

If you are physically attacked, you have the same recourse as any other citizen as well as the benefit of federal laws protecting government officials while in the performance of their official duties. If you are physically attacked, you should get to safety, call your supervisor, report the incident and seek medical attention if needed. Remember that the medical attention you receive may be used as documentation for the Agency in support of any legal action taken against the firm or the individual.

5.2.5.4.4 - NOTIFICATION OF FBI AND US 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.

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

The referenced sections in Title 18 of the U.S. Code are:

1. [Title 18 U.S.C.A. Section 111](#), which provides:

"111. Assaulting, resisting, or impeding certain officers or employees.
Whoever forcibly assaults, resists, opposes, impedes, intimidates, or interferes with any person designated in Section 1114 of this title while engaged in or on account of the performance of his official duties, shall be fined not more than \$5,000 or imprisoned not more than three years, or both.
Whoever, in the commission of any such acts uses a deadly or dangerous weapon, shall be fined not more than \$10,000 or imprisoned not more than ten years, or both. ****".
2. [Title 18 U.S.C.A. Section 1114](#), which provides:

"1114. Protection of officers and employees of the United States.
Whoever kills ***** or any officer or employee of the Department of Health and Human Services or of the Department of Labor assigned to perform investigative, inspection, or law enforcement functions while engaged in the performance of his official duties, shall be punished as provided under sections [1111](#) and [1112](#) of this title. *****".

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

5.2.6 - 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 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 information and instructions.

You are operating as an agent of the court when you serve an inspection warrant and it must be executed expeditiously once served. See IOM 5.2.5.3 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 or Compliance Officer and a U.S. Marshal with the Investigator to assist and supervise the serving of the warrant.

After obtaining an Inspection Warrant, 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 him/her 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.

5.2.7 - DISCUSSIONS WITH MANAGEMENT

After completion of the inspection, meet with the most responsible person available to discuss the objectionable conditions observed. Objectionable conditions may be identified as reportable (See IOM 5.2.3.2) or non-reportable (See IOM 5.2.3.3). During the discussion, be direct, courteous, and responsive with management.

Explain the significance of each item and relate to the applicable sections of the laws and regulations administered by the FDA.

If significant deviations are observed during the inspection, you should inform management during the closeout discussion, the conditions observed may, after further review by the Agency, be considered to be violations of the FD & C Act or other statutes. Legal sanctions available to 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.

Do not be overbearing or arbitrary in your attitude or actions. Do not argue if management voices a different view of the FDA 483 observations. Explain, in your judgment the conditions you observed may be determined by the FDA, after review of all the facts, to be violations. Make clear 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. They 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 it will be satisfactory, you can so advise management. Do not assume the role of an authoritative consultant. Do not recommend the product 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 and or organizations. Advise management if FDA receives an adequate response to the FDA 483 or FDA 4056, 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.

Report in your EIR 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 the reply or replies is necessary, enclose them in quotation marks.

5.2.7.1 - Protection of Privileged Information

You have certain responsibilities under the FD&C Act, [Section 301\(j\)](#); Sections 359(d) and 306(e) of the Public Health Service Act; and Section 1905 of the Federal Confidential Statute ([18 U.S.C. 1905](#)) regarding protection of confidential material obtained during your official duties. See IOM 1.4.

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, be alert and avoid voluntarily or unknowingly divulging information, which may be privileged or confidential and possibly compromise FDA's and your own integrity.

Management often request copies of any documents or records you obtain from their firm. There is no objection to your supplying these. When management requests copies of photos taken by you in a plant, follow IOM 5.3.4.5.

You may encounter situations when management invites outside individuals to observe the inspectional process (e.g., representatives from the press, trade associations, congressional staff, other company officials). As discussed in Section 5.1.4.3 of the IOM, the presence of representatives invited by the firm should not disrupt the inspectional process. You are to continue the inspection in a reasonable manner.

If the firm allows invited individuals to photograph, videotape, or prepare audio recordings during the inspection, you should make every effort to protect privileged information in your possession. However, it is the Agency's position that it is the firm's responsibility to protect confidential and/or proprietary information observed or

recorded by those individuals invited by the firm. Where applicable, refer to IOM 5.3.5 for additional procedures on how to prepare your own recording in parallel with the firm's recording.

5.2.7.2 - Refusals of Requested Information

Should management refuse to provide any reasonable request for information, which is not specifically required by the law, determine the reasons for the denial and report the details in the EIR. Types of refusals of interest to FDA and refusal codes to be entered in FACTS are listed in the FDA Data Codes Manual. Refusal codes' data are used when reporting to Congress. See IOM 5.2.5.4 for instructions in dealing with hostile and/or uncooperative interviewees.

5.2.8 - CONSUMER COMPLAINTS

Prior to conducting any inspection, you should review the FACTS system, OSAR 360, and the factory jacket becoming familiar with all FDA Complaint/Injury forms. You may want to request additional information to consumer compliant coordinator based on the program area to fulfill additional information if available related to establishment to be inspected. Be especially alert for ones marked "Surveillance Information for Next EIR" and make sure you investigate these during your inspection. If reviewing complaints in OSAR, the "more detail" link needs to be opened to determine if the complaint was previously followed up, or if it stills requires follow-up.

During the inspection, discuss these complaints with management without revealing the complainant's name(s). 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 5.11.4.3.11 for reporting instructions.

5.2.9 - INTERVIEWING CONFIDENTIAL INFORMANTS

When you are faced with a situation involving sources of information who want to remain anonymous, please contact your supervisor and follow the procedures here. In addition, refer to IOM 5.2.1.2 regarding your personal safety. If your management concurs with the decision to utilize a confidential source, it is particularly important you take the necessary steps to keep the identity of the source, and any information which could lead to the identity, confidential. For purposes of this subchapter, a confidential source is a person who provides information that may be of assistance to FDA without necessarily becoming a party to the actual FDA investigation. If you believe the information provided by the source could lead to a criminal investigation, please contact the Office of Criminal Investigations (OCI).

5.2.9.1 - How to handle the first contact

When you interview a person, who may become a confidential source use the following procedures:

1. Type of meeting. Try to schedule a personal interview with the person rather than a telephone interview. At a face-to-face interview you can assess the person's demeanor, body language, overall presentation, and truthfulness.
2. Meeting location. The place and time of the interview should be the choice of the person, unless there is a concern with personal safety. If the person's suggested location is unsuitable, the investigator should suggest the location. When you conduct the interview off FDA premises, notify your supervisor of your destination, purpose, and estimated time of return. When an off-site interview has been completed, check-in with your supervisor.

5.2.9.1.1 - INTERVIEWING METHODS/TECHNIQUES

It is strongly recommended you have two investigators conduct interviews of a confidential source. The lead investigator conducts the interview, while the second investigator takes notes and acts as a witness to the interview. You should:

1. Prepare carefully for the interview. The investigators should develop the questions they intend to ask the person during the interview, e.g., "establish motivation," and record and number the questions to be asked in their 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 also should discuss their interviewing strategy, and determine the method by which they will consult with each other during the interview and (during extensive interviews) share the interviewing and note-taking responsibilities;
2. Have the person tell the story chronologically, placing complex situations into logical order; and
3. If the person makes allegations, ask him or her how he or she knows the allegations are true.
 - a. How were they in a position to know?
 - b. Did they personally see, hear, or write about the information/incident?
 - c. Can they provide proof of the allegations?

5.2.9.1.2 - 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):

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?

5.2.9.1.3 - ANONYMITY

If the person is requesting anonymity, inform him or her FDA:

1. Will not divulge his or her identity, the occurrence of the interview, or the sensitive information provided to FDA if the information could lead to the identity of the person,

- unless FDA is required to disclose the information by law, e.g., the investigation leads to a hearing or trial and he or she is required to testify, and
2. Will try to corroborate all information provided by the person, minimizing the chances he or she must later testify. However, testifying remains a possibility.

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

5.2.9.2 - 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 gender, name, address, and phone number in the memorandum of interview. You should assign the confidential source a code name or number and use the identifier in memoranda and other communications relating to the confidential source (see IOM 5.2.9.2.2 item 2).

5.2.9.2.1 - ACCESS

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

5.2.9.2.2 - STORAGE REQUIREMENTS

Each program division should establish procedures, in addition to those listed below, to properly store confidential information. The following list contains information related to storage procedures.

1. Use security measures necessary to protect the confidentiality of personal information, whether it is in hard copy or electronic form, 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. Personal privacy information should be safeguarded to the extent allowed by law. Use discreet subject headers in the file labels as appropriate.
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.

5.2.9.2.3 - 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 (FOI) process, unless the sharing is done according to our regulations and

procedures. Refer FOI requests to FDA's Division of Freedom of Information (see item 3 below). See also IOM Subchapter 1.4. The following information relates 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 voice mails with the information. Avoid transmitting the non-public information by facsimile or e-mail.
3. If you receive a FOI 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, OSPOP/DIDP and, if needed, OCI.
4. Immediately retrieve information from or about a source if inadvertently disclosed. Follow FDA's Inadvertent Disclosure SOP.

5.2.9.2.4 - DESTRUCTION

Destroy personal information by shredding or similar means which physically destroys the record and/or, if the information is in electronic form, makes it unreadable.

After a matter has been referred to the Office of Chief Counsel (OCC) for litigation or enforcement action, consult with OCC if you are interested in contacting the source.

5.2.10 - 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. See IOM 5.2.10.3.

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.

5.2.10.1 - 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 following guidance in IOM 5.2.1.1, Pre-Announcement, 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:

1. 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.
2. 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.
3. Reusable cloth or plastic laundry bag(s) for clothing to be laundered. (Disposable bags can be used.)
4. Soap, water and disposable or freshly laundered individual hand (or paper) towels.
5. 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)

5.2.10.2 - 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:

1. 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.
2. 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.
3. 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.
4. Wear appropriate head coverings, as necessary. If you wear a head covering, clean and disinfect between facilities or use disposable head coverings.
5. 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.

6. If you are visiting production units with animals of multiple ages, always try to work from the youngest to the oldest.
7. Avoid direct contact with livestock or wild animals, bodily fluids or animal byproducts when visiting facilities.
8. 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 CFSAN 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.

5.2.10.3 - Special Situation Precautions

If you are required to inspect or visit a facility known or suspected to be involved in a contagious animal disease 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 CFSAN directly for specific procedures to follow. Additional decontamination steps will be required.

5.2.10.3 – 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 farms 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>

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, ORA-OFFO, CFSAN-OC and CFSAN-OFS (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.

3. 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.

4. 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.

5. 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, car 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

6. Follow the farm's own biosecurity program to the extent that it does not interfere with investigators conducting the inspection.

7. Do not enter or inspect houses where birds are known to have disease, including but not limited to, SE.

8. FDA personnel participating in the inspection cannot be bird owners. Ownership of birds disqualifies that investigator from participation in all egg farm inspections.

9. 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.

10. 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.

11. 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 ORA-OO-ORS (see contacts at the end of this document).

12. 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. Investigators should 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.

13. Use disposable cameras, when possible. Otherwise, digital cameras are to be placed within plastic bags prior to entry into the house.

14. 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.

15. Houses should be inspected from the cleanest areas to the dirtiest areas and from the youngest to oldest birds.

16. No jewelry is allowed to be worn into poultry houses.

17. 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.

18. If possible, inspectors should park their 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.

19. Eyeglasses should be cleaned and disinfected with disposable decontamination wipes.

Items 20-32 listed below represent either direct or indirect contact with Population 2 as described in item #3 of 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:

20. Not come in contact with bird feeders or bird baths for a minimum of 1 week prior to participating in an egg farm inspection.

21. Stay away from family members, friends or acquaintances that are pet bird owners or have backyard poultry flocks of any type.

22. Not visit fairs where poultry or birds are shown or exhibited.

23. Not visit live bird markets of any type, or gatherings where live birds may be present.

24. Not visit flea markets, trade shows, or swap meets where live poultry or birds of any type may be present.

25. Not visit zoos, theme or amusement parks where live birds maybe present.

26. Not visit known nesting grounds or resting place for wild birds, such as natural preserves or refuges, known breeding grounds or bird sanctuaries.

27. 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.

28. 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.

29. Not visit an ocean side town where you may come in contact with shorebirds, e.g., gulls.

30. Not visit feed stores or other retail establishments where live poultry may be sold, e.g., baby chicks, turkey poults, ducklings, etc.

31. 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.

32. 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

33. Wash the vehicle used during the inspection as specified in item #5 in the pre-inspection procedures of this directive.

34. Clean and disinfect the sampling kit(s), e.g. tubs, scissors, can openers

35. Clean and disinfect respirators in accordance with manufacturer's recommendations

Contacts

CFSAN-OC:

Doriliz De Leon, email: doriliz.deleon@fda.hhs.gov, phone: 240-402-2772

Robyn Jones, email: robyn.jones@fda.hhs.gov, phone: 240-402-2575

CFSAN-OFS

John Sheehan, email: john.sheehan@fda.hhs.gov, phone: 240-402-1488

Gerardo A Ramirez, email: gerardo.ramirez@fda.hhs.gov, phone: 713-293-1418

ORA-DDHAFO/HAFPOB

Martha Myrick, email: martha.myrick@fda.hhs.gov, phone: 616-304-6283

ORA-ORS

Michelle Markley, email: michelle.markley@fda.hhs.gov, phone: 301-796-8178

Kenneth Crombie, email: Kenneth.crombie@fda.hhs.gov,
phone: 240-402-5346

SUBCHAPTER 5.3 - EVIDENCE DEVELOPMENT

5.3.1 - TECHNIQUES

The recognition, collection, and effective presentation of admissible evidence is essential to successful litigation. Evidence is required to support your observations and reports of violative conditions.

Although the inspectional procedures to detect adulteration and contamination, etc., are described under specific headings in the IOM, 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 5.4.7 may also apply to drugs or other products. Your experience and training assists you in making this transition and enables you to detect possible violative conditions.

Keep in mind the policy announced in the 4/23/1991 memorandum from the Director, Office of Compliance: The 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 to be in compliance are not a bar to pursuing action under CGMP charges.

5.3.2 - SAMPLES

Samples, including "Factory Food Samples" (in-lines) and packaged finished products collected during inspections provide the necessary key to establish routes of contamination and/or actual product adulteration. They also document the character of products packed prior to the inspection. Collect samples for laboratory examination only when they contribute to confirming the suspected violation. Be selective since negative reports of analysis of food samples are required under [Section 704\(d\) of the FD&C Act](#) [21 U.S.C. 374 (d)] to be furnished to the firm and might give management a false picture of the firm's operation.

When possible collect duplicate subsamples to provide for the 702(b) portion of the sample. See IOM 4.3.2.1 and 4.3.7.4.1 for additional guidance and [21 CFR 2.10](#) for exemptions regarding the collection of duplicate portions.

When shipping samples collected during a foreign establishment inspection, refer to IOM section 4.5.5.10 for notification procedures.

5.3.3 - EXHIBITS

Impressive exhibits are extremely effective and important forms of evidence to establish existence of violative conditions or products. They should relate to insanitary conditions contributing or likely to contribute, filth to the

finished product, or to practices likely to render the product injurious or otherwise violative. 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.

Submit as an INV sample exhibits (except photographs) collected during an inspection or investigation. Describe each subsample and assign a unique subsample number to each exhibit. Group similar subsamples on one collection report. Examples of exhibits include:

1. Live and dead insects, insect frass, 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. ("INV Samples of Filth Exhibits.")
2. Components and finished dosage forms.
3. Samples of in-process ingredients, in-process materials and unpackaged finished products. ("Factory Food Samples" or "in-lines.") Note: Samples of packaged finished products and ingredients are official samples.
4. Manufacturing and control devices or aids.
5. Physical samples if possible and practical or, photographs with descriptions of scoops, stop-gap expediences, other unorthodox manufacturing equipment or makeshift procedures. If photos are taken, follow the procedures described in IOM 5.3.4.
6. Evidence showing the presence of prohibited pesticide residues. A method of swabbing for prohibited pesticide residues was published in Laboratory Information Bulletin # 1622. Excerpts are quoted as follows:
 - a. Apparatus - Four dram size glass vials, 95% ethanol, and cotton swabs preformed on 6" long wooden handles. Keep uncontaminated in a clean plastic bag.
 - b. Procedure - Blow away loose dirt or debris from approximately a 3" x 3" selected area. Measure approximately 2 cm of 95% ethanol in vial, dip swab into ethanol, press out excess on inside of vial and roll moist swab back and forth firmly across the selected area. Return swab to vial, swirl in alcohol, press out excess on inside of vial and again roll moist swab across the same area 90° to the previous swabbing. Re-insert swab into vial, break off swab handle and cap the vial with the swab inside.
 - c. When swab subsamples are submitted, also submit a blank control sub consisting of an unused swab placed in a capped vial containing 2 cm of the same alcohol that was used for the other swabs.
 - d. Describe the type of material swabbed (cardboard carton, metal table top, rubber inspection belt, etc.) and the area covered. A reasonable area is approximately 10 sq. inches. Always try to establish a definite link in the chain of subsamples leading towards the highest level of contamination. If possible, identify the pesticide suspected. Be sure to include a floor plan with the areas sampled identified.

Do not remove the firm's only copy of records. Whenever possible, scan, photograph or photocopy, if duplicates are not available. Reproductions should be reviewed to ensure all relevant information is readable. Records should not be accepted by email from outside USFDA.

5.3.4 - PHOTOGRAPHS

Photos taken during inspections are not investigational samples. They are exhibits. Photos are not attached to collection reports unless the photos are part of an Official Sample. See IOM 4.1.4 Official Samples and IOM 4.5.2.4 Photographs. Only use a Government issued camera to take photographs.

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, e.g., to document violations and environmental surface subsample sites. Photographs should be related to insanitary conditions contributing or likely to contribute filth to the finished product, or to practices likely to render it injurious or otherwise violative.

CAUTION: Evaluate the area where flash photography is contemplated. Do not use flash where there is a potentially explosive condition; e.g. very dusty areas or possible presence of explosive or flammable vapors. In these situations, use extremely fast film and/or long exposure time instead of flash.

Examples of conditions or practices effectively documented by photographs include:

1. Evidence of rodents or insect infestation and faulty construction or maintenance, which contributes to these conditions.
2. Routes of, as well as, actual contamination of raw materials or finished products.
3. Condition of raw materials or finished products.
4. Employee practices contributing to contamination or to violative conditions.
5. Manufacturing processes.
6. Manufacturing and various control records showing errors, substitutions, penciled changes in procedure, faulty practices, deviations from GMP's, NDA's, 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.
7. Effluent contamination of water systems. See IOM 5.4.3 for techniques in photographing this type of contamination.

When photographing labels, make sure your picture will result in a legible label with printing large enough to be read by an unaided eye. Photograph whited out documents by holding a flashlight against the whited outer side and taking a close-up photo of the reverse using high-speed film. This will produce a photo with a mirror image of the whited outer side.

If you use a Polaroid camera or color slide film, explain the facts in your EIR or on the C/R to alert reviewers that there are no negatives.

5.3.4.1 - In-Firm Photographs

Take your camera into the firm and use it as necessary just as you use other inspectional equipment. Only FDA issued cameras are to be used in official business. Don't request permission from firm management to take photographs during an inspection because taking photographs is part of the 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. Advise management 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:

1. "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. ***"
2. "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 refuses, obtain 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 inform their ORA Regional Counselor 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 film to management. Advise the firm it can obtain copies of the photos under the Freedom of Information Act. See IOM 5.3.4.5.

If management of a drug or device firm does 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. 551(j)] of the FD&C.

5.3.4.2 - Photo Identification and Submission

One of the most critical aspects about photographs or videotapes is the ability for the agency to provide testimony clearly verifying the authenticity of the conditions depicted

in the photograph or video. It makes no difference if the photo is a 35 mm print from acetate negatives, a Polaroid photo, a digital photo or video taken with a video recorder. 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 or video 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 or in the digital record. This will help identify the film or file 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 or video recording in the event you are not able to testify personally.

5.3.4.2.1 – FILM BASED PRINTS

Identify each print on the margin with exhibit number, firm name (or DOC Sample Nos., if DOC Sample), date taken or inclusive dates of inspection, and your initials. Do not place any identifying marks on the picture area of the print. (Some photo developing firms are supplying borderless prints. For this type print, 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. A narrative description may be placed on the mounting paper next to the print. If part of an EIR, include as exhibits. If part of a DOC sample, attach to the collection report with other records associated with a DOC Sample.)

5.3.4.2.2 - COLOR SLIDE IDENTIFICATION

If color slides are used, identify each slide, in the same manner as for prints. Program divisions may have special mounting frames for color slides, so the narrative description of each slide must be in the body of the report with proper reference to exhibits, or, each description may be placed on sheets of paper following the mounting frames and properly referenced.

5.3.4.2.3 - 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 envelope. Complete blocks 2, 3, (4 if DOC Sample), 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.

As applicable, submit the sealed FDA-525 or envelope as an exhibit to the EIR, with the Investigative Report as an attachment, or with the other associated records/documents with a DOC Sample.

5.3.4.2.4 - VIDEO RECORDINGS

Handle and protect the original video record just as if it were a photograph negative. Unused videotapes should generally be used to capture the video and, for subsequent copies of the original recording. Write-protect and identify the original videotape with a label with the firm name (or Sample number if it is being submitted as part of an official sample), date taken, and your initials. Seal the original copy of the electronic media 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 program division, date, firm name, firm address (include zip code), and description of the contents of the envelope.

Seal the original videotape in an FDA-525 envelope or similar envelope. 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 marked in large, bolded letters "STORE AWAY AND PROTECT FROM MAGNETIC FIELDS."

As applicable, submit the sealed FDA-525 or similar envelope as an exhibit to the EIR, with the Investigation Memorandum as an attachment, or with the other associated records and documents with a DOC sample.

If you perform any editing of the recording, you should only perform this on a copy of the original video recording to prevent possible damage to the original. Document in your regulatory notes you made a copy of the original and verified the copy is an accurate copy of the original video you took. This "original copy" should be treated just as if it is the original. When you sign the report, memorandum or other agency document, your signature certifies you are saying the content of the document, including any video recordings, is true and accurate to the best of your ability

5.3.4.2.5 – DIGITAL PHOTOGRAPHS OR VIDEO RECORDINGS

Prior to the year 2000, FDA investigators traditionally worked with silver acetate photographic film or used analog video tapes. Early digital cameras recorded photographic images directly to floppy disks or mini-CDs in which the evidence could be handled like photographic negatives.

The important difference today is digital cameras are capable of recording high resolution images on the order of twenty to thirty megapixels. The corresponding image file sizes can be over fifteen megabytes when using uncompressed file formats. To cope with the increased file sizes, digital camera manufacturers have introduced non-volatile flash memory cards which can record digital images, delete images, and be recorded over and over again. This presents a new issue since the original digital images, which are captured at the moment when the images are recorded on the memory card, will be copied at

a later time to a CD-R or other permanent storage media. Due to the cost of flash memory cards and the large file sizes, it is not feasible to purchase new memory cards for each inspection/investigation as you did using photographic film. You will be working with an “original copy” of the images which have to be copied in the exact format to a CD-R or DVD-R as they were originally recorded on the flash memory card to preserve the chain of custody. The term “other permanent storage media” includes the hard-drive on the work computer/laptop of the investigator, and not a shared or personal computer. In order to preserve the chain of custody, it is acceptable to transfer the images from the flash memory card onto the hard-drive and then burn the images onto a CD-R or DVD-R, so long as the images have not been altered in any way before being burned onto the CD-R or DVD-R.

In the same manner, digital video recordings may involve the use of different media types such as tapes, CD-Rs or DVD-Rs, or built-in hard drives. If you cannot handle the original video recording as in IOM 5.3.4.2.4, you will need to create an “original copy” of the video recording.

Despite the differences in photographic film and digital technology, you are responsible for collection, handling, documenting the chain of custody, storage, and submission of your evidence in a manner where you can testify to its authenticity in a court of law. See IOM 5.3.4.2 and 5.3.4.3.

5.3.4.2.6 – GLOSSARY OF DIGITAL TERMINOLOGY

Some basic terminology is used when referring to digital devices in IOM 5.3.4.2.4, 5.3.4.2.5, 5.3.4.3.

5.3.4.2.6.1 – Digital Data

Electronic data in binary form consisting in its simplest form as “1”s and “0”s. A computer interprets data by whether the state is on (“1”) or off (“0”).

5.3.4.2.6.2 – Analog Data

Information captured in a directly measurable signal versus an analog signal converted and stored in binary.

5.3.4.2.6.3 – Memory Card

Any non-volatile memory media that can be removed and which retains data without the need for electrical power. Examples of current memory cards are: Compact Flash (CF), Secure Digital (SD), Memory Stick (Sony), and Extreme Digital (xD).

5.3.4.2.6.4 - 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 are considered the originals and prints are considered copies. See IOM 5.3.4.2.1 and 5.3.4.2.3.

5.3.4.2.6.5 – 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 is indistinguishable from the original.

5.3.4.2.6.6 - Permanent Storage Media

A media format in which the digital files cannot be altered once written. Examples are CD-Rs, DVD-Rs and other approved media.

5.3.4.2.6.7 - Time/Date Stamp

The internal clock within the camera which records the time/date information on the image file. Set the time/date stamp for the location where the photographs or videos are being taken. In this usage, the time/date stamp does not refer to imprinting the time/date stamp within the photographic image although the time/date stamp can also be imprinted on the photograph as some film cameras could do.

5.3.4.2.6.8 - Working Copy

A copy of the original copy used when you need to make additional copies for your report, sample C/R. Creating a working copy decreases the chance the original copy is damaged.

5.3.4.3 - Preparing and Maintaining Digital Photographs as Regulatory Evidence

Assure and protect a digital photo's chain of custody (and authenticity) following this procedure:

1. Prior to using the digital camera, verify the date and time stamp is correct and there are no images stored on the memory card. Reformat the memory card using your camera's reformat command to delete any images not related to your current assignment. Depending on your inspection/investigation, camera, and memory card capacity you should consider bringing more than one memory card if possible.
2. Handle your camera and the memory cards in a manner to protect your evidence and maintain the trail of the "chain of custody" for the evidence you have collected. For example, keep the camera and memory cards in your personal possession at all times or hold under lock and key in a secure storage area. Also, keep any additional memory cards containing images in your personal possession until transferred to permanent storage media. When necessary, document these facts in your regulatory notes or written report (EIR, CR etc.).
3. As soon as practical, create an original copy of the digital photos. Some older FDA cameras will capture

images directly to a (Write-once Compact Disk Recordable (CD-R)); in this case, the CD-R from these cameras becomes the original CD-R. Identify, date and initial the CD-R as an original image record. If a CD-R/W was used, copy the images to a CD-R to create an original copy with files that cannot be altered. Follow additional instructions for creating and finishing a CD-R in step 4 below.

4. If the camera requires downloading of images to a CD-R or other media, download all the images from the digital camera to an unused CD-R or other electronic storage media to create an original copy. If there was more than one memory card used, use a separate CD-R for each memory card. The storage capacity of a CD-R is about 650 MB; thus, more than one CD-R may be needed to create an original copy of your memory card depending on your camera's resolution, the storage capacity of your memory card, and the number of pictures taken. The images should be transferred in a file format maintaining the image resolution at the time the image was captured. If possible, avoid the use of any file compression in transferring the images to the CD-R. Prior to preparing the CD-R or transferring image files, verify that the computer you are using is set to the correct date and time. Make the CD-R permanent in a format readable by any CD-R reader. Prior to making the working copy from the original copy, identify the original copy. For EIRs identify with the firm name, FEI, date taken or inclusive dates of inspection, and your initials. For sample collections identify with sample number, collection date, and your initials. 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.
5. 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 CD-R may be damaged. See the NIST document, "[Care and Handling of CDs and DVDs - A Guide for Librarians and Archivists](#)". Figure 12, page 23 shows where to identify the CD-R.
6. 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.
- 7.

Make only one working copy from each original copy. Make any additional working copies using the initial working copy. No more than one copy should be made from the original copy to preserve the original copy. After making the initial working copy, seal the original copy of the electronic media in an FDA-525 or similar envelope until submitted with the written report (e.g., EIR, 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 the images are captured or transferred to electronic storage media, refer to IOM 5.3.8.3 for the

handling of electronic storage media. If possible, the investigator (who took the photos and will authenticate them at trial) should store the sealed electronic storage media until it is submitted with the written report. If you break the seal for any reason, see IOM 4.5.4.5 – Broken Official Seals and "Temporary Seals."

8. Working copies should be used to print photos, insertion into an EIR, cropped, otherwise edited or to be included in a referral.
9. Document in your regulatory notes or written report (EIR, CR, etc.) any steps taken for any unusual editing of original photo images. For example: Superimposing over an important area of the image, image enhancement, composite images, etc.
10. Do not scan the FDA 525 or envelopes containing the photo discs 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 original officially sealed disc(s) and unsealed working copy disc(s) 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 original copy and unsealed working copy discs containing the photographs taken during the inspection are filed with the unlabeled exhibits and attachments."

5.3.4.4 - Preparing Digital Photos for Insertion in an eNSpect Establishment Inspection Report (EIR)

Digital photos taken during an inspection can be inserted into the body of a report in eNSpect or can be printed and attached to the EIR as an exhibit. Inserting digital photos can dramatically increase the file size of the eNSpect document. To maintain a minimum eNSpect document file size, the following is recommended: Do not open a digital picture/photo and use copy and paste to insert the picture/photo into the eNSpect document. Instead, save pictures/photos in a JPEG image format (.jpg file name extension) in a separate folder in preparation for inserting into eNSpect. Then resize all the JPEG pictures to a reasonable image file size. Ensure you are not using the original picture file as the file will be overwritten using this procedure. To do this:

1. Open Microsoft Office Picture Manager, select "Add a new picture shortcut." After the window opens, select the folder containing the pictures you want to edit. The window will close and the photographs contained in the folder will be available.
2. Hold the control key down and left click to select each image file(s) to be resized.
3. Right click and select "Edit Pictures." After the sidebar appears, select "Resize."
4. In the "Resize Settings" sidebar, select the button for "Predefines with X height" and select "Document – Small (800 x 600px). Click OK.

5. New resized pictures will be created in Microsoft Office Picture Manager and are denoted by an asterisk in the picture name. The files must be saved for the change to take effect. Select "File" and select "Save." The resized picture files will replace the files in the original source folder. If you want to keep the source picture files you must rename the resized files by selecting each file individually by selecting "File," then "Save As," and entering a new name.
6. The resized photograph files are now ready for insertion into the eNSpect EIR document. Remember to maintain the original image files, not the resized digital image files, for filing with the hard copy exhibits and attachments in accordance with applicable procedures

To insert a picture into the eNSpect EIR document:

1. Open the eNSpect EIR document. Position cursor to where you want to insert the picture.
2. From the menu bar, click on Insert, choose Picture, click on From File, find and select folder with resized pictures to be inserted. See Exhibit 5-7.
3. Double click on the resized picture to be inserted.
4. Picture inserted into the eNSpect EIR document can be made larger or smaller by clicking on the picture and grabbing the corner of the picture frame and dragging to achieve the desired size.
5. Include the following information in the EIR narrative: the photo number; the date the photo was taken and by whom; and a brief narrative description of what the photo depicts.

Alternative method: Digital photographs can also be submitted as Exhibits to the EIR. A narrative description may 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.

See also 5.3.8.2 - Identification of Records Collected. Photographs can be resized using Microsoft Office Picture Manager. See Exhibit 5-8 which shows the "resize" menu option.

NOTE: When any digital photos are used in an EIR, submit the original or original copy of the camera images following procedures as outlined in IOM 5.3.4.3 – Preparing and Maintaining Digital Photographs as Regulatory Evidence.

5.3.4.5 - Photograph Requests

Do not routinely advise firms 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 the Freedom of Information Act. Any request should be sent to The Food and Drug Administration, at the address listed on the FDA 482 or FDA 483 or FDA 4056. The firm must bear the cost of duplicating the photographs.

Since photographs are records in an investigative file, they are not available under the Freedom of Information Act 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.

5.3.5 - RECORDINGS

Under normal circumstances recording devices will not be used while conducting inspections and investigations. However, some firms are now recording and/or video-taping, the inspection and/or the discussion with management portion of the inspection. These firms should be advised we do not object to this procedure, but we will also record the discussion to assure the accuracy of our records. 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.

Use a clear tape cassette and identify the tape verbally as follows:

"This is Investigator _____ 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 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 will be verbally identified as follows:

"This is Investigator _____ speaking. It is now _____ 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)."

If the recording covers a different situation, the identification should be modified accordingly. If the representative of the firm refuses permission to record the discussion, continue with your discussion and report the facts in your EIR.

The tape cassette must be identified with the firm name, date of the inspection, and investigator's name. Program divisions have the option of transcribing the tape and making the transcription an exhibit for the EIR. However, the tape itself must be made a permanent part of the EIR as an exhibit.

5.3.6 - 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.

Document and fully report individual responsibility whenever;

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

Under the Medical Device Quality System regulation ([21 CFR 820.20](#)), if the management at the firm is not exercising the controls required by the regulation, the deviations may be cited on your FDA 483.

5.3.6.1 - Discussion on 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 points to consider are:

1. Who had the duty and power to detect the violation?
2. Who had the duty and power to prevent the violation?
3. Who had the duty and power to correct the violation?

5.3.6.2 - Inspection Techniques How to Document Responsibility

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

Obtain the correct name and correct title of all corporate officers or company officials. 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 and record review specifically intended to determine responsibility. Cover and report items such as:

1. Organizational charts,
2. Statements by individuals admitting their responsibility or attributing responsibility to others,
3. Company publications, letters, memos and instructions to employees, and

4. The presence or absence of individuals in specific areas at specific, significant times, and their observed activities directing, approving, etc.

In order to establish relationships between violative conditions and responsible individuals, the following types of information, would be useful:

1. Who knew of conditions?
2. Who should have known of the conditions because of their specific or overall duties and positions?
3. Who had the duty and power to prevent or detect the conditions, or to see they were prevented or detected?
4. Who had the duty and power to correct the conditions, or to see they were corrected? What was done after person(s) learned of the conditions? Upon whose authority and instructions (be specific)?
5. What orders were issued (When, by whom, to whom, on whose authority and instructions)?
6. What follow-up was done to see if orders were carried out (when; by whom; on whose authority and instructions)?
7. Who decided corrections were or were not complete and satisfactory?
8. What funding, new equipment, new procedures were requested, authorized or denied in relation to the conditions; who made the requests, authorizations, or denials.

Duties and power related to general operations should be established to supplement the specific relationships to violations. Examples of operational decisions that indicate responsibility are:

1. What processing equipment to buy.
2. What raw materials to purchase.
3. What products to produce and what procedures to follow in production?
4. Production schedules - how much to produce, what to make, when to stop or alter production?
5. What production controls to be used?
6. What standards are set for products, raw materials, processes?
7. How to correct or prevent adverse conditions; how much to spend and whom to hire to correct or prevent adverse conditions; when to clean up?
8. How products will be labeled; what products to ship; label approval?
9. When to reject raw materials or products; when to initiate a recall; acceptable quality levels for products?
10. When to hire or fire personnel?
11. Who will accept FDA 482, Notice of Inspection; refuses inspection; accept Inspectional Observations, FDA 483?
12. Who designed and implemented the quality assurance plan; who receives reports of Q.A.; who acts or should act upon the reports?
13. Who is responsible for auditing other facilities, contractors, vendors, GLP sites, etc.?
14. In the firm's business relationships, who signs major contracts, purchase orders, etc.?

In some circumstances, documenting of 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. Copies of documents between the firm and outside parties may help establish responsibilities. Do not overlook state officials as another possible source of information in selected cases.

During the course of 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, handicap, 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.

5.3.7 - GUARANTEES AND LABELING AGREEMENTS

Review the Code of Federal Regulations, [21 CFR 7.12](#), [7.13](#), [101.100\(d\)](#), [201.150](#), and [701.9](#), for information concerning guarantees and labeling agreements.

5.3.7.1 - Guarantee

Certain exemptions from the criminal provisions of the FD&C Act are provided where a valid guarantee 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 guarantee, which the firm claims to use relating to a violation noted during your inspection. No person may rely upon any guaranty unless he has acted merely as a conduit through which the merchandise reached the consumer.

5.3.7.2 - Labeling Agreement

Products regulated by 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 trade practices, to be processed, labeled, or repacked in substantial quantity at an establishment other than where 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.

5.3.7.3 - 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 the shipper is not the operator of the establishment, he 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 insure 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.

5.3.8 - 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 Good Manufacturing Practice (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 format 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 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.

5.3.8.1 - 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 your copy is an exact duplicate of the original or source record. Record in your regulatory notes you authenticated copies of records and when, where, and from whom copies were obtained.

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. The Investigator 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.

5.3.8.2 - Identification of Records Collected

Articles used as evidence in court cases must be identified so you can later testify the records entered as evidence are the very ones you obtained. This includes all records as noted in IOM 5.3.8, 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 and to 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 initials of all FDA participants, exhibit number and page number(s). Refer to ORA-OO.004, "Using eNSpect to Create, Store, and Preserve Electronic Records Associated with an Establishment Inspection Report," When you collect a sample, each page of the copied records will become part of the collection report and should be identified as noted in IOM 4.4.5. Examples include records of interstate commerce, manufacturing deviations, label and labeling violations. Records submitted with a memorandum of investigation will be identified with the firm or subject name, the date(s) of the investigation, the initials of all FDA participants, and page number.

There are occasions when a single record may include hundreds of sheets of bound paper. Abbreviated methods of identification may be used for bound records by fully identifying the first and last few pages. In some cases, firm's clearly mark each page with the sequential and total pages number (e.g., page 6 of 10, 7 of 10, etc.) and this allows you to fully mark only a few pages in the beginning and end of the exhibit.

All pages must be identifiable if not in bound records. One example of a shortened method of identifying individual exhibits containing a large number of pages (usually more than 25) is to fully identify the first few and last few pages with at least the exhibit number, date and the initials of all FDA participants. Then identify the remaining pages with the page number of the total page numbers, and your initials, e.g., "5 of 95 SHR". This may not be acceptable if you have more than one exhibit consisting of exactly 95 pages.

Whatever method is used, you must assure the record is complete and is always identifiable. This is so you can testify as to the "where", "when" and "from whom" the copies were obtained, and that the copy is a true copy of the source record based on your review of the source record. The identification method should allow any reviewer to determine if the record is complete or pages or parts are missing.

5.3.8.3 – Electronic Records, Microfilm and Microfiche

When attempting to obtain records, you may find they are stored on microfilm, microfiche, or some form of a

computerized management information system as electronic records. Records obtained during the course of the inspection in these forms are handled the same as any records following procedures outlined in IOM 5.3.8.1 and 5.3.8.2.

5.3.8.3.1 - 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 Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, even if such records are not specifically identified in agency regulations. In both instances, these records will be maintained and handled as identified in 5.3.8.3.3.

Electronic data obtained from a firm provides an investigator with a wealth of information which can be used to assess their compliance with the FD&C act and promulgated regulations. If there are no mechanisms available for a firm to securely transmit the data electronically to the investigator, the data may be provided to FDA via electronic storage media. Secure means of transmittal may include approved cloud file sharing or use of FDA Electronic Submissions Gateway. Refer to your program for approved methods of secure transmittal, as well as instructions that can be provided to regulated industry.

Data received on movable media presents a challenge with IT security as well as physical security of the media. The information obtained from the firm is commercial confidential information (CCI) and as such must be protected to the greatest extent possible. It is the responsibility of the investigator 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 along with concerns related to safeguarding the security of both FDA and firm information. ORA investigators must be very cognizant of issues that may arise with the use of electronic media and be vigilant while using it.

If secure methods of transmission are not available, electronic data can be obtained by receiving electronic media from the firm or by providing a clean, preformatted electronic media to the firm. ORA procedures for the use of electronic media will be identical for both domestic and foreign inspections/investigations. Those foreign locations which 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.

The Device Control Data Loss Prevention (DLP) tool at 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 ORA Investigators have an exception and are permitted read access to firm-provided USBs in order to transfer data onto their machines. However, they are not permitted write access, as FDA data should not be written to a device that is not FIPS 140-2 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 ISSO.

5.3.8.3.1.1 ORIGINAL COPY

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

5.3.8.3.1.2 WORKING COPY

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

5.3.8.3.2 - ELECTRONIC DATABASES AND QUERIES

Firms may use proprietary programs developed in-house or off the shelf programs to generate and/or store records used to show regulatory compliance, such as blood bank databases, drug production records, medical device complaints, and/or service records. These programs can often times be queried to generate electronic databases or summary data in a commonly used file format, such as Microsoft Excel. During an establishment inspection you may request and receive electronic databases or summary data generated by the firm from their databases. The methods used must maintain the integrity of the electronic data and prevent unauthorized changes.

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 5.10.2.1 or
- a biologics inspection where it is not practical to oversee the firm's personnel while they access their system, follow section 5.7.2.5.1 .

Secure methods of transmitting this data to the FDA for all other types of inspections may be used to obtain these files for review.

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

1. Oversee the firm's personnel accessing their system and have them answer your questions.
2. Request the firm run queries specific to the information of interest.
3. Request the firm provide the parameters used to generate the data.
4. Request the firm to transmit the electronic data securely to 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 (i.e., 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 accidentally omitted due to a programming logic error occurring at the firm.

Reviewing electronic data may require its transfer to electronic storage media for you to use in your computer if a method of secure transmittal is not available; see section 5.3.8.3.3.1 below for information on how to handle electronic storage media. Do not use the firm's equipment or personnel to perform computerized data manipulation for the purposes of review and analysis.

5.3.8.3.2.1 - REQUESTING Electronic RECORDS from databases

Before requesting a copy of computerized data, you should determine several things including information about the size and contents of the database, the program used by the firm, and the program you will use, among others. The following steps are useful in preparing for an electronic database request.

1. Determine the firm's application program used to maintain the data of interest. It is best to obtain data files in a format compatible with application programs currently used by the agency. Check the program you plan to use to ensure it can handle the file size you will be using.
2. You should 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 the inputting of 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 give 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 located in the SOPs for that computerized system. Also, 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 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 to manipulate the files as needed.

5.3.8.3.2.2 - ELECTRONIC RECORDS RECEIVED VIA SECURE TRANSMISSION OR ON ELECTRONIC STORAGE MEDIA

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".

Any request for electronic records on electronic storage media should be made with a computer application in mind and the information obtained should be useful. The electronic records should be in a format compatible with software applications knowledgeable to you and available from the Agency. Certain types of file conversion are difficult and should not be attempted without the necessary knowledge and availability of conversion type programs where applicable. Other file conversions are simple and have standard, built in conversion programs, such as converting a Microsoft Word document to an Adobe PDF. If help is needed for file conversion, assistance may be available within the program division.

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 the course of 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 assure the integrity of the data when used to support observations of potential violations or used as evidence in administrative or judicial proceedings. Seal 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, e.g. 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 5.11.5.1.

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 prior to closing the inspection. You will need to view the copied files and verify the files contain the information requested and the information is useable to you.

If you perform analysis of the data, including sorts, pivot tables, or other reviews, on the working copy of an electronic database 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 database that includes only the information of interest (e.g. an Excel spreadsheet of failures of a certain type for a specific time period), or requesting a paper copy of the information of interest.

5.3.8.3.3.1 - IDENTIFYING AND SECURING ELECTRONIC STORAGE MEDIA

When electronic storage media is used to obtain electronic records you should follow these steps to ensure its proper identification and security:

1. Label each original copy of electronic storage media
 - a. Firm name
 - b. Date and your initials
 - c. If you provide the disk(s)/USB to be used, use only new and preformatted disk(s)/USB.
 - d. The name of the appropriate software and version to ensure readability of the information.
2. Make a working copy of the electronic storage media
 - a. Virus scan the original storage media
 - i. Disconnect your machine from the FDA network, the VPN, and the internet.
 - ii. Insert the Media into your computer (USB 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. When the window identified in Figure XX appears, select "Continue."
 - (1) We do not want to "Clean" the data as it may be used as evidence if a virus or malware was detected.
 - vii. If the scan is clean, proceed forward. If the scan detects a problem, the security scanning tool should quarantine the file(s). At this point, the file(s) will not be accessible, and you should put in an ERIC ticket to report the incident (which should be assigned to the FDA Incident Response team). If the scan reveals malware or

- a virus, maintain chain of custody on the electronic media. Alert the SCSO of the issue and the steps taken.
 - b. Check the security on the storage media by viewing the "Security" tab under the "Properties" window (right click). This will ensure you have the ability to view and analyze the data.
 - c. Copy the original information from the electronic storage media onto a working copy.
 - d. Verify the data is useable.
3. Identify and place the original copy of electronic storage media as identified in 5.11.5.1.
 4. Prepare electronic record(s) for inclusion in the EIR, Memorandum, or C/R.

5.3.8.5 - 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.

5.3.8.6 - Patient and/or Consumer Identification on Records

During the course of many types of inspections and investigations you will review and collect records which specifically identify (by name) patients or consumers. Under most state Privacy Laws this information is confidential. Some firms we inspect 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 is then required to maintain the confidentiality of the records/files, as with any confidential record you collect. See IOM 5.10.5. Any disclosure of the information contained in the record(s) can only be by Law, i.e., 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 FDA access to the patient records.

General, routine guidance is as follows:

1. For records copied as a result of injury or complaint investigation, where you obtain patient identification, the identification should remain intact and stored in the official FDA files. Frequently, medical releases must be obtained from a complainant, consumer or "next-of-kin". At least one or two extra should be obtained and stored in the files.

2. 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.
3. For most others, 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) 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, obtain the data. It is always easier to delete later than to return to obtain the information, especially in the few cases 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, i.e., 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.

5.3.9 - REQUEST FOR SAMPLE COLLECTION

There are times one program division will request another program division to collect surveillance or compliance samples for it. The requesting program division should provide as much of the following information as is available on specific shipments, using the FACTS Create Sample Assignment Screen. See IOM Exhibit 5-9.

The following fields must be completed in order to save the assignment: Requesting Organization, Priority, Subject, POC Name, Op Code, Accomp Org, Num of Ops, and PAC. When you create a sample collection assignment, which will require laboratory analysis, you should also create an assignment for the laboratory, using operation 41.

The screen is organized in sections.

5.3.10 - POST-INSPECTION NOTIFICATION LETTERS

Issuance of Post-inspection notification letters have been discontinued in all program areas. See [FMD 145](#).

SUBCHAPTER 5.4 – FOOD AND COSMETICS INSPECTIONS

5.4.1 - FOOD and COSMETIC INSPECTIONS

Food inspections are conducted to evaluate the methods, facilities, and controls used in manufacturing, storage and distribution of foods.

Cosmetic Inspections are conducted to determine whether cosmetics are being manufactured in a manner that ensures products adequately meet all statutory and regulatory requirements so as to be safe for consumers to use.

See CFSAN Office of Compliance's intranet website for the most current guidance (e.g., compliance programs, field assignments, field guidance).

5.4.1.1 - Preparation and References

Before undertaking an inspection of food see items 1-11 below. For inspection of cosmetics see items 1,2,3,5,6,7, and 8 below:

1. Review the program division files of the firm to be inspected and acquaint yourself with the firm's history, related firms, trademarks, practices and products. The review will identify products difficult to manufacture, require special handling, special processes or techniques, and hours of operation, which is especially important in bacteriological inspections. Remove, for subsequent investigations and discussion with management, Complaint/Injury Reports, which are marked for follow-up during the next inspection. See IOM 5.2.8.
2. Become familiar with current programs relating to the particular industry involved and relevant DDHAFO Inspection Guides. Become familiar with any applicable Compliance Policy Guide .
3. Understand the nature of the assignment and whether it entails certain problems, e.g., *Salmonella* or other bacteriological aspects.
4. Review the [FD&C Act Chapter IV](#) - Food.
5. Review and become familiar with the appropriate parts of 21 CFR pertaining to foods and cosmetics. All CFRs can be found [here](#).

<u>Food</u>	<u>21 CFR 101-190</u>
<u>Cosmetics</u>	<u>21 CFR 700-740</u>
<u>Control of Communicable Disease</u>	<u>21 CFR 1240</u>
<u>Interstate Conveyance</u>	<u>21 CFR 1250</u>

6. Determine the type operation to be inspected to ensure application of the appropriate regulations.

7. Ensure that you have received all necessary training that may be required. Consult your supervisor with questions.
8. Review implementation dates of regulations to ensure application of the appropriate regulations.
9. Review reference materials on food technology and other subjects.
10. If you are assigned to inspect food-service establishments under the FDA - Secret Service Agreement, you should use the most current copy of the "Food Code" and be standardized in its use. All Food Service Specialists and most Interstate Travel Sanitation Specialists are standardized in use of the code.
11. Be familiar with the "Food Chemicals Codex". See IOM 5.4.4.3.

5.4.1.2 - Inspectional Authority

See IOM subchapter 2.2 for broader information on this topic.

Authority to Obtain Records and Information in LACF and Acidified Foods Plants:

FDA's regulation in [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 FDA. The demand for these records must be in writing on an FDA 482a, Demand for Records, signed by you and must identify the records demanded.

5.4.1.2.1 - WRITTEN DEMAND FOR RECORDS

To obtain the records:

1. Prepare an FDA 482a, "Demand for Records", listing the records demanded. Describe the processing records to be reviewed and/or copied as accurately as you can, e.g., "All thermal process, production, and quality control records, including analytical records and maintenance records which may document any changes to the equipment or the thermal process that are mandated by 21 CFR 108, 113 and 114 for all Low Acid Canned Food (LACF) or Acidified Food (AF) produced at this facility."

If only a specific record is desired list it specifically as follows: e.g., "Fill Weight Records for #2 Filling Machine for the period of 4-15-17 through 6-7-17."

2. Sign the form.
3. Issue the original to the same person to whom the FDA 482, "Notice of Inspection", was issued.
4. Submit an exact copy with your EIR.

5.4.1.2.2 - WRITTEN REQUEST FOR INFORMATION

[21 CFR 108.35\(c\)\(3\)\(ii\)](#) states commercial processors engaged in thermal processing of low-acid foods packaged in hermetically sealed containers shall provide FDA with any information concerning processes and procedures necessary by FDA 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 his files a letter or other written documentation from a processing authority delineating the recommended scheduled process and associated critical factors.

You may encounter situations where you believe control of certain factors is critical to the process and there is no evidence to document these factors were considered when the process was established (e.g., a change in formulation which could affect consistency). It is appropriate to issue a written request for a letter or other written documentation from a processing authority, which delineates the recommended scheduled process and associated critical factors. 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 delineated in the process authority's recommendation or the filed process, obtain all available information about the situation. 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 the Center for Food Safety and Applied Nutrition, Division of Enforcement (HFS-605) 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. If requested to obtain the information:

1. Prepare an FDA 482(b) - Request for Information listing the specific information requested. Specify each product involved by food product name and form, container size and processing method. For example, "All documents and records mandated by 21 CFR 108, 21 CFR 114.83 and 21 CFR 113.83 relating to or having a bearing on the adequacy of processes for all Low Acid Canned Food (LACF) or Acidified Food (AF) products that are manufactured, processed or packed by this firm.
2. Sign the form.
3. Issue the original to the same person to whom the FDA 482, "Notice of Inspection", was issued.
4. Submit the carbon copy or exact copy with your EIR.

5.4.1.3 - Records Access Under Sections 414 and 704 of the FD&C Act

The Food Safety Modernization Act amended Section 414 of the Act to provide FDA with access and the ability to copy records under the following circumstances:

1. FDA has a reasonable belief that an article of food, and any other article of food that FDA reasonably believes is likely to be affected in a similar manner:
 - a. Is adulterated and presents a threat of serious adverse health consequences or death to humans or animals, and
 - b. The records are needed to assist FDA in determining whether the food is adulterated and presents a threat of serious adverse health consequences or death to humans or animals.
2. FDA believes that there is a reasonable probability that use of or exposure to an article of food, and any other article of food that the FDA reasonably believes is likely to be affected in a similar manner:
 - a. Will cause serious adverse health consequences or death to humans or animals, and
 - b. The records are needed to assist FDA in determining whether there is a reasonable probability that the use of exposure to the food will cause serious adverse health consequences or death to human or animals.

If, during an inspection, you believe the above conditions exist, and:

1. The firm refuses to provide access to the records, or
2. Based on past experience, the program division anticipates that the firm may refuse to provide access to records, or
3. The firm requests FDA to provide a separate written request for records,

Notify your supervisor and consult with your program division Compliance Branch.

Program division management will obtain DE concurrence before you issue the Form FDA 482c Notice of Inspection - Request for Records See Exhibit 5-10. Program division management will notify FDA's Office of Emergency Operations (OEO) of any situation requiring issuance of Form FDA 482c. (OEO contact number: 1-866-300-4374 or 301-796-8240 - 24 hours/day.) OEO will notify CFSAN or CVM, as appropriate, OHAFO, DE and OCC according to standard operating procedures to obtain a determination that the situation warrants issuance of Form FDA 482c. DE, in consultation with CFSAN or CVM OEO, OHAFO and the Program division, will determine if the standards for records inspection in paragraphs (1) or (2) of section 414(a) have been met and identify the scope of the records to request. Issue an FDA 482c, Notice of Inspection - Request for Records. See Exhibit 5-10 according to their instructions.

FDA may at a later time, request additional records related to the same article of food, or other article of food that is likely to be affected in a similar manner, as long as the

criteria in 414(a)(1) or (a)(2) continue to be met. The request for additional records may be verbal or written as necessary to facilitate access to the records.

Investigators should document in the EIR a firm's refusal to allow access to records or a firm's request for a written request for records and issuance of Form FDA 482c.

5.4.1.4 - Food and Cosmetic Defense Inspectional Activities

Food and cosmetics security inspectional activities should be conducted during all routine food and cosmetics safety inspections. During the normal course of the inspection be alert to opportunities for improvement or enhancement of the firm's food and cosmetics security preventive measures, as compared to those recommended in the guidance documents described below. You should not perform a comprehensive food and cosmetics security audit of the firm or conduct an extensive interview of management or employees in an attempt 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 on the subject of food and cosmetics security.

5.4.1.4.1 - FOOD AND COSMETIC SECURITY

Inspectional activities relative to food and cosmetic security for routine food and cosmetic establishment inspections should include:

1. Discussion with firm management of relevant FDA guidance documents including:
 - a. FDA Firm Resources
 - b. Draft Guidance for Industry: Mitigation Strategies to Protect Food Against Intentional Adulteration.
 - c. Retail Food Stores and Food Service Establishments: FSMA Final Rule for Mitigation Strategies to Protect Food Against Intentional Adulteration

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](#).

2. Identification of opportunities for improvement or enhancement of the firm's food and cosmetic security preventive measures, as compared to those recommended in the guidance documents, and encouragement of management to make such improvements or enhancements to their security system.

Keep in mind that guidance does not represent mandatory conditions or practices; some of the recommended food and cosmetics security 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 to consider the goals of the food and cosmetics security preventive measures; evaluate the goals relative to the specifics of their operation; and address those that are relevant to the extent practical.

Food and cosmetics security observations should not be listed on form FDA-483, Inspectional Observations, unless they likewise constitute deviations from Current Good Manufacturing Practice. Security discussions 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 summary section of the EIR. For example, under a section heading titled "Food and Cosmetics Security" 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 and cosmetics security issues were discussed with (name of firm official)." The details of inspectional findings regarding security should **NOT** be recorded. You should also minimize the quantity and detail of notes taken relative to the firm's food and cosmetics security program, recording only items needed to serve as a "memory jog" during the discussion with management.

5.4.1.4.2 - RECONCILIATION EXAMINATIONS

During routine food and cosmetic inspections, conduct one reconciliation examination during each food and cosmetic establishment inspection. The examinations are to be 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 factory jacket 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; and 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 6.4.3. For imported food and cosmetics, a reconciliation examination should be conducted:

1. Per Part A [IOM 5.4.1.4.3] 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 [IOM 5.4.1.4.4]).

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 in IOM 5.4.1.4.3 to IOM 5.4.1.4.4 below for domestic and import reconciliation exams.

5.4.1.4.3 - RECONCILIATION EXAMINATION GUIDANCE PART A

Reconciliation examinations are performed to ensure that:

1. The food or cosmetic is what it purports to be
2. There are not unexplained differences in the quantity of product ordered, shipped, and received, and
3. 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:

1. The actual goods in a lot are the same as those that are declared in the shipping documents
2. There is consistency in the manufacturer declared on the product labeling, bulk product packaging, and shipping documents; and
3. 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 [IOM 5.4.1.4.4] of this guidance while conducting a detailed reconciliation exam.

5.4.1.4.4 - 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:

1. Product identity on the package that does not match the identity declared on the shipping documents
2. Mixed product sizes within a carton or within the lot;
3. Product sizes that do not match the sizes declared on the shipping documents
4. Differences in product configuration or package type (e.g. plastic containers mixed with glass jars or aluminum or steel cans)
5. Easily apparent variations in weight
6. Product labels that display crude, unprofessional, or inconsistent styles of print, color or use of language
7. Unusual placement of labels (e.g. off-center)
8. 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
9. Differences between the actual can codes in the lot and those listed on the shipping documents
10. The existence of a tamper-evident notice on the labeling when the packaging does not contain a tamper-evident feature
11. Product that is beyond its expiration date
12. 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:

1. Differences between the product and that which is declared on the label
2. Color differences in the product between containers of the same lot
3. 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)
4. 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.

5.4.1.4.5 - SPECIAL SAFETY PRECAUTIONS

See IOM Chapter S - Safety, specifically S.8, S.8.1, S.9, S.9.1 through S.9.12.

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.

5.4.1.5 - Food Registration

Section 415 of the FD&C Act (21 U.S.C. 350d) requires most domestic and foreign facilities that manufacture/process, pack, or hold food for human or animal consumption in the United States to register with FDA before operations commence. Section 415 also requires food facilities to renew their registration biennially. FDA requires renewals to be submitted between October 1 and December 31 of each even-numbered year. Facilities may register electronically at <http://www.access.fda.gov>, by mail, or by CD-ROM for multiple submissions, to Food and Drug Administration, Food Facility Registration, HFS-651, 5100 Paint Branch Parkway, College Park, MD, 209932, or by fax to 301-436-2804. FDA maintains the registration information in the Food Facility Registration Module (FFRM) within the FDA Unified Registration and Listing System (FURLS) database. A facility is not registered until all required fields have been completed in FFRM. Upon completion, the registrant is issued a system generated 11-digit registration number.

For food facilities that are required to register, the owner, operator, or agent in charge of a facility must provide the following:

1. Facility name, address, phone number, and emergency contact phone number;
2. Parent company name, address, and phone number (if applicable);

3. Name, address, and phone number of the owner, operator, or agent in charge;
4. Email address for the contact person of the facility or, in the case of a foreign facility, the U.S. agent for the facility;
5. All trade names the facility uses;
6. Applicable food product categories, as listed on the registration form;
7. Name, address, and phone number of a foreign facility's U.S. agent and phone number of the facility's emergency contact if it is someone other than the U.S. agent;
8. Certification that the information submitted is true and accurate and that the person submitting the registration is authorized to do so; and
9. Assurance that FDA will be permitted to inspect the facility at the times and in the manner permitted by the FD&C Act (section 415(a)(2)).

Section 415(b) of the FD&C Act also provides FDA with authority to suspend the registration of a facility when:

1. FDA determines that food manufactured, processed, packed, received, or held by a registered facility has a reasonable probability of causing serious adverse health consequences or death to humans or animals (SAHCODHA); and
2. That facility:
 - a. Created, caused, or was otherwise responsible for that reasonable probability of SAHCODHA; or
 - b. Knew of, or had reason to know of, the reasonable probability of SAHCODHA, and packed, received, or held such food.

The purpose of registration is to provide FDA with sufficient and reliable information about food facilities. Registration will help provide information on the origin and distribution of food that may be associated with a real and potential threat to public health. In the event of a foodborne outbreak of illness, registration information will enable FDA to notify the food facility representatives and to investigate the source and cause of the outbreak. It will also enable FDA to identify and contact other facilities that might be associated with the food causing the outbreak.

Under section 301(dd) of the FD&C Act (21 U.S.C. 331(dd)), the failure to register a food facility is a prohibited act. Food from a foreign facility that is not registered may be held at the port of entry (section 301(l) of the FD&C Act (21 U.S.C. 381(l))).

Low Acid and Acidified Food Registration

21 CFR 108.25(c)(1) and 21 CFR 108.35(c)(1) require all commercial processors, when first engaging in the manufacture, processing, or packing of acidified foods (AF) or low-acid canned Foods (LACF) to register their facility with FDA and file information including the name of the establishment, principal place of business, the location of each establishment in which that processing is carried on,

the processing method, and a list of foods so processed in each establishment by using form FDA 2541.

In addition to registering the facility, AF processors must provide FDA with information, using Form FDA 2541e, on the scheduled processes for each acidified food in each container size (21 CFR 108.25(c)(2)). LACF processors must file processes using either Form FDA 2541d, 2541f or Form FDA 2541g.

Both registration and filing can either be done electronically (<https://www.access.fda.gov/>) or by mail by using the appropriate forms.

5.4.1.5.1 – FOOD FACILITY REGISTRATION EXEMPTIONS

The following food facilities do not have to register (21 CFR 1.226):

1. A foreign facility, if food from such facility undergoes further manufacturing/processing (including packaging) by another facility outside the U.S. A foreign facility is not exempt under this provision if the further manufacturing/processing (including packaging) conducted by the subsequent facility consists of adding labeling or any similar activity of a *de minimis* nature. The facility conducting the *de minimis* activity also must register.
2. Farms that are devoted to the growing and harvesting of crops, the raising of animals (including seafood), or both. Washing, trimming of outer leaves of, and cooling produce are considered part of harvesting. The term “farm” includes:
 - a. Facilities that pack or hold food, provided that all food used in such activities is grown, raised, or consumed on that farm or another farm under the same ownership; and
 - b. Facilities that manufacture/process food, provided that all food used in such activities is consumed on that farm or another farm under the same ownership.
3. Retail food establishments whose sales to consumers exceed their sales to non-consumers (businesses are considered non-consumers).
4. Restaurants that prepare and serve food directly to consumers for immediate consumption.
5. Nonprofit food establishments in which food is prepared for, or served directly to, the consumer.
6. Fishing vessels, including those that not only harvest and transport fish but also engage in practices such as heading, eviscerating, or freezing intended solely to prepare fish for holding on board a harvest vessel. However, those fishing vessels that otherwise engage in processing fish are required to register. For the purposes of this

section, “processing” means handling, storing, preparing, shucking, changing into different market forms, manufacturing, preserving, packing, labeling, dockside unloading, holding, or heading, eviscerating, or freezing other than solely to prepare fish for holding on board a harvest vessel.

7. Facilities that are regulated exclusively, throughout the entire facility, by the U.S. Department of Agriculture under the Federal Meat Inspection Act (21 U.S.C. 601 et seq.), the Poultry Products Inspection Act (21 U.S.C. 451 et seq.), or the Egg Products Inspection Act (21 U.S.C. 1031 et seq.).
8. Other exemptions from registration in the final rule are based on the definition of food included within the scope of the registration regulation. Facilities that manufacture/process, pack, or hold food contact substances (including packaging materials) (21 CFR 1.227(b)(4)(i)(A)) or pesticides (21 CFR 1.227(b)(4)(i)(B)) are exempt from registration.

5.4.1.5.2 - FOOD FACILITY REGISTRATION RESOURCES

Additional information relating to food facility registration is available at the following website:

<http://www.fda.gov/Food/GuidanceRegulation/FoodFacilityRegistration/default.htm>.

See the guidance in [Compliance Policy Guide Sec. 110.300 Registration of Food Facilities Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002](#).

If a facility (domestic or foreign) is required to register but is operating with no registration, a suspended registration, an invalid registration, or a cancelled registration, make sure that firm’s management is aware of the food facility registration requirements, see registration exemptions in Section 5.4.1.5.1 - FOOD FACILITY REGISTRATION EXEMPTIONS. Inform the firm’s management that information regarding food facility registration and penalties for failure to register is available at the following website:

<http://www.fda.gov/Food/GuidanceRegulation/FoodFacilityRegistration/default.htm>. Encourage electronic registration and provide them with the web site address for electronic registration <http://www.access.fda.gov>. Send an email to CFSANFoodFacilityRegistration@fda.hhs.gov with FORM-000173 with the required fields completed (1-32, 42-48).

If a facility (domestic or foreign) has a current registration but information obtained during the inspection/investigation is different from the information in FFRM, make sure that 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)). Inform the firm's management that information regarding food facility registration and penalties for failure to update their register is available at the following website:

<http://www.fda.gov/Food/GuidanceRegulation/FoodFacilityRegistration/default.htm>. Provide a copy of the Update Facility Registration Tutorial located at <https://www.fda.gov/food/registration-food-facilities-and-other-submissions/online-registration-food-facilities>. Send an email to CFSANFoodFacilityRegistration@fda.hhs.gov with FORM-000173 with the required fields completed (1-32, 42-48) to include an explanation of what firm information is different than FFRM.

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 registration form to complete and submit by mail at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM071977.pdf>. Also encourage the firm to submit the optional information on the registration form to assist and facilitate FDA's future communications with the firm.

5.4.2 - PERSONNEL

5.4.2.1 - Management

Follow the guidance described in IOM 5.3.6 when documenting individual responsibility including obtaining the full name and titles of the following individuals:

1. Owners, partners, or officers.
2. Other management officials or individuals supplying information.
3. Individuals to whom credentials were shown and FDA 482 Notice of Inspection, FDA 482d Request for FSVP Records and other inspectional forms issued.
4. Individuals refusing to supply information or permit inspection.
5. Individuals with whom inspectional findings were discussed or recommendations made.

Regulations require plant management take all reasonable measures and precautions to assure control of communicable disease, employee cleanliness, appropriate training of key personnel, and compliance by all personnel with all requirements of [21 CFR 110.10](#), [112 Subpart C](#), [113.10](#), and [114.10](#).

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

5.4.2.2 - Employees

Improper employee habits may contribute to violative practices in an otherwise satisfactory plant. Observe the actions of employees during all phases of the inspection. Observe employees at their work stations and determine their duties or work functions.

Note whether employees are following food hygiene and food safety practices, including wearing outer garments suitable to the operation in a manner that protects against allergen cross contact and contamination, maintaining adequate personal cleanliness, and store personal items properly. Note whether employees eat while on duty. 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 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 which may be expected to result in contamination.

Under no circumstance should you swab a sore, touch or remove a bandage from an employee in an attempt to obtain bacteriological data. 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 it affects possible 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 record insanitary employee practices or actions showing employees handling or touching insanitary or dirty surfaces and then contacting food products or direct food contact surfaces. 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 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. See IOM 5.4.7.2.2.

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. Sanitizers work most effectively on hands, which have been first cleaned by washing with soap and water.

Conversations with employees doing the work may provide information on both current and past objectionable practices, conditions and circumstances. These should be recorded in your notes.

Where appropriate, determine employee education and training. Also determine type, duration, and adequacy of firm's training programs, if any, to prepare employees for their positions and to maintain their skills.

5.4.3 - PLANTS AND GROUNDS

Grounds must be kept in a condition that will protect against the contamination of food. Building structures at produce farms may include fully or partially enclosed structures and fields. 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 contribute to rodent, bird, insect or other sanitation problems.

5.4.3.1 - 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. Determine the approximate size and construction (e.g., brick and concrete block) of building 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. Determine any construction defects or other conditions such as broken windows, cracked floor boards, sagging doors, etc. which may permit animal entry or harborage.

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. Evaluate the firm's attitude toward maintenance and cleaning operations.

5.4.3.2 - 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.

Suspected dumping of sewage effluent into nearby streams, lakes, or bay waters near water intakes can be documented by color photographs and water-soluble fluorescein sodium dye. Place approximately two ounces 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. Color photographs should be taken.

Determine collecting or flushing methods used to remove waste from operating areas. If water is used, determine if it is recirculated and thus may 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., which contain pesticide residues. Determine how this is segregated from waste material which contains no residues, and which may be used for animal feed.

5.4.3.3 - 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.

5.4.4 - 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 or 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. Materials should be stored so they are accessible for inspection. Thoroughly check ceilings, walls, ledges, and floors in raw material storage areas for evidence of rodent or insect infestation, water dripping or other adverse conditions.

5.4.4.1 - 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.

5.4.4.2 - 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 HAF Division. If the documentation shows the product was imported, contact your corresponding [import division](#) to determine if the product is subject to Import Alert and 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.

5.4.4.3 - 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.

Determine whether firm is aware of this publication and whether or not they comply.

5.4.5 - EQUIPMENT AND UTENSILS

By arriving before processing begins, you are able to 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.

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.

5.4.5.1 - 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.

5.4.5.2 – 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. 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.

5.4.5.3 - Conveyor Belt Conditions

Equipment used to convey, hold, or store raw materials and other ingredients, work-in-process, rework, or other food must be constructed, handled, and maintained during manufacturing, processing, packing, and holding in a manner that protects against allergen cross-contact and against contamination.

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 4.3.7.7.3 for procedure on taking In-line Sample Subs.

5.4.5.4 - 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.

5.4.5.5 - 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.

5.4.5.6 - UV Lamps

If firm is using ultra violet (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.

5.4.5.7 - 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.

5.4.5.8 - 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. If chlorine is used, 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. 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.

5.4.6 - 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.

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 identify Preventative Control Points. 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 or sanitized after contact with insanitary surfaces. For example:

1. Workers do general work, then handle the product;
2. Containers contact the floor, then are nested or otherwise contact product or table surfaces;
3. Workers use common or dirty clothes or clothing for wiping hands;
4. 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 re-used or re-worked into the process (e.g., candy and macaroni products), observe the methods used in the re-working and evaluate from a bacteriological standpoint. Re-working procedures such as soaking of macaroni or noodle scrap to soften or hand kneading of scrap material offers an excellent seeding medium for bacteria.

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

5.4.6.1 - 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.

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.

5.4.6.2 - 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 refuse the quantitative formula.

If formula information is refused, attempt to reconstruct formula by observing:

1. Product in production,
2. Batch cards or formula sheets,
3. Raw materials and their location.

5.4.6.3 - Food Additives

Refer to the food additives programs in CP (Chapter 9) for instructions on conducting establishment inspections of firms manufacturing food additive chemicals. Information is also available in ORA'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:

1. Unauthorized and illegal as listed in the Food Additive Status List (safrole, thiourea, et al), and
2. Restricted as to amount in finished food.

Because of special problems, exclude the following additives from coverage during routine inspections:

1. Packaging materials,
2. Waxes and chemicals applied to fresh fruit and vegetables (unless covered under the Produce Safety Regulation),
3. Synthetic flavors and flavoring components except those banned by regulations or policy statements (these products will be covered under other programs), and
4. 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](#)) and the [Food Additives Status List \(FASL\)](#) found on the CFSAN website 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 Food Additives Status List (FASL). Such substances will include:

1. 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.;
2. Synthetic flavoring substances because of their indefinite status;
3. Substances pending administrative determination,
4. 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 FASL. 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 actually put into the batch.

5.4.6.4 - 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 of these links can be found on the CFSAN website. 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 colors additives. 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 online Color Certification Database system maintained by the Food and Drug Administration, Color Certification Branch. Contact the Color Certification Branch to be granted user privilege.

Where decertified or restricted-use colors additives are used in manufacturing food, drug, device, or cosmetics products, proceed as follows:

1. Collect an Official Sample consisting of the color additives and the article in which it is being used. Make every effort to collect interstate shipments of the adulterated 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 additives 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 decertified color additives after the decertifying date. Documentation should include batch formula cards, employee statements, code marks indicating date of manufacture, color certification number, etc. The presence of a color additive in the finished product will be confirmed by your servicing laboratory.

5.4.6.5 - 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.

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.

5.4.6.5.1 - 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 food or feed purposes.

5.4.6.5.2 - 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.

5.4.6.5.3 - 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\(b\)](#).

5.4.6.6 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 manner in which 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.

5.4.6.6.1 - QUANTITY OF CONTENTS

If slack fill is suspected, weigh a representative number of finished packages. See IOM 4.3.8 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.

5.4.6.6.2 - LABELING

Check the sanitary condition of labelers and equipment feeding cans to, and away from, the labeler. Determine if old product is present on any equipment which touches the can end seams, in the presence of moisture carry-over from the can cooling operation. 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.

Labeling that identifies the by-product by the common or usual name must be affixed to or accompany human food by-products for use as animal food when distributed.

Determine what labels are used. 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.

5.4.6.6.3 – 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 subingredients 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.

5.4.6.6.4 – 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.

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.

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.

5.4.6.6.5 – SANITARY FACILITIES AND CONTROL

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 waste water or sewage and piping systems that carry water for food or food manufacturing.

5.4.6.6.6 Labeling violations

Refer to 21 CFR part 701 (Cosmetic Labeling) or 21 CFR part 740 (warning statements), 21 CFR Part 112 (Produce Safety) and applicable sections of CPGM 7329.001 for information on labeling requirements. Collect and review labels as required by a particular assignment. For routine inspections, samples of labels are not required unless significant violations are noted.

5.4.6.6.7 Cosmetic product labeling making drug claims

See [CPGM 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. 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:

- 1- product labels, including outer containers and all inserts
- 2- 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:

- 3- samples of product
- 4- samples of the active ingredient used in the cosmetic and ingredient certificate of analysis
- 5- records showing usage of the active ingredient in manufacturing of a cosmetic product batch

(NOTE: As stated in CPGM 7329.001 III.A, CDER and CFSAN have concurrent jurisdiction over any product purported as a cosmetic that meets the legal definition of a drug.)

5.4.6.6.8 – 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](#).

5.4.7 - SANITATION

Documented observation of the conditions under which food products are processed, packed, or stored is essential to the proper evaluation of the firm's compliance with the law. This involves the determination of whether or not 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.

5.4.7.1 - 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, or filth in insect or rodent contaminated raw materials may carry over into the finished product. IOM Section 4.3.7 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 Compliance Program (CP) or **DDHAFO Inspection Guides**.

5.4.7.1.1 - 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 routes of contamination with insect filth are encountered, identify the insects generally, e.g., weevils, beetles, moths, etc. If qualified, identify as to species. You must be correct in your identification. See IOM Appendix A.

5.4.7.1.2 - RODENTS

Rodent contamination of the finished product may result from using rodent defiled raw materials, exposure to rodents during processing, and by rodent depredation of the finished product. When evidence of rodents is discovered, you should thoroughly describe its composition, quantity, estimated age and location. Explain its significance and potential for product contamination.

See IOM Section 4.3.7.4.2.3 – Summary of Sample for Rodent Evidence.

5.4.7.1.3 - PESTICIDES

Pesticide contamination of the finished product may be the result of mishandling of food products at any stage in growing, manufacturing or storage. The use of toxic rodenticides or insecticides in a manner, which may result in contamination, constitutes an insanitary condition. Where careless use of these toxic chemicals is observed, take photographs and provide other documentation showing its significance in relation the food products.

Additional guidance can be found in 21 CFR as follows:

1. [Part 117.10\(b\)](#) - Personnel
2. [Part 117.20\(b\)](#) - Plant Construction and Design
3. [Part 117.35\(c\)](#) - Pest Control
4. [Part 117.40\(a\)](#) - Equipment and Utensils

Additional guidance can be found in 40 CFR Part 180 - Tolerances and Exemptions From Tolerances For Pesticides in Food Administered by The Environmental Protection Agency as follows:

1. [Part 180.521](#) - Fumigants for grain-mill machinery; tolerances for residues, and
2. [Part 180.522](#) - Fumigants for processed grains used in production of fermented malt beverages; tolerances for residues.

Be alert for:

1. Possible 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 used in food plants. 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.
2. Possible mix-up of pesticides or industrial chemicals with food raw materials.
3. Improperly stored pesticides or industrial chemicals (lids open, torn bags in close proximity to foods, signs of spillage on floors, pallets, shelves, etc.).
4. Incorrect application methods including excessive use. Many pesticide labels give instructions for use and precautions on the container.
5. Improper disposal or reuse of pesticide or industrial chemical containers.
6. Evidence of tracking powder or improper use of bait stations or baited traps.
7. 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.

8. Use of unauthorized pesticides.
9. Use of foods treated with pesticides and marked "Not For Human Consumption" (e.g., Treated seed wheat, etc.).
10. Noticeable odor of pesticides.
11. Careless use of machinery lubricants and cleaning compounds.
12. Chemical contaminants in incoming water supply.

When inspecting products with a known potential for metals contamination, determine whether the firm tests for such contamination in raw materials.

Determine who administers the firm's rodent and insect control program. Determine responsibility for the careless use of toxic materials.

If pesticide misuse is suspected, obtain the following information;

1. Name of exterminator and contract status,
2. Name of pesticide,
3. Name of pesticide manufacturer,
4. EPA registration number,
5. Active ingredients, and
6. Any significant markings on pesticide containers.

Fully document the exact nature of any pesticide or industrial chemical contamination noted or suspected. If samples are to be collected to document misuse, exercise caution to prevent contamination of the immediate area of use, product or yourself.

5.4.7.1.4 - OTHER

Contamination of food products by bats, birds and/or other animals is possible in facilities where food and roosting facilities are available. Examine storage tanks, bins, and warehousing areas to determine condition and history of use. There have been instances where empty non-food use containers were used for food products.

Birds and other animals are normal in a farm operation. Evaluate the farm's wildlife management and their actions if there is any contamination or concerns.

5.4.7.2 - Microbiological Concerns

During the inspection, identify likely sources and possible routes of contamination of the product with pathogenic microorganisms.

See IOM sections 4.3.7.6 and 4.3.7.7 for 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. See IOM 4.3.7.7 for instructions on sampling for pathogens. 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 the particular processing step, and **the length of time** the product has been delayed prior to the next step). Also, 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.

5.4.7.2.1 - 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.

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.

5.4.7.2.2 - 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. Did employees handle product in an insanitary manner (cross contaminating raw product with cooked product, etc., how many, how often).

5.4.7.3 - 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.

5.4.7.3.1 - FOOD TRANSPORT VEHICLES

During food sanitation inspections, (See IOM 5.2.2.2 regarding issuance of FDA 482, Notice of Inspection while inspecting vehicles.), conduct inspections of food transport vehicles to include:

1. Evidence of insanitary conditions,
2. Conditions which might lead to food adulteration,
3. Physical defects in the vehicle,
4. Poor industry handling practices.

The following types of transport vehicles should be covered:

1. Railroad boxcars, both refrigerated and non-refrigerated, and hopper cars.
2. Any type of truck used to transport foods; both refrigerated and non-refrigerated.

3. 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.
4. Vessels used to transport food in I/S commerce. Direct coverage primarily to intercoastal type vessels, including barges.
5. On farm vehicles used in covered produce activities such as trailers, farm trucks, fork lifts, tractors, equipment used between growing/harvesting, etc.

Coverage should be limited to food transport vehicles used for long haul (I/S) operations. Long haul vehicles are defined as those which travel at least 150 miles between loading and unloading or which do not return to the point of loading at the end of the day.

Regulatory actions are possible if unfit cars are loaded and, as a result of loading, adulteration occurs. Fully document any violations noted with appropriate samples and photographs. When vehicle insanitation is observed, it is imperative the carrier's and shipper's responsibility for the food adulteration be documented by appropriate evidence development, such as:

1. The nature and extent of the conditions or practices, and
2. The mechanical or construction defects associated with the food transport vehicle.
3. Individual responsibility for vehicle or trailer cleaning, vehicle assignments, load assignments, etc.

If gathering evidence about a single carrier, seek a series of occurrences at numerous locations involving as many different shippers as possible.

Basically, two types of vehicles will be covered.

5.4.7.3.2 - VEHICLES AT RECEIVERS

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, collect a sample(s) for regulatory consideration. Samples collected from vehicles, which have moved the product in interstate commerce are official samples. You may also collect Documentary (DOC) Samples from the vehicle to substantiate the route of contamination.

5.4.7.3.3 - VEHICLES AT SHIPPERS

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 he/she can contact the FDA

program division where the consignee is located for possible follow-up. You may also collect samples from the load. These samples will become official when the Bill of Lading is issued.

5.4.8 - DISTRIBUTION

Report the general distribution pattern of the firm. 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.

5.4.8.1 - Promotion and Advertising

Determine the methods used to promote products and how the products reach the ultimate consumer. Determine what printed promotional materials are used and whether they accompany the products or are distributed under a separate promotional scheme. Check on the possibility of oral representations, i.e., door-to-door salesmen, spielers, etc. and obtain copies of brochures, pamphlets, tearsheets, instructions to salespersons, etc. Where indicated, obtain the lecture schedule of any promotional lecture program. If applicable, determine the general pattern of the media used for promotion and advertising.

5.4.8.2 - Recall Procedure

Determine the firm's recall procedure. Audit enough records to determine the effectiveness of established procedures. Firms that are subject to Preventative Controls have specific requirements for recall plan. Refer to [21 CFR 117.139](#).

Note: Produce farms are not required to have a recall procedure.

5.4.8.3 - Complaint Files

Review the firm's complaint files. Where possible, copy the names and addresses of representative complainants; include a brief 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 5.2.8 for discussion of complaints with management and IOM 5.11.4.3.11 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 5.2.8, 5.4.1.1 and 5.11.4.3.11. Complaints can be accessed by clicking on the Consumer Complaint link in FMS, or by clicking the "Firm 360" link in OSAR.

5.4.9 - OTHER GOVERNMENT INSPECTION

See IOM 3.1 for general procedures on cooperating with other Federal, State, and local officials.

During Establishment Inspections determine the specific type of inspection service and inspecting units, which cover the firm, such as the name of the federal, state, county, or city health agency or department. Obtain the name and title of the inspectional official, and general method of operation.

5.4.9.1 - Federal

Do not inspect firms, or those portions of the plant, subject to compulsory, continuous inspection under USDA's [Meat Inspection Act](#), [Poultry Products Inspection Act](#), or [Egg Products Inspection Act](#), except on specific instructions from your supervisor or assignment document.

Ingredients or manufacturing processes common to both USDA and FDA regulated products should be inspected by FDA. See IOM 3.2.1.4 for FDA-USDA Agreements in specific areas.

Provide routine FDA coverage of such firms as breweries and wineries, which may be intermittently inspected on a compulsory basis by the U.S. Treasury Department, U.S. Public Health Service, or other agencies.

All products inspected under the voluntary inspection service of the Agriculture Marketing Service (AMS), USDA, and the National Marine Fisheries Service (NMFS), US Department of Commerce, are subject to FDA jurisdiction and are usually given routine coverage. However, formal written Agreements or Memoranda of Understanding between FDA and other agencies are often executed and may govern the agreeing agencies' operations on this type of inspected plants. When assigned this type of plant for inspection, always check to see if an Agreement or a Memorandum of Understanding exists between FDA and the agency involved to determine the obligations of both agencies. See IOM 3.1.2.1 and 3.2.

If you are assigned to cover a Federally Inspected plant which is under either compulsory or voluntary inspection, present your credentials and an FDA 482 Notice of Inspection to management and:

1. Identify yourself to the inspector(s) and invite him/her to accompany you on the inspection but do not insist on their participation.
2. At the conclusion of the inspection, offer to discuss your observations and provide the in-plant inspector with a copy of your Inspectional Observations (FDA 483).

5.4.9.2 - State and Local

State and local officials usually have extensive regulatory authority over firms in their area regardless of the interstate movement or origin of the food products involved. Joint FDA-State or local inspections are frequently conducted. These are usually arranged by program division administrative or supervisory personnel. See IOM 3.1.2 and 3.3.

5.4.9.3 - 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 the Milk Specialist. Grade A milk plants, milk, and milk products labeled as Grade A are inspected by state inspectors and check rated by FDA's 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 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). 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 particular 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. Also, 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.

5.4.10 - FOOD STANDARDS

The Federal Food, Drug, and Cosmetic Act requires the Secretary of Health and Human Services to promulgate reasonable definitions and Standards for food to promote honesty and fair dealing in the interest of consumers. When a Standard 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 Standard and supplies much of the data upon which the regulation is based.

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.

5.4.10.1 - Food STANDARDS Inspection

Food Standard (FS) inspection assignments usually originate from CFSAN. 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 the CFSAN has not already done so. If the firm selected does not choose to cooperate, it may be necessary to visit additional plants in order to obtain the desired information. Selection of additional firms should be done in consultation with the CFSAN.

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 through the use of 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.

5.4.10.2 - Food Inspection Report

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 the CFSAN and one copy kept for the program division 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.

5.4.10.2.1 - ESTABLISHMENT INSPECTION RECORD (EI RECORD)

In order 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 through the use of codes, which cannot be traced back to the firm.

5.4.10.2.2 - BODY OF REPORT

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 in regard to 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.

5.4.10.2.3 - 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."

5.4.10.3 - 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.

5.4.12 - PESTICIDES

5.4.12.1 - 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.

This requires directing coverage to two major areas:

1. Pesticide practices in the production and processing of field crops.
2. Application of pesticide chemicals in establishments storing and processing raw agricultural products.

Pesticide coverage must be provided during all food establishment inspections. Coverage of raw agricultural products will generally be on a growing-area basis.

Problem areas include:

1. Improper use of pesticides around animals - gross misuse of sprays and dips in animal husbandry may 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.

5.4.12.2 - Current Practices

Cooperative Activities - important sources of information relative to evaluating the "Pesticide Environment" include:

1. 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.

The contact point at USDA for pesticide residue matters is:
 Martha Lamont, Director
 Monitoring Program Office, Science Division
 Agricultural Marketing Service, USDA
 8609 Sudley Road, Suite 206
 Manassas, VA 20110
 703-330-2300

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.

5.4.12.3 - 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.

5.4.12.3.1 - 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.

5.4.12.3.2 - 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.

5.4.12.4 - 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.

5.4.12.5 - 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.

5.4.12.6 - 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.

5.4.12.7 - Sample Collections

See IOM Sample Schedule Chart 3 - Pesticides.

5.4.13 – COSMETIC INSPECTIONS

There is no FDA pre-approval for cosmetic products or ingredients, with the exception of 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 and 602, respectively, of the Food Drug and Cosmetic Act. Inspections cover three major areas:

- 1- Control of processes and quality of products - Products are manufactured in an adequate state of control to meet the firm's established quality standards.
- 2- Sanitation, cleanliness and hygiene – The facility is clean and orderly, sanitary conditions are being maintained and workers are attentive to preventing contamination
- 3- 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 5.4.13.3 (Contaminated Cosmetics) and 5.4.13.5 (Specific Types of Cosmetic Safety Concerns))

5.4.13.1 Preparation and References

Refer to this section and the Compliance Program Manual titled "Cosmetics Program: Import and Domestic" (CPGM 7329.001) when performing a cosmetic site inspection. Refer to any direction from CFSAN or the district having to do with a concern about a particular product. Refer to the sections 5.1, 5.2, 5.3, 5.4.1.1, 5.4.6.1.1, 5.4.6.6.4, in the IOM, and read or be familiar with all pertinent references provided in this subchapter (5.4.13). Be familiar with the statutory requirements and definitions and parts of the Code of Federal Regulations Title 21 (21 CFR) applicable to cosmetics. For more background information on cosmetic site inspections see [Inspection of Cosmetics](#).

Related Resources:

- [Cosmetics Compliance Program: Import and Domestic \(PDF 310 KB\) \(CPGM 7329.001\)](#)
- [GMP Draft Guidance for Industry: Cosmetic Good Manufacturing Practices](#)
- [Import Alerts for Cosmetics](#)

5.4.13.2 – 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.

5.4.13.3- 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:

- 1- Overall cleanliness of the facility and sanitation practices (including programs and systems for pest control and waste disposal)

- 2- Personal hygiene and employee health (including training of staff and monitoring of employees by supervision)
- 3- Handling of ingredients, materials and products by employees (including procedures for making transfers, training and use of PPE)
- 4- 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)
- 5- Water systems (including system design and control and monitoring of microbiological quality)
- 6- Equipment design (including potential for stagnant water)
- 7- Cleaning and sanitization of equipment surfaces contacting process stream or products (including utensils and shared equipment)
- 8- 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 CPGM 7329.001 section on *Adequacy of Preservation* for more information. Also refer to preceding sections 5.4.7.1 and 5.4.7.2 for more information about documenting routes of contamination and microbiological concerns.

See CPGM 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.

5.4.13.4- 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.

5.4.13.5 – Specific Types of Product Safety Concerns

You should be aware of certain cosmetic products that CFSAN/OCAC has identified as posing unusual safety hazards due to concerns about the product ingredients. Examples include:

- 1- tattoo inks
- 2- ingredients or products labeled “organic” or “natural”
- 3- products lacking traditional preservatives
- 4- products containing stem cells or human tissue
- 5- wet wipes (used by infants/children and adults)
- 6- cosmetic non-alcohol oral care products
- 7- eye area products
- 8- 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 CFSAN/OCAC.

5.4.14 – Foreign Supplier Verification Program

See Subchapter 6.8 Foreign Supplier Verification Program for inspectional instructions.

SUBCHAPTER 5.5 - DRUGS

5.5.1 - DRUG INSPECTIONS

Authority for inspection is discussed in IOM 2.2. [FD&C Act Sections 501\(a\)-\(d\)](#) and [501\(j\)](#) [21 U.S.C. 351(a)-(d), (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 FDA. Therefore, the purposes of a drug inspection are:

1. To evaluate a firm's adherence to the concepts of sanitation and good manufacturing practice; i.e., production and control procedures include all reasonable precautions to ensure the identity, strength, quality, and purity of the finished products;
2. To identify deficiencies that could lead to the manufacturing and distribution of products in violation of the Act, e.g., non-conformance with Official Compendia, super/sub potency, substitution;
3. To determine whether a firm is distributing drugs that lack required FDA approval including counterfeit or diverted drugs;
4. To obtain correction of those deficiencies;
5. To determine if drugs are manufactured by the same procedures and formulations as specified in the Drug Application documents;

6. To determine the drug labeling and promotional practices of the firm;
7. To 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. To determine if the firm is complying with the requirements of the Prescription Drug Marketing Act (PDMA) and regulations; and
9. To determine the disposition of Drug Quality Reports (DQRS) received from the Drug Surveillance and Data Reporting Branch (DSDRB)/CDER; and
10. To determine if the firm is complying with 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), and [600.80](#) (therapeutic biological products), and [Section 760 of the FD&C Act](#) (non-application nonprescription products) [21 U.S.C. 379aa].
11. For pharmacy compounding inspections determine if compounded drug products meet the conditions of section 503A or 503B of the FDCA

5.5.1.1 - Preparation and References

Become familiar with current programs related to drugs. Determine the nature of the assignment, i.e., a specific drug problem or a routine inspection, and if necessary, consult other program division personnel, such as chemists, microbiologists, etc., or center personnel, such as office of compliance staff. Review the establishment program division files of the firm to be inspected including:

1. Establishment Inspection Reports,
2. Firm Profiles,
3. OTC monographs and other pertinent references for non-application products,
4. Drug Applications (New, Abbreviated and Investigational) and the Knowledge Transfer Memo, if the Center has provided it for a specific pre-approval inspection,
5. Therapeutic Biologics License Applications,
6. Sample results,
7. Complaints and Recalls,
8. Regulatory files,
9. Drug Quality Reports (DQRs), NDA Field Alert Reports (FARs), and Biological Product Deviation Reports (BPDRs),
10. Drug Registration and Listing
11. Facility Dossier where applicable
12. Inspection Assignment memo where applicable.

During this review identify products which:

1. Are difficult to manufacture,
2. Are complex dosage forms,
3. Require special tests or assays, or cannot be assayed,
4. Require special processes or equipment,
5. 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 FDCA
Review the factory jacket, FACTS OEI and registration/listing data, and all complaint reports which are marked follow-up next inspection. These complaints are to be investigated during the inspection and discussed with management. See IOM 5.2.7.

Become familiar with current regulations and programs relating to drugs, [CP 7356.002](#), et al. When making GMP inspections, discuss with your supervisor the advisability of using a microbiologist, analyst, engineer, or other technical personnel 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](#) 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 guideline entitled "[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 1.10.3 for special regulatory information by product category.

Review [21 CFR 203](#) "Prescription Drug Marketing", [21 CFR 205](#) "Guidelines for State Licensing of Rx Drug Distributors", and CP 7356.022, Enforcement of the Prescription Drug Marketing Act (PDMA).

Before conducting drug preapproval inspections (CP 7346.832) it is important to be familiar with the application and coordinate accomplishment of Center goals communicated by (1) inspectional memos, (2) pre-inspection briefings, and/or (3) Center participation on the inspection team.

The Office of Manufacturing Quality (OMQ) in CDER has established two mechanisms for you to obtain technical assistance before, during, or after an inspection:

1. [Office of Manufacturing Quality \(OMQ\)](#). This webpage contains organizational charts, names and phone numbers of OMQ individuals identified as technical specialists in various areas.
2. [Questions and Answers on Current Good Manufacturing Practices for Drugs](#). This forum 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. These questions and answers generally clarify statements of existing requirements or policy.

5.5.1.2 - Inspectional Approach

Follow Compliance Program Guidance Manual (CPGM) 7356.002 and others as appropriate when conducting drug CGMP inspections. In-depth inspection of all manufacturing and control operations is usually not feasible or practical. 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 information, contact Office of Compliance/Recalls and Shortages Branch via email at cderrecalls@fda.hhs.gov) The latter group 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 CDER- led combination product, see also IOM 5.12.

CPGM 7356.002 incorporates the systems-based approach to conducting an inspection and identifies six (6) systems in a drug establishment for inspection: Quality, Facilities and Equipment, Materials, Production, Packaging and Labeling and Laboratory Control Systems. The full inspection option includes coverage of at least four (4) of the systems; the abbreviated inspection option covers of at least two (2) systems. In both cases, CPGM 7356.002, indicates the Quality System be selected as one of the systems being covered. During the 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 marketing a number of drugs meeting the risk criteria, the following may help you identify suspect products:

1. Reviewing the firm's complaint files early in the inspection to determine relative numbers of complaints per product.
2. Inspecting the quarantine, returned, reprocessed, and/or rejected product storage areas to identify rejected product.
3. Identifying those products which have process control problems and batch rejections via review of processing trends and examining reviews performed under [21 CFR 211.180\(e\)](#).
4. Reviewing summaries of laboratory data (e.g., laboratory workbooks), OOS investigations, and laboratory deviation reports.

5.5.2 - DRUG REGISTRATION & LISTING

Registration and listing is required whether or not interstate commerce is involved. See Exhibit 5-12 and IOM 2.9.1.1 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 5.1.1.11 - Multiple Occupancy Inspections for additional information.

Independent laboratories providing analytical or other laboratory control services on commercially marketed drugs must register.

FACTS 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 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.

5.5.3 - PROMOTION AND ADVERTISING

[21 CFR 202.1](#) which pertains only to prescription drugs, covers advertisements in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communication systems. Determine what department or individual is responsible for promotion and advertising and how this responsibility is demonstrated. Ascertain what media (radio, television, newspapers, trade journals, etc.) are utilized to promote products.

Do not routinely collect examples of current advertising. Advertising should be collected only on assignment, or if, in your opinion, it is clearly in violation of [Section 502\(n\) of the FD&C Act](#) [21 U.S.C. 352 (n)] or 21 CFR 202.1.

5.5.4 - GUARANTEES AND LABELING AGREEMENTS

Determine the firm's policies relative to receiving guarantees for raw materials and issuing guarantees on their products. Also determine firm's practices regarding shipment of unlabeled drugs under labeling agreements. See IOM 5.3.7.2.

5.5.5 - OTHER INSPECTIONAL ISSUES

5.5.5.1 - Intended Use

Please see the discussion of jurisdiction in section IOM 5.11.4.3.6.

5.5.5.2 - Drug Approval Status

The investigator 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.

5.5.5.3 – 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 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 the Office of Compounding Quality Compliance in CDER's Office of Compliance at 301-796-3100 or Compounding@fda.hhs.gov.

5.5.5.4 – Verification of Compliance with PDMA Requirements

The investigator should ascertain whether a manufacturer uses samples of prescription drugs to market their products. If so, they need to comply with the regulations at 21 CFR 203 Subpart D – Samples. Refer to CPGM 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 the Office of Compliance at 301-796-3100 or DrugSupplyChainIntegrity@fda.hhs.gov.

5.5.5.5 - Drug/Dietary Supplement Status

In instances where the drug/dietary supplement status of a product is unclear, the investigator should collect all related labeling and promotional materials including pertinent Internet web sites. This labeling and promotional material is often useful in determining the intended use of a product (See [21 CFR 201.128](#)). Labeling, promotional materials and Internet web sites often contain information, for example, disease claims, that can be used to determine the intended use of a product and thereby if it is a dietary supplement or a drug and an unapproved new drug.

5.5.5.6 - 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 ask your designated pre-approval manager for CMC information of the targeted drug application. You may take the program division's copy of the NDA into the plant as a reference during the inspection. Document and report all deviations from representations in the NDA even though they may appear to be minor.

5.5.5.7 - Investigational Drugs

Follow the instructions in pertinent programs in your CPGM or as indicated in the specific assignment received.

5.5.5.8 - Clinical Investigators and/or Clinical Pharmacologists

Inspections in this area will be on specific assignment previously cleared by the Administration. Follow guidance in the CPGM or assignment.

5.5.5.9 – 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 drug inspection. If you are unsure whether an action taken by a firm constitutes delaying, denying, limiting, or refusing drug inspection, contact 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 1.10.1.

5.5.8 - DRUG INSPECTION REPORT

See IOM 1.1 English language requirement. The requirements in IOM 5.11.4.3, and any applicable Compliance Program Guidance Manuals can be used to help you prepare your report.

This 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 guidance in IOM 5.11.4 about the depth of reporting required. Follow the instructions and format for a human drug inspection report as contained in IOM 5.11.4.2 and 5.11.4.3.

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 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.

SUBCHAPTER 5.6 - DEVICES

5.6.1 - DEVICE INSPECTIONS

See IOM 2.2 for discussion of statutory authority.

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 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](#).

Inspections involving devices should be made only by those individuals qualified by training and experience in the device area. Electronic product radiation is defined in [21 CFR 1000](#). Because of the specific nature of inspections and investigations involving radiation, only personnel who have special training in this field should be assigned such work. However, others may participate for training

purposes. Specific Compliance Program Guidance Manuals designate the type of individual and special training required for work in these areas.

CAUTION: Radiation-emitting devices and substances present a unique hazard and risk potential. Every effort should be taken to prevent any undue exposure or contamination. Monitoring devices must be used whenever radiation exposure is possible. Investigators should also 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, e.g., ethylene oxide, high voltage, pathogenic biomaterials, etc. See IOM Chapter S. Specifically, S.15.2-Radiation Hazards, S.12.6.3 - Ethylene Oxide (EtO), and S.15.1.3 - Energy Hazards.

5.6.1.1 - Technical Assistance

Each program divisions have engineers and radiological health personnel available for technical assistance and consultation. Do not hesitate to make use of their services.

Engineers, quality assurance specialists, and national expert investigators in OMPTO as well as in OHAFO are available for on-site consultation and assistance in problem areas. Refer to FMD-142. The subject matter experts are also available by telephone for consultation and to answer questions regarding regulation and program interpretation and QS/GMP application. Additionally, the CDRH Office of Health Technologies, within the Office of Product Quality (organized by device product) can be contacted as necessary.

WEAC has various personnel (biomedical, sterility, electronic, materials, mechanical, nuclear and plastics engineers) available for telephone consultation and on-site assistance at 781-756-9700.

5.6.1.2 - Sample Collection During Inspection

Because of the limited funds available for samples and the relatively high cost of device samples, it is essential you consider, in consultation with your supervisor, the following factors before collecting a physical sample of a device:

1. If follow-up to a QS/GMP deviation, will sampling demonstrate the deviation and/or a defective product? Documentary Samples may be more suitable for QS/GMP purposes.
2. Likelihood of the analysis showing the device is unfit for its intended use.
3. Samples costing over \$250.00.
4. Laboratory capability to analyze the sample. See IOM 4.5.5.3.6 for sample routing information.

If you are still uncertain, discuss with your supervisor and contact the CDRH Laboratory or WEAC 781-756-9700 for assistance.

Contact CDRH for assistance as follows:

In-vitro Diagnostic Devices - Office of Science and Engineering Laboratories (HFZ-113).

NOTE: Device samples do not require 702(b) portions. Include in the FDA 525 and with the C/R, if destined for different locations, a copy of the firm's finished device specifications, test methods and acceptance and/or rejection criteria.

5.6.1.3 - Types of Inspections

General device inspections will be conducted under various Compliance Programs found in the Compliance Program Guidance Manual. The majority of these will be QS/GMP inspections, but often the reason for the inspection will vary. For example, inspections may be conducted to assist the pre-market clearance process (PMA or Class III 510(k)), to specifically address MDR concerns, or to assure in-depth coverage of an aspect of manufacturing (sterility). The following describes some of these inspections. If the inspection is conducted for CDRH- led combination product see also IOM 5.12.

5.6.2 - MEDICAL DEVICE QUALITY SYSTEM/ GOOD MANUFACTURING PRACTICES

Section 520(f) of the FD&C Act [21 U.S.C. 360j(f)] provides the Agency with authority to prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of medical devices conform to good manufacturing practices. The medical device Quality System/Good Manufacturing Practices Regulation (QS/GMP) ([21 CFR 820](#)) became effective on June 1, 1997.

21 CFR 820 is established and promulgated under the authority of Sections [501](#), [502](#), [510](#), [513](#), [514](#), [515](#), [518](#), [519](#), [520](#), [522](#), [701](#), [704](#), [801](#) and [803](#) of the FD&C Act (21 U.S.C. 351, 352, 360, 360c, 360d, 360e, 360h, 360i, 360j, 360l, 371, 374, 381 and 383). Failure to comply with the provisions of 21 CFR 820 renders a device adulterated under Section 501(h) of the FD&C Act [21 U.S.C. 351(h)].

The regulations promulgated under 21 CFR 820 establish minimum requirements applicable to finished devices, as defined in [820.1\(a\)](#). This regulation is not intended to apply to manufacturers of components or parts of finished devices, but instead recommended to them as a guide. In some special cases, components have been classified as finished devices (dental resins, alloys, etc.) and are subject to the QS/GMP. Manufacturers of human blood and blood components are not subject to this part, but are subject to [21 CFR 606](#).

The QS/GMP includes regulations regarding Purchasing Controls, [21 CFR 820.50](#), Receiving, In-process and Finished Device Acceptance, [21 CFR 820.80](#), and Traceability, [21 CFR 820.65](#), that require finished device manufacturers exercise more control over the components they use in their devices. The preamble of the QS/GMP states: "Since FDA is not regulating component suppliers, FDA believes that the explicit addition to the CGMP requirements of the purchasing controls...is necessary to provide the additional assurance that only acceptable

components are used." And "...inspections and tests, and other verification tools, are also an important part of ensuring that components and finished devices conform to approved specifications." It further states, "...traceability of components must be maintained so potential and actual problem components can be traced back to the supplier."

The medical device QS/GMP is an umbrella GMP that specifies general objectives rather than methods. It is left to the manufacturer to develop the best methods to meet these objectives. You must use good judgment in determining compliance with the QS/GMP, keeping in mind that it is an umbrella GMP and all requirements may not apply or be necessary. The purpose of the QS/GMP is to assure conformance to specifications and to ensure that all requirements that will contribute to assuring the finished device meets specifications are implemented. You should 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 QS/GMP.

5.6.2.1 - Pre-Inspectional Activities

Prior to the start of any medical device inspection, the factory jacket or establishment history of the establishment should be reviewed. You should review the previous inspectional findings and subsequent correspondence between the establishment and FDA; any MDR or consumer complaints where it was determined follow-up would occur at the next inspection; and any notifications of recalls since the last inspection.

MDR data most useful in preparing for an inspection includes specific MDRs for the manufacturer (i.e., query by establishment's short name) for the time frame since the last inspection, or MDRs for the generic devices manufactured by that establishment (i.e., query by product code) for some reasonable time frame. This data assists you in determining potential problem areas in the manufacture or design of the device, or lot or batch specific issues. MDR information can be accessed through the Total Product Lifecycle Reports (TPLC). A medical device report data request may be submitted to Office of Health Technologies, within the Office of Product Quality. The agency's Voluntary Malfunction Summary Reporting Program grants an alternative that permits manufacturer reporting of certain device malfunction MDRs in summary form on a quarterly basis. For general questions regarding MDR reporting requirements, contact the MDR Team at MDRPolicy@fda.hhs.gov.

The establishment's reported registration and listing data should be verified during any GMP inspection to assure there have been no changes and the registration and listing data is accurately reported.

510(k) and PMA data assists you in determining what devices the establishment is manufacturing and whether any new devices have been designed or changed since the last inspection. This data is useful in focusing the inspection on new or changed devices as well as devices that are

higher risk devices, i.e., Class II or III versus Class I. This information can be accessed through IMAGE 2000 plus and TPLC.

Since information about medical device firms is distributed in many different databases, CDRH information is pulled into Total Product Life Cycle (TPLC) reports and ORA created Establishment History Reports (EHR1). EHR1 Reports combine detailed recall and inspection history information. TPLC Reports combine registration and listing, premarket, adverse event (MDR), and CDRH complaint details as well as high level recall and inspection information. ORA investigators can run these reports in order to prepare for inspections.

It is necessary to have access to both Business Objects and ORADSS in order to run EHR1 and TPLC reports. If you require access, send a request to the Employee Resource & Information Center (ERIC). You need to specify in your request to ERIC that you need access to the TPLC reports.

Accessing EHR1 reports

Go to

<http://inside.fda.gov:9003/it/Applications/ORAApplcations/default.htm>

Under ORADSS click go

Click the Documents Tab; then click Folders

Navigate (by hitting the plus sign) into Public Folders and then the Domestic Reports subfolder

Double click on the Establishment History Report subfolder

Select EHR1 and double click

*Note: For initial inspections, there will not be any inspection history in the EHR1 report

Accessing TPLC reports

Go to [BI launch pad \(fda.gov\)](#)

In the upper left corner, there are tabs labeled "Home" and "Documents". Click on "Documents". At the bottom left, are tabs labeled "My Documents", "Folders", "Categories" and "Search". Click on "Folders". Find folder that is labeled "Public Folders". Click on the folder. Navigate (by hitting the plus sign) on CDRH and then into the TPLC. The TPLC reports will appear to the right. Select a report by double clicking the report name

Beneficial reports include:

- TPLC Manufacturer Name – displays information on a firm based on the Manufacturer name entered. The manufacturer name entered must be in upper case as the reports are case sensitive. Since company names vary with the inclusion of commas, abbreviations (INC vs. INC. vs. INCORPORATED), or division names, it is best to first use the shortest name possible with a wild card character (%). For example, to search for "XYZ SURGICAL CO (PVT) LTD", it

would be best to first use "XYZ%". This will return all manufacturers that have a name beginning with that phrase. Given that some firms might have similar names, the report might return several companies with a name beginning with "XYZ". The best option then is to look at those companies returned in the report and modify the name used in the search.

- TPLC Product Code Reviewer - displays information on one or more specific product codes entered. Ensure that the product codes entered are in upper case as the reports are case sensitive.

For general questions or for help accessing this information, contact your CDRH Regulatory Inspections and Audits Team (RIAT) or OMDRHO Operations at ORADeviceInspectionPOC@fda.hhs.gov.

Firm participation in the [Medical Device Single Audit Program \(MDSAP\)](#) must be verified by accessing the MDSAP [Master List](#) before conducting routine medical device inspections. MDSAP participating firms are not subject to FDA routine device inspections. Verifications should be performed by searching the list for both firm name and address. If additional verification is required by contacting an MDSAP subject matter experts (SMEs) via email at MDSAP@fda.hhs.gov.

When the reason for an inspection at a firm participating in MDSAP is not routine (e.g. for-cause, EPRC) alert CDRH RIAT 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 reference number for a Warning Letter. This allows the FDA MDSAP SMEs to be aware of ORA follow-up activities in the event the firm challenges FDA on the need for an inspection.

If the reason for an inspection at an MDSAP participating firm is related to a specific assignment, generated by either ORA or CDRH, the ORA Division should email ORA OMDRHO Operations at ORADeviceInspectionPOC@fda.hhs.gov at least ten days prior to initiating the inspection. The email should contain the name and FEI of the firm, the nature of the complaint or quality issue, and any other relevant firm/device information prior to ORA investigators conducting the inspection or investigation. In these situations, a teleconference between the FDA CDRH MDSAP SMEs and ORA may be needed to discuss the scope of any planned inspection or investigation and allow additional information to be exchanged between CDRH and ORA.

IOM 5.2 should be followed in regards to pre-announcement of medical device inspections.

5.6.2.2 - Quality Audit

The inspectional approach for identifying inadequate auditing of a quality assurance program is limited by the agency's policy, which prohibits access to audit results. The policy is stated in [CPG section 130.300](#) (7151.02). Under the QS/GMP regulation ([21 CFR 820.180](#) (c)) this prohibition extends to evaluations or audits of suppliers, [21 CFR 820.50\(a\)](#), and Management Reviews conducted per [21 CFR 820.20](#). Evidence of inadequate auditing may be discovered without gaining access to the written audit reports. See the Guide to Inspections of Medical Device Manufacturers or Guide to Inspections of Quality Systems for inspectional guidance.

The preamble to the QS/GMP specifically states, "FDA will review the corrective and preventive action procedures and activities performed in conformance with those procedures without reviewing the internal audit reports. FDA wants to make it clear that corrective and preventive actions, to include the documentation of these activities, which result from internal audits and management reviews are not covered under the exemption at 820.180(c)." Therefore, these corrective and preventive actions and documentation are not excepted from inspectional scrutiny.

The QS/GMP regulation (21 CFR 820.180(c)) requires a manufacturer to certify in writing that audits and reaudits have been conducted whenever requested to do so by an investigator. Investigators through their supervisors should consult with CDRH Office of Regulatory Programs (HFZ-320) prior to requesting such certification.

5.6.2.3 - Records

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. Manufacturers who have petitioned for and obtained exemption from the QS/GMP are not exempted from FDA authority to review and copy complaints and records associated with investigation of device failures and complaints.

You may advise manufacturers they may mark as confidential those records they deem proprietary to aid FDA in determining which information may be disclosed under Freedom of Information Act.

Records must be maintained for as long as necessary to facilitate evaluation of any report of adverse performance, but not less than two years from the date the device is released for distribution. Records required by the Radiation Control for Health and Safety Act must be maintained for five years. It is permissible to retain records in electronic or

photocopy form, providing the copies are true and accurate reproductions.

5.6.2.4 - Complaint Files

Complaints are written or oral expressions of dissatisfaction with finished device identity, quality, durability, reliability, safety, effectiveness or performance. Routine requests for service would not normally be considered complaints. However, service requests should be reviewed to detect complaints, and as part of any trend analysis system, and to comply with 820.200(a)(3).

FDA has the authority to require a device firm to open its complaint files, and review and copy documents from the file.

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, e.g., financial data, which are exempt from disclosure to FDA.
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 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.

QS/GMP requirements for complaint files are found in [21 CFR 820.198](#). GMP requirements for complaint files first became effective on December 18, 1978. The Quality System Regulation, which went into effect on June 1, 1997, added to and modified the requirements for complaint handling. The regulation contains a provision that records maintained in compliance with the QS/GMP must be available for review and copying by FDA ([21 CFR 820.180](#)). Complaint files are QS/GMP required records; therefore, the manufacturer must make all complaints received on or after December 18, 1978 and the records of their investigation available for FDA review and copying. EIRs should contain enough information to allow cross-referencing between complaints and MDRs.

[21 CFR Part 803](#) requires medical device manufacturers to report deaths, serious illnesses, and serious injuries to FDA for which a device has or may have caused or contributed, and manufacturers must also report certain device malfunctions. The MDR reportable events must be maintained in a separate portion of the complaint files or otherwise clearly identified. These complaints must be

investigated to determine whether the device failed to meet specifications; whether the device was being used for treatment or diagnosis; and the relationship, if any, of the device to the reported incident or adverse event.

When a firm determines complaint handling will be conducted at a place other than the manufacturing site, copies of the record of investigation of complaints must be reasonably accessible at the actual manufacturing site.

5.6.3 - STERILE DEVICES

Inspections of sterile device manufacturers are conducted per Compliance Program Guidance Manual 7382.845, as a production process under the Production and Process Control Subsystem. See the Guide to Inspections of Quality Systems for further guidance.

5.6.4 - LABELING

Specific labeling requirements for in vitro diagnostics (IVDs) are contained in [21 CFR 809.10](#).

Part 809.10(a) contains explicit labeling requirements for the individual IVD containers, and for the outer package labeling and/or kit labeling. Part 809.10(b) contains special labeling requirements for the product insert, which must be included with all IVD products. These two sections also contain the requirements for: lot numbers, allowing traceability to components (for reagents) or subassemblies (for IVD instruments); stability studies for all forms of the product; an expiration date, or other indication to assure the product meets appropriate standards; and, the requirements for establishing accuracy, precision, specificity and sensitivity (as applicable).

Part 809.10(c) lists the labeling statements required for IVDs which are being sold for investigational and research use. Determine whether the firm is limiting the sale of IVDs, labeled as such, to investigators or researchers. Document any questionable products and submit to CDRH OHT7:Office of Invitro Diagnostics and Radiological Health for review.

Warning and caution statements recommended for certain devices, along with certain restrictions for use, are described in [21 CFR 801](#). This same section also contains the general labeling regulations, which apply to all medical devices.

5.6.5 - GOVERNMENT-WIDE QUALITY ASSURANCE PROGRAM (GWQAP)

Inspections under the GWQAP are conducted upon request by Office of Enforcement and Import Operations (OEIO), Division of Compliance Systems (DCS). Each assignment is specific and may involve more than a single compliance program. Specific questions arising during or as a result of these inspections should be directed to OEIO/DCS.

5.6.6 - CONTRACT FACILITIES

Device manufacturers may employ the services of outside laboratories, sterilization facilities, or other manufacturers (i.e., injection molders, packagers, etc.). The finished device manufacturer is responsible for assuring these contractors comply with the QS/GMP and that the product or service provided is adequate. These contractors are subject to FDA inspection and some are subject to the QS/GMP regulation. This "...includes but is not limited to those who perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions," per [21 CFR 820.3\(o\)](#). Whether under contract or not if a firm manufactures a finished device by the definition found in 21 CFR 820.3(l) "*Finished device*" means any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled, or sterilized they are subject to QS/GMP. NOTE: if the product manufactured by the contractor also meets the definition of a component *and* a finished device, the contractor is subject to the QS/GMP regulation.

Determine how a manufacturer evaluates and selects potential contractors for their ability to meet the manufacturer's requirements, as required by [820.50](#), Purchasing Controls. Conducting audits can be an effective method for assessment. However, not all contractors allow audits. Audits may not be feasible in some instances. In other instances, the activity the contractor is conducting may not have a significant impact on the device safety or function; therefore, expending the resources necessary to audit the contractor may not be warranted.

Evaluations may be accomplished by other means such as requesting that the potential contractor fill out a questionnaire about their quality system, asking other customers of the contractor about their experiences with the firm, or basing assessments on past performance. Evaluations must be documented. The extent to which a manufacturer has evaluated a contractor, as well as the results of the evaluation, should govern the degree of oversight exercised over products and services supplied by the contractor.

5.6.7 - SMALL MANUFACTURERS

When inspecting one-person or very small manufacturers for compliance with the QS/GMP master record and written procedure requirements, the investigator should realize that detailed written assembly, process, and other instructional procedures required for larger firms may not be needed. In a small firm, division of work is at a minimum, with one person often assembling and testing the finished device. In many cases, blueprints or engineering drawings could be adequate procedures. The QS regulation requires that certain activities be defined, documented and implemented. The regulation does not require separate procedures for each requirement and often several requirements can be met with a single procedure. The

complexity of the procedures should be proportional to the complexity of the manufacturer's quality system, the complexity of the organizational structure and the complexity/risk of the finished device being produced. In assessing the need for detailed or lengthy written procedures, the investigator should make judgments based on training and experience of the individuals doing the work and the complexity of the manufacturing process. However, this does not mean small manufacturers have any less responsibility for complying with the QS regulation or assuring safe and effective devices are produced.

5.6.8 - BANNED DEVICES

[Section 516 of the FD&C Act](#) [21 U.S.C. 360f] provides a device for human use may be banned by regulation ([21 CFR 895](#)) if it presents substantial deception or an unreasonable and substantial risk of illness or injury. Investigators should become familiar with this regulation. When you determine, during an inspection or investigation, that banned devices are being distributed, the distribution, manufacture, etc., should be documented as for any other violative product.

5.6.9 – REPORTS OF CORRECTIONS AND REMOVALS

Manufacturers, importers, and distributors of medical devices are to promptly report to the FDA any corrections or removals of a device undertaken to reduce a risk to health posed by the device or to remedy a violation of the FD&C Act caused by the device which may present a risk to health as provisioned by the Safe Medical Devices Act of 1990 and 21 CFR Part 806. Refer to IOM Ch. 7 – RECALL ACTIVITIES and 7.2.3 MEDICAL DEVICE RECALLS for more information.

5.6.10 – TRACKED MEDICAL DEVICES

A "tracked medical device" is a device regulated by CDRH and for which the firm has received "tracking orders". CDRH has a dedicated mailbox to manage inquiries about tracked devices and the related regulation at TrackedDevicesMailbox@FDA.HHS.GOV.

5.6.11 - DEVICE INSPECTION REPORTS

See IOM 1.1, English language requirement. You should write your EIR following the guidance in IOM 5.11.4, 5.11.4.1, 5.11.4.2, 5.11.4.3. Section headings can be added to address the needs of other Compliance Program Guidance Manuals such as 7383.001 for pre-market and post-market PMA inspections. Include in your report the systems, processes, products, and product classification covered during the current inspection.

SUBCHAPTER 5.7 - BIOLOGICS**5.7.1 - 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 Federal Food, Drug, and Cosmetic Act (FD&C Act).

Veterinary biologics are subject to the animal Virus, Serum, and Toxin Act which is enforced by USDA (21 U.S.C. 151-158).

5.7.2 - BIOLOGICS INSPECTIONS

The periodic CGMP inspections and compliance operations of plasma fractionated products, allergenic products, vaccines, gene and cell therapy products, and biological in vitro diagnostic devices are led by investigators from ORA's Office of Biological Products Operations (OBPO). OBPO investigators also lead inspections of unlicensed CBER-regulated medical devices (e.g., blood establishment software). See IOM 2.2 for a discussion of statutory authority. CBER maintains the lead for pre-licensing and most pre-approval inspections of biological products, while ORA customarily leads PMA/510(k) inspections.

5.7.2.1 - Authority

Biological products are regulated under the authority of [Section 351 of the Public Health Service Act](#) and under the Food, Drug, and Cosmetic 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 FD&C Act, source plasma and recovered plasma may have the legal identity of either a drug or device depending on its intended use. Section 351(a) of the PHS Act provides for licensure of biological products and inspection of the products covered is per 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, investigations of blood grouping serum, reagent red blood cells, and anti-human globulin in-vitro diagnostic products may be exempted ([21 CFR 312.2\(b\)](#)).

5.7.2.1.1 - BLOOD AND SOURCE PLASMA INSPECTIONS

For blood bank and source plasma establishment inspections ([CP 7342.001](#) & [7342.002](#)) 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](#).) 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. This would generally be Parts 606 and 640 of the regulations in the case of blood bank and source plasma establishments.

5.7.2.1.2 – HUMAN TISSUE INSPECTIONS

21 CFR [Part 1271](#) contains six subparts:

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, i.e., to those 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, with the exception of two provisions ([Sec. 1271.150\(c\)](#) and [1271.155](#)) subparts D and 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."

5.7.2.2 – Donor Confidentiality

Blood bank, source plasma, and human tissue establishments are sensitive to maintaining confidentiality of donor names. The mere reluctance to provide records is

not a refusal. However, FDA has the authority under both the PHS and the FD&C Acts to make inspections and [21 CFR 600.22\(g\)](#) and [1271.400\(d\)](#) provides for copying records during an establishment inspection. For prescription drugs, [section 704 of the FD&C Act](#) 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 5.2.5 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 5.3.8.6.

5.7.2.3 – 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. The inspectional objective for HCT/Ps 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 conformance with:

1. Provisions of the PHS Act and FD&C Act,
2. Applicable regulations in:
 - 21 CFR [210-211](#)
 - 21 CFR 600-680, and
 - 21 CFR [820](#)
3. HCT/P regulations in [21 CFR 1270](#) and [1271](#).
4. FDA Policies, which include guidance to the industry, and the [Compliance Policy Guides Chapter 2](#).

5.7.2.4 - Preparation

Review the program division files of the facility to be inspected and familiarize yourself with its operation and compliance history. 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, and recalls;

Through guidance documents, CBER sets forth its inspection policy and regulatory approach. A list of these documents is attached to the current Compliance Program Guidance Manuals (CP) available on the CBER internet site at ([CBER CP Website](#)).

The OSHA regulation [29 CFR 1910.1030](#) dated December 6, 1991, was intended to protect health care workers from blood borne pathogens, including those involved in the collection and processing of blood products. The regulation defines expectations for the use of gloves, hand washing

facilities, decontamination of work areas, waste containers, labeling and training of employees and exemptions for volunteer blood donor centers. FDA Investigators should adhere to these safety guidelines during inspections or related activities in establishments that process biologically hazardous materials.

Become familiar with the OSHA regulations and their applicability to [21 CFR 606.40\(d\)\(1\)](#) and (2), which require the safe and sanitary disposal of trash, items used in the collection and processing of blood and for blood products not suitable for use. Consult your program division biologics monitor for copies of the above references. Additional copies may be obtained from OO, OMPTO, Division of Medical Products and Tobacco Program Operations or see [CBER's web site](#).

5.7.2.5 - Inspectional Approach

Use the Compliance Program (CP) for inspectional instructions. Particular attention should be given 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.

Complaints, in particular those involving criminal activity, must be promptly investigated and coordinated with other agency components as needed.

For blood banks and source plasma establishments, refer to CP 7342.001 and 7342.002 for a discussion of the systems approach to inspection. The CP incorporates a systems-based approach to conducting an inspection and identifies five (5) systems in a blood bank and source plasma establishment operation for inspection. Each system may not be in a particular establishment operation; therefore, the inspection should focus on the systems present. The CP directs an in-depth audit of the critical areas in each system. A multi-layered system of safeguards has been built into the blood collection, manufacturing and distribution system to assure a safe blood supply.

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.

If Investigators encounter products not specifically referenced in the regulations, they should contact CBER/OCBQ/ Division of Inspections and Surveillance for guidance.

5.7.2.5.1 Access of Electronic Databases and Queries

Overseeing the firm's personnel while they access their system is not always practical. For these reasons, if all the following criteria are met, OBPO investigators are permitted to access a firm's records using a read-only account, dummy terminal, or comparable mechanism when necessary:

- 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, establishment inspection report, or investigational memorandum accordingly.

5.7.2.6 - Regulations, Guidelines, Recommendations

Guidance documents for industry are made available to the public in accordance with good guidance practice regulations 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 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. During the discussion with management, the relationship of the deviation to the regulation or law, or accepted standard of industry, 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 the email address for industry in order to obtain additional information from CBER at industry.biologics@fda.hhs.gov.

If a firm claims approval for an alternative procedure, verify by reviewing the firm's written approval letter. Approved alternative procedures may be verified by contacting CBER/Division of Blood Applications or the appropriate CBER product office.

5.7.2.7 - Technical Assistance

The services of National Experts and Program Experts in ORA/OMPTO are available for telephone or on-site

consultation and assistance in problem areas (see FMD-142).

5.7.2.8 Biologics Establishment Inspection Reports

See IOM 1.1, English language requirement. You should write your EIR following the guidance in IOM 5.11.4, 5.11.4.1, 5.11.4.2, 5.11.4.3. Section headings can be added to address the needs of 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 must 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, such as complaint follow-up or center-directed assignments include information to appropriately cover the assignment. Follow specific instructions included in any associated assignment memorandum.

5.7.3 - REGISTRATION, LISTING AND LICENSING.

5.7.3.1 - Registration and Listing

See IOM 2.9.3.1

5.7.3.1.1 – TRANSFUSION SERVICES

Most transfusion services are exempt from registration under [21 CFR 607](#). 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. Such facilities include establishments:

1. Collecting, processing and shipping blood and blood components under documented emergency situations,
2. Performing therapeutic phlebotomy and therapeutic plasma exchange after which the product is discarded,
3. Preparing recovered human plasma and red blood cells,
4. Pooling products/platelets for in-house transfusion,
5. Thawing frozen plasma or cryoprecipitate for transfusion.

All VA Blood Banks and Hospital Transfusion Services must register with FDA since they are not inspected by CMS.

5.7.3.1.2 - 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 FDA. Establishments manufacturing HCT/PS regulated as drugs and/or biological products must register and list with FDA pursuant to 21 CFR 207. Establishments manufacturing HCT/PS regulated as medical devices must register and list with FDA pursuant to 21 CFR 807.

5.7.3.1.3 - LABORATORIES

Laboratories performing infectious disease testing of donors of blood or blood components or HCT/P are an FDA obligation and required to register. Clinical laboratories were previously exempted from registration by [21 CFR 607.65\(g\)](#), but FDA revoked this regulation. Your inspections should focus on activities relevant to blood product and HCT/P testing operations.

5.7.3.1.4 - MILITARY BLOOD BANKS

Inspection of military blood banks is an ORA 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; although each individual establishment may be licensed or unlicensed, all are required to register. Program divisions should notify the appropriate military liaisons 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.

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.

Ensure the firm's current registration forms reflect actual operations.

5.7.3.2 – 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 these

facilities that engage in minimal manufacturing in order 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 as such. See Federal Cooperative Agreements Manual - FDA/HCFA MOU.

5.7.3.3 - Biologics License

See IOM 2.9.3.2. 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 ORA to participate in or may request ORA 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. These inspection reports can also be located in eNSpect and OSAR.

5.7.3.4 - 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. ORA Investigators customarily inspect the CBER regulated devices, which are subject to PMA/510(k) applications.

5.7.4 - 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:

1. licensed or
1. 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 has met equivalent requirements as determined by CMS.

Instructions for inspecting testing laboratories are included in the appropriate CP. 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.

5.7.5 - 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 manufacture 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 inspections, 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.

SUBCHAPTER 5.8 - TOBACCO PRODUCTS

5.8.1 - DEFINITIONS

The term "tobacco product" is defined in FD&C Act Section 201(rr) and means any product made or derived from tobacco 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 definition of certain tobacco products can be found in the FD&C Act under section 900.

5.8.2 – TOBACCO INSPECTIONS

See IOM 2.2 for discussion of statutory authority

Inspections involving tobacco product(s) at manufacturing facilities are led by ORA's Tobacco Operations Staff (TOS) within the Office of Medical Products 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 review process. Assignments may also be issued to conduct investigations and sample collections. CTP Subject Matter Experts may accompany ORA's Tobacco Operations Staff during 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>.

5.8.3 - RETAIL COMPLIANCE CHECK INSPECTION CONTRACTS

FDA issues contracts to assist with compliance check inspections of tobacco retail establishments to help enforce the Youth Access and Advertising Regulations that took effect on June 22, 2010, and were amended on August 8, 2016, to deem additional tobacco products within FDA's jurisdiction. FDA has a goal of establishing a contract, where feasible, with every U.S. State and Territory, but some States and Territories, for a variety of reasons, have been unable to do so. Therefore, FDA 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 FDA was unable to contract with a government agency. 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, FDA may also conduct inspections using FDA personnel.

5.8.4 - GUIDANCE, COMPLIANCE & REGULATORY INFORMATION

The [Center for Tobacco Products](#) website contains resources for legal, regulatory, and policy issues related to tobacco products and information for small business assistance (SmallBiz.Tobacco@fda.hhs.gov)

SUBCHAPTER 5.9 - VETERINARY MEDICINE

5.9.1 - CVM WEBSITE

The [Center for Veterinary Medicine](#) website contains; a listing of current and planned Guidance Documents; and on-line access to the [Animal Drug@fda](#) database listing new animal drug approvals. There is a "search" feature allowing you to search for documents containing various words or phrases. The website also contains organizational information for the Center and an explanation of the various

laws and regulations which the Center enforces. Information on the website can provide guidance for inspectional efforts related to CVM obligations.

5.9.2 - 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 or prevention of disease. Production drugs are used for economic enhancement of animal productivity. Examples include: growth promotion, feed efficiency and increased milk production.

Pre-approval inspections are conducted pursuant to pending NADA or ANADA applications.

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 veterinary drugs approved 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.

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 describe what is 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 on 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 CPG on Compounding of Drugs for Use in Animals (CPG 608.400). A copy can be found on CVM's website. 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. You should contact the Division of Compliance (HFV-230) at 240-276-9200 to report instances of compounding or to seek guidance on inspectional issues, or regulatory and enforcement policies.

5.9.3 - MEDICATED FEEDS AND TYPE A ARTICLES

Animal feed is defined under [section 201\(w\) of the FD&C Act](#) [21 U.S.C. 321 (w)]. CVM is responsible for control of medicated and non-medicated animal feeds, Type A medicated articles and pet foods.

The regulations for animal food labeling are in [21 CFR Part 501](#). The regulations for medicated feed mill licensure are in [21 CFR Part 515](#). The cGMPs for Medicated Feeds are in [21 CFR Part 225](#). The cGMPs for Type A Articles are in [21 CFR Part 226](#).

Inspections are routinely conducted of medicated feed mills and manufacturers of Type A Medicated Articles.

If you have questions related to cGMPs and enforcement policies and strategies concerning Medicated Feeds and Type A Articles you should contact the CVM/Division of Food Compliance at CVMAnimalFoodPrograms@fda.hhs.gov.

Guidance on pet food labeling requirements can be found on CVM's website.

5.9.4 - BSE ACTIVITIES

CVM is responsible for FDA's industry education and regulatory activities involving BSE and animal feed. BSE is "Bovine Spongiform Encephalopathy" and is often referred to as "mad cow disease." There are two BSE-related feed regulations: 21 CFR 589.2000, entitled "Animal Proteins Prohibited in Ruminant Feed" which was adopted in 1997, addresses the feeding of ruminant animals. A second rule, 21 CFR 589.2001, entitled "Cattle Materials Prohibited in Animal Food or Feed to Prevent the Transmission of Bovine Spongiform Encephalopathy" was adopted in 2009. 21 CFR 589.2001 prohibits the use of certain cattle-origin materials in the feed of all animals and is aimed primarily at rendering operations.

CVM has [Guidance Documents](#) in place dealing with BSE. The guidance documents address renderers, protein blenders, feed manufacturers, distributors and on farm feeders. The Compliance Program Guidance Manual and the inspection checklist are available on the CVM website, as are a variety of other BSE information, including a database containing a summary of the most recent inspection of each firm.

Questions on inspectional assignments and regulatory activities in the BSE area should be addressed to the CVM/Division of Food Compliance (HFV-236) CVMAnimalFoodPrograms@fda.hhs.gov.

5.9.4.1 – Biosecurity Procedures for BSE Inspections at Poultry Facilities and Farms

Given our recent experiences with highly pathogenic animal viruses such as porcine epidemic diarrhea virus (PEDV) in 2013 and 2014, and highly pathogenic avian influenza (HPAI) in 2015, we expect everyone conducting feed inspections on FDA's behalf to observe routine, simple, biosecurity precautions for all of your routine feed inspection work going forward.

In summary: and in addition to FDA's Biosecurity Guidance/procedures:

- 1) Follow the biosecurity plan for the facility being visited if they have one.
- 2) Plan your daily work so you do not carry contamination from one location to another. As much as possible, plan to work from cleanest to dirtiest 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 hand-washing and bathing.
- 5) Change or clean your shoes between inspection sites if they get dirty or wear disposable shoe coverings.
- 6) Visiting a farm to conduct a feed inspection should not require any contact with farm animals in most situations, and animal contact should be avoided unless it is absolutely necessary.
- 7) Be cognizant of recent contact with any livestock or poultry, including your own or those belonging to friends, families or neighbors, pet birds, and things like hunting, and consider it as you plan your work.
- 8) As much as possible, avoid going from one farm to another on a single day. If you do need to go from one farm to another, it may be necessary to change clothes or shoes, or even take a shower which is why we are encouraging the planning of work in such a way that contamination is not carried from one site to another.
- 9) Make an appointment to conduct routine on-farm inspections.

For the most part, the information above is a brief, high-level summary of Section 5.2.10. "Routine Biosecurity Procedures for Visits to Facilities Housing or Transporting Domestic or Wild Animals

CVM asks that all routine assigned work (covered in the work-plan or an assignment) involving on-farm feed inspections be pre-announced. This will allow the CSO the opportunity to ask about biosecurity procedures and help make sure someone is present.

5.9.5 - 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/Food Safety Inspection Service (FSIS).

Drug residues are commonly caused by medicating animals prior to marketing and 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. Although your investigation may begin at the USDA slaughter establishment or person named on the USDA/FSIS "Violation Notification Letter," you may inspect and/or visit more sites as part of your overall investigation. You may have to visit an auction barn, dealer, trucker, veterinarian, drug supplier, slaughter facility (USDA firm management or State personnel), etc. One or more of these establishments may be responsible for the drug residue. Thus, each establishment's activities may warrant a recommendation for regulatory action such as Warning Letter, Injunction, etc. when 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, which will include all operations required to complete the CVM assignment. This could include multiple inspections, sample collections and/or investigations. You may not be aware of all the establishments you will visit prior to beginning your investigation. Appropriate operations should be added to or deleted from the program division assignment.

Each site visit is unique, and each produces its own set of unique documents and evidence requiring individual reporting by establishment. You should use good judgment during case development to assure you document your investigation thoroughly. Explain the chain of events and evidence, from the initial drug residue report, and how other establishments were involved. Collect samples (usually DOC samples) as appropriate. Consultation with your supervisor and/or compliance branch during these operations is essential to assure all evidence necessary 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 program division Compliance Branch, with a copy to the originating CVM office. This Memo will 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 obtain information on the animal from the USDA inspection personnel on site; and obtain verification from management 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 may be important to establish whether the drugs which caused the drug residue(s) were prescribed and, if so, how they were prescribed. When there is reason to believe off-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" for in depth instructions on how to conduct a drug residue inspection.

For information on drug residue violations and activities you should contact the CVM/Division of Food Compliance (HFV-236) CVMAntimalFoodPrograms@fda.hhs.gov.

5.9.6 - 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) (ASKOCS@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) (ASKOCS@fda.hhs.gov).

5.9.7 - 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\(j\)](#) 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.

5.9.8 – 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.

SUBCHAPTER 5.10 – BIORESEARCH MONITORING (BIMO)

Inspectional activities in the bioresearch monitoring (BIMO) program involve all product areas and centers. Establishments inspected include Sponsors, Monitors, Contract Research Organizations, Clinical Investigators, Sponsor-Investigators, Institutional Review Boards, In Vivo Bioequivalence / Bioanalytical Clinical and Analytical Sites, and Nonclinical Laboratories. BIMO also includes Post market Adverse Drug Experience (PADE) reporting and Risk Evaluation and Mitigation Strategies (REMS), both of which are post approval activities. 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.

5.10.1 – BIMO Establishment Type Definitions

Clinical Investigator – A person who conducts a research study (i.e., 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) – An entity employed or contracted by sponsors or CROs to oversee the progress of an investigation. A monitor is not a regulated entity unless they have assumed one or more obligations from the sponsor in writing. In such case, the monitor is regulated as a contract research organization.

Institutional Review Board – Also known as Institutional Review Committee for Human Studies and 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 Bioequivalence/Bioanalytical Clinical Site – A facility or individual involved in the screening and/or dosing of human subjects for obtaining biological specimens (e.g., 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 Bioequivalence/Bioanalytical 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. 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 – A clinical investigator who is also responsible for initiating an investigational study. This person has the responsibilities of both a sponsor and a clinical investigator.

Postmarket 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 Food and Drug Administration 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.)

5.10.2 – BIMO Assignments

Assignments are issued by the product centers to ORA. These assignments are primarily issued to conduct inspections of entities engaged in nonclinical or clinical research and were involved in studies submitted as part of an application for approval of new product. Typically, inspections are conducted well after a nonclinical or clinical study has been completed. Inspections may also be conducted of on-going research. Assignments may also be issued for-cause for allegations for 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 to be inspected and provide instruction on what to cover during the inspection. The areas of coverage relate to the specific regulatory requirements of each establishment type.

Assignments are prepared by each center using a template that was harmonized across all centers for the BIMO program. The assignment memo will identify the type of establishment to be inspected, the Compliance Program, the Program Assignment Code, background information, general instructions and any special instructions for inspectional coverage. Assignments are issued to ORA HQ, reviewed and assigned to the appropriate division. Assignments are received by the Director, Investigations Branch and then disseminated to the appropriate supervisory group for assignment to an investigator.

Occasionally, center personnel will participate in inspections with field investigators. Center personnel are subject matter experts on the products or processes which are the focus of the nonclinical or clinical research. In these cases, the ORA investigator will be the lead investigator. See IOM 5.1.2.5 – Team Inspections.

Assignments in BIMO will usually have background materials, which will be available to you via a link to Enterprise Content Management Server/System (ECMS). Background materials may include the protocol for the study you are assigned to inspect, certain line listing of data included in the application such as reported adverse events and measurements taken during the study, and the assignment memo. If there are specific areas to focus on during the inspection, the assignment memo will discuss these areas and there may be specific data included in the background materials for you to verify during your inspection.

Centers have final classification authority for inspections in the BIMO program. When inspections are completed and the EIR reviewed by your supervisor, an initial inspection classification will be assigned through eNSpect. The

centers will determine and assign the final classification for the inspection after their review of the EIR and evidence collected is completed.

5.10.2.1. READ-ONLY ACCESS TO ELECTRONIC DATABASES DURING BIORESEARCH MONITORING INSPECTION ASSIGNMENTS

As the conduct of clinical and non-clinical trials increasingly moves toward 100% electronic data capture, to include electronic case report forms, medical records, patient-reported outcomes, informed consent systems and other electronic study records, it has become necessary for bioresearch monitoring investigators to have access to these electronic systems and databases in order to successfully perform inspections. Overseeing the firm's personnel while they access their system is not always practical in BIMO inspections, as this can result in the firm having to dedicate an individual to this task.

For these reasons, if all the following criteria are met, bioresearch monitoring investigators are permitted to access a firm's records via a read-only account, dummy terminal or comparable mechanism when necessary:

1. Responsible management at the firm is agreeable to allowing read-only access to electronic systems and/or databases;
2. Access to electronic systems/databases is read-only and will not permit you to change or alter data or programming in any manner;
3. You obtain written program supervisory approval to gain read-only access to the firm's electronic systems/databases in advance of doing so;
4. 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
5. You document this read-only access in your establishment inspection report or investigational memorandum accordingly.

While you may complete a form needed by the firm in order to obtain read-only access, such as an account request form, you will not sign such form as per section 5.1.2.3. You may acknowledge via email that you have completed any required training necessary for access.

5.10.2.2 ELECTRONIC REGULATORY NOTES FOR BIMO OPERATIONS

As per section 1A.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.

5.10.3 – BIMO Compliance Programs

BIMO Compliance Programs are posted on the internet at:

<https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-program-guidance-manual-cpgm/bioresearch-monitoring-program-bimo-compliance-programs>

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

7348.808 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

5.10.4 – Postmarket Adverse Event Reporting

FD&C Act section 760 [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 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 a life-threatening event, and if the event was expected (labeled) or unexpected (unlabeled) for the product. Responsible firms must submit adverse event information to FDA in expedited or periodic reports in an electronic format as described in the regulations. Adverse event information submitted to

FDA should be complete and accurate based on the data received.

Refer to the Compliance Program Guidance Manual (CP) (section 7353.001) for the description of the program and for detailed instructions for conducting inspections.

5.10.5 - Risk Evaluation and Mitigation Strategies (REMS)

FD&C Act Section 505-1 [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), or 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 as amended by 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 FDA 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.

5.10.6 BIMO Establishment Inspection Reports (EIRs)

In general, refer to IOM 5.11 for reporting requirements following BIMO inspections with a few exceptions as follows. The Summary of Findings format is not to be used for BIMO EIRs. For foreign inspections where the firm has been previously inspected and the current inspection will be classified NAI, an abbreviated report may be used as per section 5.11.4.3.1 under the heading Routine Surveillance—NAI Reports as outlined below.

Domestic BIMO EIRs and EIRs for foreign inspections not meeting the above criteria will utilize the Standard Narrative 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, e.g., Authority and Administration, Protocol, Institutional Review Board, Subjects' Records, etc. for a clinical investigator inspection.

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 within 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 BIMO EIRs include:

Manufacturing/Design Operations, Manufacturing Codes (may be applicable for Bioequivalence), and Recall Procedures. All other headings should be included. If they do not apply to your inspection (e.g., Sample Collection, Refusals), simply insert "N/A" into that section, but do not delete.

For foreign inspections where the firm has been previously inspected and the current inspection will be classified NAI, the abbreviated report should include the information required in section 5.11.4.3.1 Routine Surveillance—NAI Reports (to include change reporting) as well as the following:

- BIMO program specific information (i.e., 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 – name, number, sponsor
 - # Subjects
Screened/Consented/Enrolled/Randomized/Completed (whichever descriptions fit best)
 - Records Reviewed (including Subjects) and Recordkeeping Practices
 - Adverse events
 - Primary Endpoints
 - Discussion items (including minor protocol deviations or recordkeeping issues)

5.10.7 BIMO Affidavits

Affidavits will be obtained in accordance with IOM 4.4.8. In the BIMO program, affidavits (FDA 463a) will generally be obtained to document violative conditions or unusual circumstances observed during an inspection.

Additionally, an affidavit will accompany all sample collection reports, whether or not the firm provides a statement on company letterhead attesting that the test and reference product reserve samples are representative of those used in inspected BA/BE studies, and that they were stored under conditions specified in accompanying records, e.g. protocol or labeling. This is because all bioequivalence samples are official samples, and as such must be accompanied by an affidavit.

5.10.8 BIMO Collection Reports (CRs)

Samples collected under the BIMO program primarily include bioequivalence samples. Refer to IOM 4.4.10 for reporting these sample collections. All subs collected for a bioequivalence sample including investigational product, reference, and placebo, will be included on one collection report. A scanned copy of the collection report and all associated documents will be uploaded into eNSpect as an attachment to the EIR.

Additional instructions specific to certain fields on BIMO CRs are as follows:

5.10.8.1 Sample Type

The sample type for all bioequivalence samples will be "Official". Select "Domestic-Import" if applicable. Note: Domestic-Import samples are also Official, however, this is the way the drop-down menu is set up.

5.10.8.2 Sample Description

Ensure that the field includes a description of the investigational product collected as well as the reference and placebo if applicable.

5.10.8.3 Reason for Collection

Reference the compliance program (e.g., CP 7348.003, "In vivo Bioavailability- Bioequivalence Studies- Clinical", the assignment memo, and the inspection dates (if applicable). There will not be a suspected violation for surveillance samples. Add the following statement and edit as appropriate, "Sample of bioequivalence investigational product, reference control and placebo. Sample is representative of test product used in study supporting Protocol (insert Study #)." You will specify the analysis desired as follows: "Collected for drug assay analysis." Include the application number, e.g., ANDA 12345.

5.10.8.4 Associated Firms

List all firms related to the investigational product. Associated firms for the reference and placebo can be listed in the Collection Remarks field or on a continuation sheet.

5.10.8.5 Product Code and Product Name

The product code and product name listed should be that of the test article.

5.10.8.6 Brand Name

List the brand names for the test article, reference and placebo (if applicable.)

5.10.8.7 Product Label

Quote the label and labeling from the test article, reference and placebo (if applicable.) Be sure to use Collection Remarks or a continuation if necessary and specify which labeling goes to which product.

5.10.8.8 Sample Flags

There should be no sample flags for bioequivalence samples, unless the sample is a complaint sample. This is rare.

5.10.8.9 Estimated Value

It may be difficult to estimate the value of a bioequivalence sample. If the firm is not able to provide you with the value of the lot remaining after sampling, use the estimated cost of the innovator if possible. If you cannot estimate, leave blank and note in the Collection Remarks, "Estimated Value is unknown."

5.10.8.10 CR & Records Sent To FACTS Org

For domestic CRs, select your division from the list of values and send the hard copy CR and all associated documents to the director of investigations for your division when complete. For samples collected on foreign inspections, select the appropriate center/division (e.g. CDER-CP for bioequivalence samples) from the drop-down menu and send the hard copy CR and all associated documents to the center/division office contact specified in the assignment memorandum.

SUBCHAPTER 5.11 – REPORTING

Following an inspection, you are required to prepare a report of your findings. Reporting includes the data and summary entered using eNSpect, a narrative report, attachments and exhibits. As soon as practical you have access to eNSpect after the close of an inspection, ensure the start and end date are entered. Investigators must select a suggested "Inspection Conclusion" in eNSpect for each process covered.

Reports must be completed within time frames commensurate with the inspection classification, the current regulatory action time frames for the anticipated regulatory action, applicable FMDs, SOPs, RPM and/or the assignment deadline, if any.

Your narrative report should be prepared to accurately and concisely communicate the findings of your inspection and be adequate for its intended use. For example, an inspection of a new firm, one that FDA has not inspected previously, should be a comprehensive inspection focused on assessing the firm's compliance with applicable regulations. The resulting report would detail the products manufactured, the processes used to manufacture those products, the conditions of the environment in which products are manufactured or stored, any violations observed, persons responsible for the firm's operations, their actual duties and their responsibility for observed violations, distribution practices, and so on, providing information responsive to each of the required elements.

For establishments that have been previously inspected, you should determine what changes in operations and responsible individuals have occurred since the previous inspection, detail those changes in the narrative report and report on the areas of concern for the current inspectional outcome. For example, a non-violative inspection may only require a Summary of Findings report with the information required in the Summary, Administrative Data, General Discussion with Management, Voluntary Corrections, Refusals, Samples Collected, Exhibits Collected and Attachments (see IOM 5.11.4.1).

An OAI follow-up inspection that reveals continuing violations supporting a regulatory action would require the Summary, Administrative Data, Individual Responsibility and Persons Interviewed, Objectionable Conditions and Management's Response, Supporting Evidence and Relevance, Discussion with Management, Exhibits Collected, Attachments, and if appropriate, Refusals, Samples Collected, and Voluntary Corrections. Additionally, any information related to changes in previous operations would also need to be included in this type of report.

The key for you to remember in writing your narrative report is to communicate the findings of your inspection so that others may take the appropriate action. Notice that the required elements always include the product, interstate commerce, the violations observed and responsibility of firm officials. This is to document the elements of proof – Jurisdiction, Interstate Commerce, Violation and Responsibility (JIVR). Write your EIR with the intended use in mind. Your report may be a brief summary of an inspection of a firm in a state of compliance with applicable regulations all the way to a firm where the agency must take regulatory action to correct deficiencies.

5.11.1 - ESTABLISHMENT INSPECTION REPORT (EIR)

See IOM 1.1 English language requirement. The EIR consists of the following: the eNSpect Establishment Inspection Report, investigator's narrative report, attachments and exhibits. Regarding the use of checklists that are completed during the inspection (such as the BSE Checklist), the original checklist should be submitted with unlabeled attachments. If you maintain the data in your

regulatory notes, instead of entering the data directly on the checklist during the inspection, then a copy of the checklist that was completed using the data from your regulatory notes should be included with the EIR. The signed original report is maintained electronically and is available in OSAR.

See IOM 5.10.6 for additional requirement for Bioresearch Monitoring EIRs.

See [SOP-000063 "Submission and Processing of International Food Inspection and Investigation Reports"](#) for additional information regarding the processing of foreign food reports.

5.11.2 – ENDORSEMENT

Supervisory Investigators evaluate inspection findings, determine the classification of the inspection, and recommend an action, in accordance with applicable compliance programs, assignments or policy. The final content of the endorsement of the establishment inspection report is determined by the supervisory investigator. However, Investigators should prepare proposed endorsement 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 identify 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 5.11.4.1.

Normally the endorsement consists of:

1. The reason for the inspection, i.e., workplan, or assignments from headquarters. State the subject of the assignment and reference.
2. A brief history of previous findings (e.g., FDA 483 observations, FDA 4056 observations, and discussion items) including classification of previous inspection, any action taken by the program division and/or corrective action 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 the firm's management.
5. Identify FDA received consumer complaints covered during inspections and follow up disposition.
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.

- Distribution consistent with program division policy and the requirements of the specific compliance programs and requirements as noted in IOM 1.7.3.

Note: When endorsing in eNSpect, include notification to the Division of Import Operations and Management (DIOM) when any violative, imported products are identified.

Note: In rare situations (e.g., extended leave, retirement, 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 5.11.4.3.21)

The existence of Personal Safety Alerts (IOM 5.2.1.3) or Personal Safety Plans (IOM 5.2.1.4) pertaining to the firm should be included in the endorsement section only and not in the EIR.

The signed endorsement should be updated to indicate if an amendment to the EIR (IOM 5.11.7) or an amended FDA 483 or and FDA 4056 (IOM 5.2.3.1.6.1 and 5.2.3.1.6.2) 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 ORA Field Investigators, Supervisors and Compliance Officers from ORA and Centers.

See Exhibit 5-14 for more information on profiling CGMP/QS Compliance Status.

5.11.2.1 – 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.

Both FACTS and eNSpect are used to report verified corrective actions, which are not the result of legal action. When you are unable to enter the action in eNSpect because the PAC is not available or the 483 was issued outside of eNSpect, investigator should enter corrective actions into FACTS CARS as directed in 5.11.2.1.1.

The supervisor may enter the correction if the investigator is unavailable.

5.11.2.1.1 - REPORTING CRITERIA

There are three criteria for reporting into the FACTS CARS system:

- The detection or identification of the problem. A problem may be observed by FDA, other federal officials, or by state or local authorities and referred to FDA; and as a result of an inspection, investigation, sample analysis, or detention accomplished by ORA or states under contract to ORA.
- The correction of the problem. The correction is directly attributable to the efforts of ORA or state officials under

contract to ORA (involving contract products only); and is unrelated to the filing of a legal action, i.e., seizure, prosecution, injunction.

- The verification of the correction of the problem. The correction is verified by the FDA, other federal officials or state or local 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.

5.11.2.1.2 - DATA ELEMENTS

For instruction on entering corrective actions in eNSpect refer to the [user manual](#).

For instruction 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):

- PAC. Should there be insufficient space to code all corrections verified on an occasion, record the most significant corrections.
- 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.
- 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.
- 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.
- 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.
- 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.
- 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.

5.11.3 – eNSpect ESTABLISHMENT INSPECTION REPORT COVERSHEET

Per SOP-000051, each ORA Program Division and HQ Office is responsible to ensure all investigators verify, correct, and enter changes to the OEI (including Profile data for profilable firms) on the firm's maintenance

screens in eNSpect during each inspection, investigation and during any OEI update. Consult with your supervisor and your OEI Coordinator to assure data is accurately updated.

Inspectional accountable time reported into eNSpect consists of the hours devoted to file reviews (operational preparation), actual onsite inspectional time, document preparation (attachments and exhibits) and EIR (narrative) write-up. Accountable time does not include travel time. One occasional exception could be when more than one participant prepares and discusses the assignment while they are traveling together.

You should report the actual amount of inspection accountable time it took you. Do not report the module time given in the ORA Workplan. Additional time required to complete the assignment due to giving or receiving training should be reported separately from inspectional time.

5.11.3.1 – Inspection Basis

The inspection basis is the underlying reason for conducting an inspection.

Compliance – A directed inspection to evaluate potential violative situations that the agency has become aware of at the firm or industry and have not already resulted in an official agency action. These may include complaints (trade or consumer) which are not the primary reason for the inspection, recalls not classified as Class I, MedWatch Reports, Adverse Drug Experience Reports, information from confidential informants, etc.

Consumer Complaint – A directed inspection in which the primary purpose is to follow up on a consumer complaint. When a consumer complaint is received, and the follow-up action chosen is to conduct an inspection to confirm allegations within the complaint or root causes that may have led to the condition described in the complaint, this value should be selected.

F/U to Class I Recall – A directed inspection in response to a Class I Recall conducted by the establishment. The inspection is conducted to determine the root cause and corrective actions addressing the violation(s) associated with the product.

F/U to Class I Recall and F/U to Injunction – A directed inspection conducted in response to a Class I Recall conducted by the establishment AND pursuant to Permanent Injunction and in accordance with the Consent Decree. In this instance, a firm under permanent injunction has conducted a Class I Recall and the inspection is conducted to determine the root cause and corrective actions addressing the violation(s) associated with the product. Additionally, the inspection covers the requirements of the Consent Decree for the Injunction.

F/U to Class I Recall and F/U to Warning Letter – A directed inspection conducted in response to a Class I Recall conducted by the establishment AND to follow up on issues cited in a Warning Letter issued to the

establishment. In this instance, a firm that has received a Warning Letter has conducted a Class I Recall and the inspection is conducted to determine the root cause and corrective actions addressing the violation(s) associated with the product in addition to covering corrective actions responsive to the violations cited in the Warning Letter. The Warning Letter may have issued as a result of the previous inspection or other circumstance.

F/U to Class I Recall and OAI Inspection F/U – A directed inspection conducted in response to a Class I Recall conducted by the establishment AND to follow up to a previous OAI-classified inspection, where a regulatory or administrative action has not been completed. This value captures the situation where the previous inspection of the firm was classified OAI, but no official action was taken, and the firm has conducted a Class I Recall. The inspection is focused on the root causes of the violations leading to the recall and may also address previously cited violations. Before conducting an inspection of a firm where the previous inspection was classified OAI with no regulatory action taken, be sure to discuss what areas to cover with your supervisor and/or compliance officer.

F/U to Injunction – An inspection conducted pursuant to Permanent Injunction and in accordance with the Consent Decree.

F/U to Warning Letter – An inspection conducted to follow up on issues cited in a Warning Letter issued to the establishment. This inspection is focused on the firm's actions to resolve issues cited in the Warning Letter.

OAI Inspection F/U – An inspection conducted to follow-up previous OAI-classified inspection where a regulatory or administrative action has not been completed. There can be a number of situations where an action is not taken although the observations cited during the previous inspection met the threshold for an OAI classification. Consult your supervisor and/or compliance officer prior to initiating these types of inspections.

Surveillance – An inspection conducted as a routine assignment with no other indicators of non-compliance. For example, an inspection of a firm whose previous inspection was classified NAI; there have not been any complaints or recalls, etc.

5.11.4 - NARRATIVE REPORT

See IOM 1.1, English language requirement. You should use eNSpect for all EIRs. The narrative report is the written portion of the EIR, which accurately describes the investigator's inspectional findings. The narrative report may be prepared in two formats depending on the type of inspection and inspection classification. A Summary of Findings narrative report may be used for NAI and VAI classified, non-initial inspections (IOM 5.11.4.1 and IOM 5.11.4.2), or as directed by your supervisor. The full Standard narrative report is used for initial and potential Official Action Indicated (OAI) classified inspections (IOM 5.11.4.3.1). Additional requirements for human drug and medical device establishment inspection reports are described in IOM 5.5.8 and 5.6.9. For all reporting formats,

include additional information as directed by your assignment, Compliance Program Guidance Manual, or your Supervisor.

EIRs populated in eNSpect should automatically include the firm name and FEI. Those populated outside of eNSpect should include the firm name, FEI in the header and the footer should include the page number.

All reports should be prepared or uploaded into eNSpect.

Your Establishment Inspection Report (EIR) should:

1. Be factual, objective, and free of unsupportable conclusions.
2. Be concise and descriptive while covering the necessary aspects of the inspection.
3. Not include opinions about administrative or regulatory follow-up.
4. Not include information that could identify confidential or anonymous informants (See IOM 5.2.9.2)
5. Generally, be written in the first person using the active voice.
6. 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.

Refer to IOM 5.11.7 for an Amendment to EIR.

5.11.4.1 – Summary of Findings report for NAI Inspections

Investigators should use "Summary of Findings", stand-alone, narrative reports for NAI domestic establishments, unless otherwise directed by your supervisor, the assignment or the Compliance Program Guidance Manual. Use the report format given in 5.11.4.3.1- Standard Narrative Report, Comprehensive Reports- for all foreign inspections.

The Summary of Findings Report may not be written solely in the eNSpect provided "Inspection Summary" heading. The Summary of Findings report should include:

1. The reason for the inspection;
2. The date, final classification and findings of the previous inspection;
3. The actual inclusive dates of the inspection (these may be included as part of a header or in the body of the EIR.)
4. Report the current registration(s) status or any changes to registration status. Per CPG section 110.300, do not report the FURLS Registration number.
5. The name of the person to whom credentials were shown and the FDA-482, Notice of Inspection or FDA 482d Request for FSVP Records was issued and the person's authority to receive the FDA 482 or FDA 482d. Explain if you were unable to show credentials or issue forms to top management. Include the name of the person to whom the FMD-145 correspondence should be directed to and their email

address. If an email address does not exist for this person, then this should be noted.

6. The inspectional approach (comprehensive or directed); the scope of the inspection; a brief description of the business; a description of the products produced; and a brief description of the products, processes or systems covered during the inspection. Indicate which aspects of the firm's processes or systems you observed versus those which the firm described to you;
7. The manufacturing codes and if necessary their interpretation.
8. Significant changes (e.g., personnel, facilities, products, processes) since the previous inspection;
9. Voluntary Corrections
10. Samples collected
11. Exhibits collected;
12. Attachments
13. The investigator's signature.

5.11.4.2 – Summary of Findings for VAI Inspection

Investigators should use "Summary of Findings", stand-alone, narrative reports for VAI domestic establishments, unless otherwise directed by your supervisor, the assignment or the Compliance Program Guidance Manual. Use the report format given in 5.11.4.3.1 - Standard Narrative Report, Comprehensive Reports for foreign inspections.

All violative EIR's should in addition to the information required for non-violative reports contain the following:

1. The objectionable conditions or practices described in sufficient detail so someone reading the report will clearly understand the observation(s) and significance.
2. The objectionable conditions or practices cross-referenced to FDA 483 or FDA 4056 citations, samples collected, photographs, or other documentation including exhibits attached to the EIR.
3. Information as to when the objectionable conditions or practices occurred, why they occurred, and who is or was responsible, developed to the highest level in the firm.

5.11.4.3 - Individual Narrative Headings

There are many acceptable ways of organizing a narrative report. The key is to cover the required information in IOM 5.11.4, 5.11.4.1 and 5.11.4.2, or as required by the assignment, Compliance Program Guidance Manual, or your supervisor. The appropriate use of headings should not result in repetition of the same information in different sections. You are encouraged to create headings as necessary to present the inspectional findings in the most concise manner. For NAI and VAI classified inspections, a single heading such as "Summary of Findings" is sufficient (for exceptions, see IOM 5.11.4.1 and 5.11.4.2). eNSpect should be used to generate the FDA 483, FDA 483a, and FDA 4056. In certain instances, if you experience computer problems, do not delay the issuance of the FDA 483, FDA

483a, or FDA 4056. See IOM 5.2.3. You should use eNSpect for all EIRs.

5.11.4.3.1 - STANDARD NARRATIVE REPORT

This is intended to outline the minimal information needed to produce a narrative report that supports further agency regulatory action, as warranted. Investigators are encouraged to add additional report headings as needed to communicate important information about the inspection, relevance of inspectional observations that may impact public health, and /or to address specific requests from directed assignments.

Comprehensive Reports (Include all applicable sections)

A comprehensive EIR should be prepared for initial inspections as well as foreign inspections in all program areas. It is essential to describe the products manufactured, the process the manufacturing and storage environment, distribution patterns/interstate commerce, individual responsibility of key employees, history of business, all objectionable conditions observed, etc. All things pertinent to the operations and management of the establishment should be included in these reports. The comprehensive report may also be used for other situations requiring full reporting such as Routine Surveillance - OAI. An abbreviated inspection does not necessarily equate to an abbreviated report.

Required elements

- 5.11.4.3.2 – Summary
- 5.11.4.3.3 – Administrative data
- 5.11.4.3.4 – History
- 5.11.4.3.5 – Interstate (I.S.) Commerce
- 5.11.4.3.6 – Jurisdiction (Products Manufactured and/or Distributed)
- 5.11.4.3.7 – Individual Responsibility and Persons Interviewed
- 5.11.4.3.8 – Firm’s Training Program
- 5.11.4.3.9 – Manufacturing/Design Operations
- 5.11.4.3.10 – Manufacturing Codes
- 5.11.4.3.11 – Complaints
- 5.11.4.3.12 – Recall Procedures
- 5.11.4.3.13 – Objectionable Conditions and Management’s Response
- 5.11.4.3.13.1 – Supporting Evidence and Relevance
- 5.11.4.3.13.2 - Discussion with Management
- 5.11.4.3.14 – Refusals
- 5.11.4.3.15 – General Discussion with Management
- 5.11.4.3.16 – Additional Information
- 5.11.4.3.17 – Samples Collected
- 5.11.4.3.18 – Voluntary Corrections
- 5.11.4.3.19 – Exhibits Collected
- 5.11.4.3.20 – Attachments

Routine Surveillance – NAI Reports

When FDA has an inspectional history for the firm and no deficiencies were observed by the investigator, a brief report may be prepared. The intent of this report is to include only the required information about the firm and what areas were covered during the inspection. “Change reporting” means information that differs from the previous inspection report such as changes in management, products produced, manufacturing processes, etc. Where these changes have occurred, the applicable section heading in the EIR should be included. The elements may also be captured in a “Summary of Findings Only” report without header information. See IOM 5.11.4.1.

Required elements

- 5.11.4.3.2 – Summary
- 5.11.4.3.3 – Administrative data
- 5.11.4.3.10 – Manufacturing Codes
- 5.11.4.3.14 – Refusals
- 5.11.4.3.15 – General Discussion with Management
- 5.11.4.3.17 – Samples Collected
- 5.11.4.3.18 – Voluntary Corrections
- 5.11.4.3.19 – Exhibits Collected
- 5.11.4.3.20 – Attachments

Change reporting only

- 5.11.4.3.4 – History
- 5.11.4.3.6 – Jurisdiction (Products Manufactured and/or Distributed)
- 5.11.4.3.7 – Individual Responsibility and Persons Interviewed
- 5.11.4.3.8 – Firm’s Training Program
- 5.11.4.3.9 – Manufacturing/Design Operations

Routine Surveillance – VAI Reports

For firms with an inspectional history and the outcome of the inspection is a VAI classification, the below elements would be required, plus change reporting. Note that the difference in the NAI versus the VAI report is the inclusion of narrative addressing objectionable conditions observed during the inspection. Each objectionable condition or practice must be documented in the EIR along with discussion of the evidence, relevance and discussion with management.

Required elements

- 5.11.4.3.2 – Summary
- 5.11.4.3.3 – Administrative data
- 5.11.4.3.10 – Manufacturing Codes
- 5.11.4.3.13 – Objectionable Conditions and Management’s Response
- 5.11.4.3.13.1 – Supporting Evidence and Relevance
- 5.11.4.3.13.2 - Discussion with Management

- 5.11.4.3.14 – Refusals
- 5.11.4.3.15 – General Discussion with Management
- 5.11.4.3.17 – Samples Collected
- 5.11.4.3.18 – Voluntary Corrections
- 5.11.4.3.19 – Exhibits Collected
- 5.11.4.3.20 – Attachments

Change reporting only

- 5.11.4.3.4 – History
- 5.11.4.3.6 – Jurisdiction (Products Manufactured and/or Distributed)
- 5.11.4.3.7 – Individual Responsibility and Persons Interviewed
- 5.11.4.3.8 – Firm’s Training Program
- 5.11.4.3.9 – Manufacturing/Design Operations

Routine Surveillance – OAI

For an OAI surveillance inspection, follow the guidance under Comprehensive Reports.

OAI Follow-up Inspection Reports

OAI follow-up inspections are inspections conducted following an OAI classified inspection. Inspections of this nature are conducted to determine whether corrective actions have been implemented or significant violations continue. The outcome of these inspections may range from NAI to OAI. The intended use of the EIR should be the driving force of the content of these EIRs. Typically, the follow-up should be done relatively soon after the previous inspection, so changes to products, process, personnel, etc. should be minimal. The NAI and VAI reports should focus on corrective actions implemented by firm management to correct the violative conditions observed during the previous OAI inspection. Those reports may be Summary of Findings only or may follow the other NAI and VAI report formats above. An OAI follow-up inspection may lead to a regulatory action such as seizure, injunction and/or prosecution. Those reports should focus on documenting the continuing violations, responsibility for those violations, any corrective actions implemented or inadequate corrective actions and defining the new scope of violations observed including the products affected. Scope should include additional lots, products, timeframe and distribution. These reports should document all elements of JIVR (Jurisdiction, Interstate Commerce, Violation and Responsibility). This allows for the report to support whatever regulatory action is deemed necessary.

Required elements

- 5.11.4.3.2 – Summary
- 5.11.4.3.3 – Administrative data
- 5.11.4.3.7 – Individual Responsibility and Persons Interviewed

- 5.11.4.3.10 – Manufacturing Codes
- 5.11.4.3.13 – Objectionable Conditions and Management’s Response
- 5.11.4.3.13.1 – Supporting Evidence and Relevance
- 5.11.4.3.13.2 - Discussion with Management
- 5.11.4.3.14 – Refusals
- 5.11.4.3.15 – General Discussion with Management
- 5.11.4.3.17 – Samples Collected
- 5.11.4.3.18 – Voluntary Corrections
- 5.11.4.3.19 – Exhibits Collected
- 5.11.4.3.20 – Attachments

Change Reporting Only:

- 5.11.4.3.5 – Interstate (I.S.) Commerce
- 5.11.4.3.6 – Jurisdiction (Products Manufactured and/or Distributed)
- 5.11.4.3.9 – Manufacturing/Design Operations
- 5.11.4.3.11 – Complaints

5.11.4.3.2 - SUMMARY

1. Provide the reason for the inspection including if it was announced or unannounced (e.g., compliance program(s), by assignment number, trip number, etc.);
2. The inspectional approach (comprehensive or directed); the scope of the inspection; a brief description of the business; a description of processes used, and the products produced.
3. Provide a summary of the findings, date, and final classification of the previous inspection and the firm’s response/corrective actions.
4. List the products, profile, 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.
5. Provide a summary of the current findings (i.e., reportable observations, nonreportable observations, and discussion items), refusals, samples collected, warnings given to management, and a summary of management’s response or voluntary corrections.

5.11.4.3.3 - ADMINISTRATIVE DATA

1. The firm name, address, phone, fax, website address, and e-mail address of the firm
2. Report the names and titles of the Investigator(s), Analyst(s), non-FDA officials, etc. 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 5.1.1 and 5.2.2.
3. The inclusive date(s) of the current inspection, i.e., list the actual dates in the plant.

4. If a team inspection and some individuals were not present during the entire inspection, indicate dates in plant for each team member.
5. For foreign inspections with Locally Engaged Staff (LES)/Foreign Service National (FSN) participation include this language:

This inspection was supported by _____ (during the period of _____), who is a Locally Engaged 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 _____ (LES) that supports the Form FDA 483, Inspectional Observations (if Form FDA-483 was issued), FDA 483a FSVP Observations, Form FDA 4056, Produce Farm Inspectional Observations and the Establishment Inspection Report (EIR) was collected in collaboration with the FDA investigator(s).

Report:

1. Full names and titles to whom FDA Official Credentials were shown,
2. 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),
3. Full name, title, address (if different from the address of the inspected establishment), and email address of the top management official to whom the FMD 145 letter should be addressed. If an email address does not exist for this person, then this should be noted.
4. 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
5. If this was a team inspection, who wrote which section of the EIR.
6. Full names and titles of inspectors from other government agencies (i.e. federal, state, local or foreign) at the facility during the inspection.
7. Full names and titles of who provided translation of foreign language documents.
8. 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 5.1.1.9)
9. Full name and title of the individual provided with guidance documents and list the documents provided.

5.11.4.3.4 - HISTORY

1. Report the legal status of the firm (corporation, partnership, limited liability company, sole proprietorship, etc.), and the state and year of incorporation.
2. List the parent corporation, corporate address and relevant subsidiaries with respective FEIs.
3. Provide a summary of any agency actions and prior warnings (do not cite any action only recommended but not approved). You should also report any significant/relevant inspectional history pertinent to the current EI or recommendation.
4. Include any relevant recalls, market withdrawal, etc. since the last inspection.
5. Report the hours of operation and any changes from past inspections (include seasonal variations).
6. Report all current registration(s) status or any changes to registration status. Describe any inaccuracies identified in the firm's registration(s). Per [CPG section 110.300](#), do not report the FURLS Registration number.
7. Report if the firm is located on tribal land, or is owned/operated by a federally recognized Indian tribe or tribal member.

5.11.4.3.5 - INTERSTATE (I.S.) COMMERCE

1. Report the estimate of the percentage of products shipped outside of the state (or exported to the U.S.) and the basis of the estimate.
2. Report the firm's general distribution patterns.
3. If there is an apparent violative product, provide examples of interstate shipments of violative product(s); or
4. If no such shipments, provide examples of interstate shipments of major components of apparent violative products - with complete interstate documentation in either case.
5. For foreign inspections, list significant U.S. consignees to whom the firm's products are shipped.
6. For Human Drugs - domestic firms, identify the general types of customers and provide the names and addresses for several regular customers of a few of the firm's products.

5.11.4.3.6 - JURISDICTION (PRODUCTS MANUFACTURED AND/OR DISTRIBUTED)

1. 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, in-

- dustry or technology; or as directed by your supervisor.
3. Report the firm's general promotion patterns (i.e. website, advertisements, etc.).
 4. 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, the label, labeling and promotional materials are a critical part of determining a product's intended use.

1. 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 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 audio and video tapes.
2. 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 can be used for the treatment of any disease.

5.11.4.3.7 - 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. Who provided relevant information,
2. Who accompanied you during the inspection,
3. Who refused access to required records or any other refusal of information (Note: a separate heading for Refusals may be needed if refusals are significant, extensive or an Inspection Warrant is anticipated),
4. Who refused to permit inspection (IOM 5.2.5.1) and
5. For Human Drug inspection reports, also include the name, title, physical mailing address, phone, and fax number and e-mail address for any U.S. Agent or broker who represents the company when dealing with the FDA, and

Describe roles and authorities of responsible individuals, including the full names and titles of individuals providing you with information.

Describe roles, authorities and responsibilities of officials at headquarter or corporate organizations for this firm; including their names, titles and addresses.

Report changes to the following:

1. Who is the most responsible individual at the inspected firm? Who is the responsible head or designated correspondent? Refer to IOM 5.3.6, 5.3.6.1, and 5.3.6.2.
2. Report full names and titles of owners, partners, and corporate officers. Who has the duty, power and responsibility, and authority to prevent, detect, and correct violation(s), and how is this demonstrated and/or documented? See IOM 5.3.6.2.

3. Report the chain of command; include an organizational chart (create if necessary).
4. Obtain a copy of public annual report, if any.
5. List the names and titles of key operating personnel.

5.11.4.3.8 - FIRM'S TRAINING PROGRAM

Explain coverage of the firm's training program as stated in the applicable compliance program and/or as it correlates to the deficiencies observed during the inspection.

The firm's training programs are of particular significance where inspectional findings find people may not be adequately trained.

5.11.4.3.9 - MANUFACTURING/DESIGN OPERATIONS

1. Report only changes to the firm's general overall operations, including significant changes in equipment, processes, or products since the previous inspection. Include schematics, flow plans, photographs, formulations and diagrams, if useful.
2. List names and sources of 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 which the firm described to you.

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

1. Describe the product(s) covered and include basic food information: finished product name, product description with packaging; pertinent ingredients, intended use and conditions of storage and distribution.
2. Describe the process flow (receiving through distribution) and a description of the process at each step.
3. For full scope preventive control or HACCP inspections describe the results of the hazard analysis and the adequacy and implementation of written programs.
4. Describe the firm's general sanitation procedures.
5. Describe any coverage of additional food safety regulations that apply to the product(s) inspected (e.g. LACF, infant formula, bottled water, etc.).

For human drug inspection reports:

This section of the EIR should be organized by system covered during the EI as outlined in CP 7356.002. In each section, include a brief summary of what you reviewed in order to meet the key system element outlined in the CP. You should add more detail for the system elements found

to be deficient, or the subject of an FDA-483 observation.

For medical device inspection reports:

1. Describe manufacturing operations by sub system covered in your inspection (Management Controls, Design Controls, Production and Process Controls, Corrective and Preventive Action Controls, Material Controls, Facility and Equipment Controls, and Records/Documents/Change Controls). For ALL Level 2, 3, and "for cause" inspections: for production and process controls - indicate which production processes were covered/ reviewed. If a subsystem was not specifically covered during your EI, you do not need to separately describe the general operations of that subsystem.
2. For all inspections covering CAPA - indicate which data sources were available for review and which were actually reviewed; include a brief statement regarding coverage or non-coverage of applicable tracking requirements, MDRs, sterilization, and reports of corrections and removals.
3. If the Design Control system was covered, indicate the design project(s) covered during the inspection. Where design activities occur at a location other than the manufacturing site, list the name, address of the design location and responsibilities of those performing the design activities.
4. If applicable, identify the name and address of the specification developer if different from either the manufacturing site or where design activities occur.

5.11.4.3.10 - 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 (for applicable finished devices).

5.11.4.3.11 - COMPLAINTS

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

1. Report your review of the firm's complaint file(s).
2. In addition, if returned goods and/or documents for returned goods are examined, describe findings. If not examined, so indicate.
3. Report your follow-up of FDA received complaints including complaint number and action taken by the firm. Correlate consumer/trade complaints, Adverse Event Reports, MDR's, MedWatch reports to specific objectionable conditions observed.

5.11.4.3.12 - 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.

5.11.4.3.13 - OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

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

NOTE: Observations of a verbal nature (i.e., Discussion Items) should be reported in sufficient detail under the General Discussion with Management (correlate any Exhibits, samples, etc. to any "verbal" observations).

5.11.4.3.13.1 - Supporting Evidence and Relevance

Sufficiently describe the observation as necessary to relate the facts as you found them.

1. 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.
2. Describe verbal statements (verbatim if possible) by firm officials having knowledge, duty, power, and responsibility to detect, prevent, or correct the apparent violation.
3. Identify the responsible party for each apparent violation (i.e., if known.)
4. Identify which team member (if applicable) was responsible for the observation.
5. When appropriate explain how this observation relates to the overall situation; i.e., impact on the product, batches, or lots involved, and any relationship to other products, processes, or other FDA 483 or FDA 4056. observations.
6. The duration of the problem.

5.11.4.3.13.2 - Discussion with Management

Discussion with management:

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

For medical device inspection reports:

1. For each observation based on sampling of records, indicate which Sample Table and level of confidence was used and the actual number of records sampled.
2. If the number sampled is different than the actual number reviewed, so indicate.

5.11.4.3.14 - REFUSALS

Provide full details of all refusals of/for requested information, statutory information, photography, entry, etc. received during the inspection, including who made the refusal and, if available, why the refusal was given.

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

5.11.4.3.15 - GENERAL DISCUSSION WITH MANAGEMENT

General Discussion with Management:

1. Report the names and titles of all present, including those present via electronic media (describe).
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 deemed not to merit inclusion on the FDA 483, FDA 483a, or FDA 4056. (IOM 5.2.3)
4. A description of each warning, recommendation, or suggestion given to the firm, and to whom given.
5. 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 the conditions observed may, after further review by the Agency, be considered to be violations of the FD & C Act or other statutes. Legal sanctions available to 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.
8. Report all significant conversations with management or management representatives.

5.11.4.3.16 - ADDITIONAL INFORMATION

Report changes as appropriate.

1. Describe contractors used and for what purpose. **For Medical Device inspection reports:** also include names and addresses of all applicable third-party installers or servicing organizations used by the manufacturer. Include their responsibilities.
2. Describe suppliers (major raw material, active ingredient, etc.) used and for what.
3. During inspections, when violative products imported into the U.S. or intended to be imported into the U.S., are encountered, document the product and foreign manufacturer in the EIR. Violative products could be rejected APIs due to non-conformance with the USP or applicable compendium, foods without appropriate labeling, etc. Send a copy of the EIR to OEIO/DIO. See IOM 5.2.1 and 5.11.2.
4. For initial inspections, verify distribution patterns for the firm's products, raw materials, and components to firms which warehouse or further process products which may be subject to FDA regulations. Program divisions should incorporate information obtained into their Official Establishment Inventory improvement activities and complete form FDA 457, Product/Establishment Surveillance Report as appropriate. See IOM 8.1.5.4.
5. Report pertinent facts, which do not fit another section of the EIR. (For firms located in foreign countries, include information relative to lodging and travel; for domestic firms, include information relative to location of firm if difficult to find; etc.)
6. In accordance with IOM 5.3.4.3, 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."
7. In accordance with IOM 5.11.5.1, 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 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 SOP's. Significant problems which 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.

5.11.4.3.17 - SAMPLES COLLECTED

List and describe samples collected during the inspection.

5.11.4.3.18 - VOLUNTARY CORRECTIONS

1. Provide a brief description of improvements initiated by the firm in response to a previous inspection, report of observations and/or a warning letter.
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.

5.11.4.3.19 - EXHIBITS COLLECTED

List all exhibits attached. See IOM 5.11.5, Exhibits.

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

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.

5.11.4.3.20 – ATTACHMENTS

List all attachments. See IOM 5.11.6, 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 and/or forms (e.g., FDA 463a, FDA 482, FDA 483, FDA 4056).

5.11.4.3.21 - SIGNATURE

All participants will sign the final narrative portion of the EIR. The prescribed format is to include each person's name and title. Refer to current eNSpect user guide for guidance on electronic signatures for multiple participants.

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 read and approve, 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 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".

5.11.5 - EXHIBITS

Exhibits are materials collected from the firm after the FDA 482 Notice of Inspection or FDA 482d Request for FSVP Records is issued and before the FDA 483, FDA 483a, or FDA 4056 is issued or the inspection is closed out. Collect only records and documents which 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 document violations. Exhibits include flow plans, schematics, layouts, batch records and procedures, etc. Reference and explain exhibits in your narrative report. Copies of procedures, patient records, etc., that do not serve as evidence of a violation should not be collected unless you are directed to do so.

Labeling exhibits should show the entire label and must be legible and easy to read. Pertinent portions of exhibits in foreign languages should be translated, 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 5.3.4.4.

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 all FDA participants, exhibit number, and page number(s). See IOM 5.3.8.2. Refer to the SOP titled, "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. If the materials collected from the firm are not needed as exhibits, they should be destroyed in accordance with your Program Division or office policy.

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. When copies of these records are requested internal to FDA, they should be redacted by obliterating the patients full name (keeping first and last initial only), social security number, date of birth, race, personal address and any other personal identifiers. All external requests should

be handled by the FOI officer. Submit at least three copies of new or suspect labeling or other material collected as exhibits for labeling purposes. See IOM 4.4.9 for exceptions. These should be mounted in a manner so complete sets are submitted that can be reviewed by individuals in separate offices, i.e., labels 1-10 in each of three sets.

5.11.5.1 - 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 5.3.8.3.3.1. Electronic records should be protected from degradation, including preventing exposure of the electronic storage media to extreme temperatures and magnetic fields where 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 5.11.5 Exhibits and 5.11.6 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 section 5.11.4.3.16 - Additional Information item # 7 for specific details.

For information on handling photographic storage media see IOM 5.3.4.3 Preparing and Maintaining Digital Photographs as Regulatory Evidence.

5.11.6 ATTACHMENTS

Attachments as referred to here are any material 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 material attached to the narrative portion of the EIR should be identified as "Attachments" similar to IOM 5.3.8.2. 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. See the opening sentence of IOM 5.10.5. List and attach copies of associated reports (Recall Attachment B Report, etc.).

5.11.7 - 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, e.g. dates, incorrect names, lot numbers, type of operation, or 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 accompany the word Amendment. Example "Amendment 1". Changes made to correct errors in the text of the EIR should remain visible; bold all additions and strike through all removals. The amended narrative report will be processed through eNSpect.

The coversheet must be re-endorsed by the supervisor. 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.

SUBCHAPTER 5.12 – COMBINATION PRODUCTS

5.12.1 – COMBINATION PRODUCT INSPECTIONS

As set forth in part 3 (21 CFR part 3), a combination product is a product comprised of any combination of a drug and a device; a device and a biological product; a biological product and a drug; or a drug, a device, and a biological product (see also 2.7.1.3.7). 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 5.5, 5.6, and 5.7, 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 System (QS) Regulation (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 QS regulation (drug CGMP-

based streamlined approach, see 21 CFR 4.4(b)(1)) or with the device QS regulation and specific provisions from the drug CGMPs (device QS regulation-based 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.

5.12.1.1 – 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 5.5. For a CDRH-led combination product inspection, review IOM 5.6. For CBER-led combination product inspection, review IOM 5.7.

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.

5.12.1.2 – 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 OBPO supervisory staff and CBER for assistance.

5.12.1.3 – 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.

5.12.1.4 – 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.

5.12.1.5 – Limitations on Inspection

The limitations on the agency's ability to access audit results (see IOM 5.6.2.2) 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. p.m.
	6. NUMBER AND STREET 579 Main Street		
	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))	
<i>Sidney H. Rogers</i>		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."

5-3 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 <input checked="" type="checkbox"/> A.M. <input type="checkbox"/> 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 [<i>or specify product</i>] that were produced in this firm since the last FDA inspection.			
10. SIGNATURE (<i>Food and Drug Administration Employee(s)</i>) <i>Sidney H. Rogers</i>		11. TITLE FDA EMPLOYEE Investigator	

FORM FDA 482b (6/11)

PREVIOUS EDITION IS OBSOLETE.

REQUEST FOR INFORMATION

PSC Publishing Services (301) 443-6740 EF

5-5 FORM FDA 483

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION			
DISTRICT OFFICE ADDRESS AND PHONE NUMBER Minneapolis District 250 Marquette Ave. South, Suite 600 Minneapolis, MN 55401 Industry information: www.fda.gov/oc/industry		DATE(S) OF INSPECTION 10/5-7/2008	
		FEI NUMBER 0000112233	
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED TO: William S. Gundstrom, Vice President, Production			
FIRM NAME Topline Pharmaceuticals "T.L.P."		STREET ADDRESS 2136 Elbe Place	
CITY, STATE AND ZIP CODE Jackson, MN 55326		TYPE OF ESTABLISHMENT INSPECTED Tablet Repacker	
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:			
List your significant observations ranked in order of significance. See IOM 5.2.3, 5.2.3.1, 5.2.3.2, and 5.2.3.3			
SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE <i>Sylvia H. Rogers</i>	EMPLOYEE(S) NAME AND TITLE (<i>Print or Type</i>) Sylvia H. Rogers, Investigator	DATE ISSUED 10/7/2008

The observations of objectionable conditions and practices listed on the front of this form are reported:

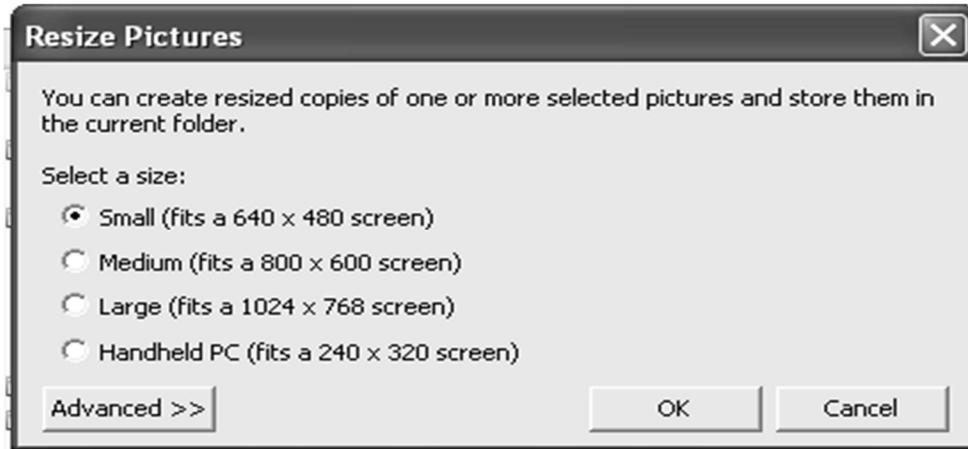
1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

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."

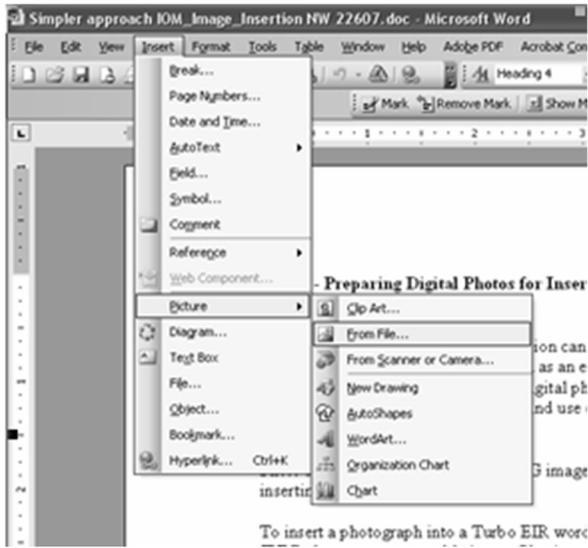
5-6 INSERTING DIGITAL PHOTOS INTO eNSpect (RESIZE PHOTO)

Screenshot - Resizing Pictures using Windows Explorer:



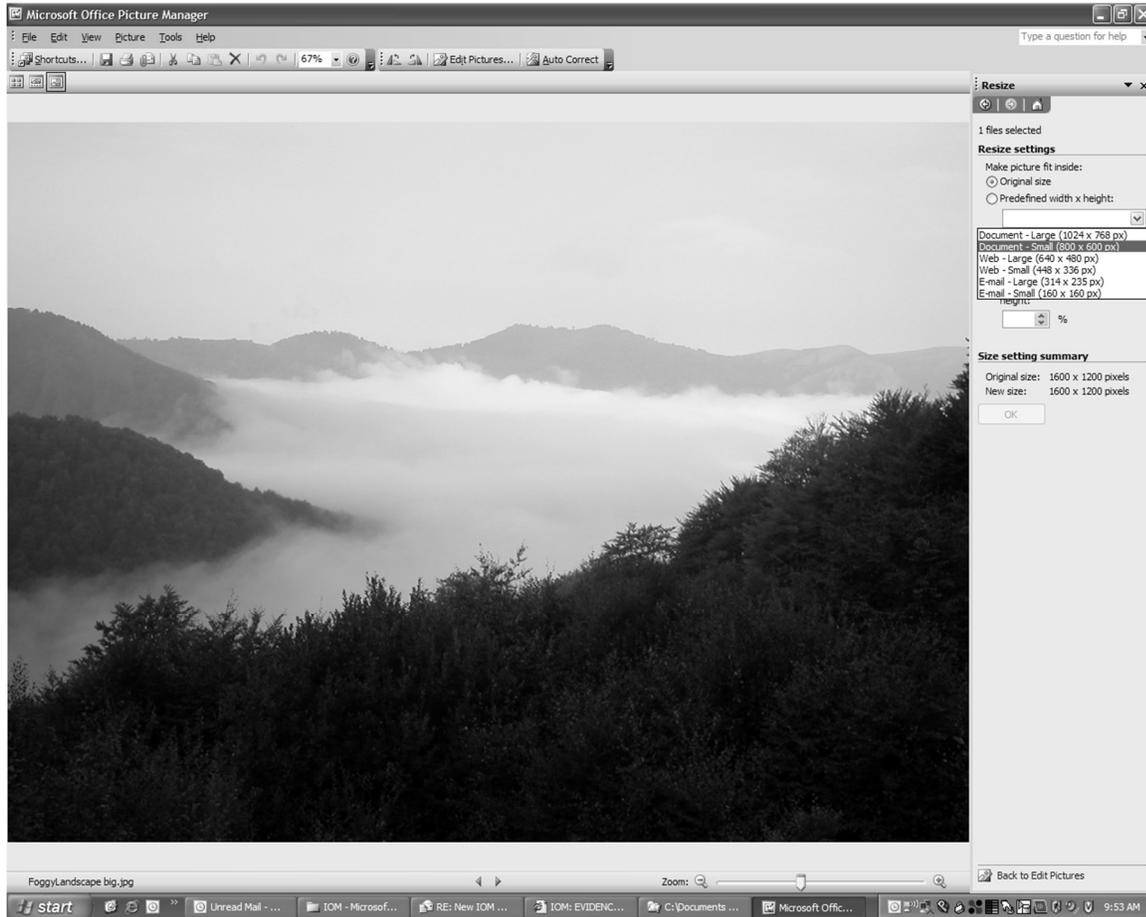
5-7 INSERTING DIGITAL PHOTOS INTO eNSpect (INSERT PHOTO)

Inserting a resized picture into Microsoft Word.



5-8 INSERTING DIGITAL PHOTOS INTO eNSpect (RESIZING USING MS OFFICE PICTURE MANAGER)

Screenshot - Using Microsoft Office Picture Manager to Resize a picture to 800 x 600 pixels.



5-9 FACTS CREATE SAMPLE ASSIGNMENT SCREEN

FACTS Version 4.9.01 - [Create Assignment]

Action Edit Options Related Info Reports Navigate Trading FACTS Help Window Help

Assignment

Requesting Organization: MIN-IB-SPV Requester Completion Date: 11/21/2005 Priority: High ORA Req'd: N/A Compliance Number: 145 - 0

Subject: Pharma-Mix Digitalis ORA Cntrnc Num: Survey Num:

Remarks: Request for samples as follow-up to violative EI Reporting Method: Notify SI DoMore by phone when accomplish

Background Information: Firm's manufacturing practices may lead to low potency POC Name: James W. DoMore

Operations

Op Code: 31 Sample Collection Rqstr Prty: High

Subject: Pharma-Mix Digitalis Target Date: 11/21/2005

Requester Remarks: Collect 12/100 tab bottles of lot DC-01234 as follow-up to vi

Estmtd Hours: 4 Estmtd Smpl Cost: \$150.00 Reimbursable:

Organizations

Accomp Org	Num Of Ops	Perf Org (Adhoc Work)
NWJ-DO	1	

Buttons: Add, Delete, Prev Op, Next Op, Delete

PACS & Products

PAC	Description	Product Code	Description
56002	DRUG PROCESS INSPEC	63 F C E 04	Digitalis (Cardiotonic); Human - Rx/

Buttons: Add, Delete

Firms & Cross References

FEI B	Name	Code	Value
3000900992	Drug Distributors, I		

Buttons: Add, Delete

Lab References

Sample Number: PAF: LID:

Buttons: Add, Delete

FACTS Editor

Collect 12/100 tab bottles of lot DC-01234 as follow-up to violative EI of Pharma-Mix, Minneapolis, MN (FEI 3000901012), conducted on 9/31-10/05/2005. 30 cases were shipped to Drug Distributors Inc., 3910 Riverside St., Newark, NJ on 10/03/05 via Cross Country Express, Kansas City, MO. Invoice # 8328 10/05/05, B/L A-3026, 10-3-05.

Search OK Cancel

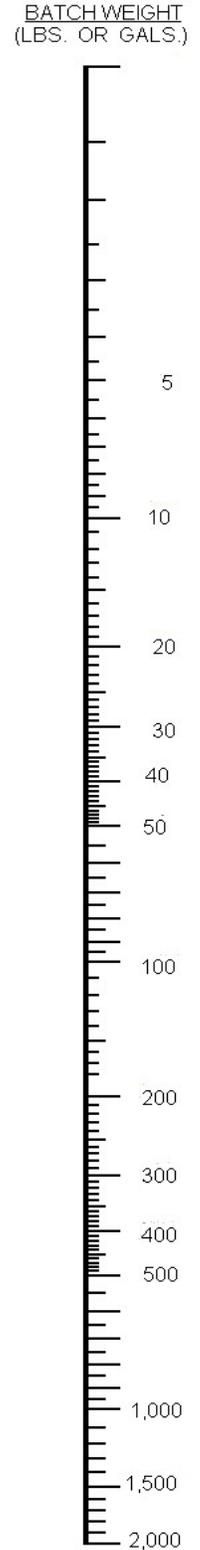
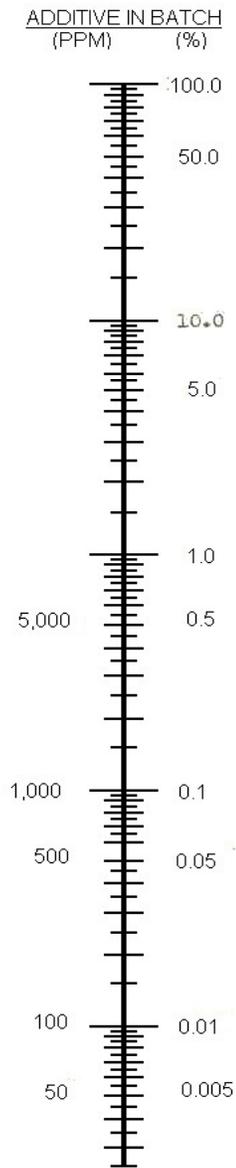
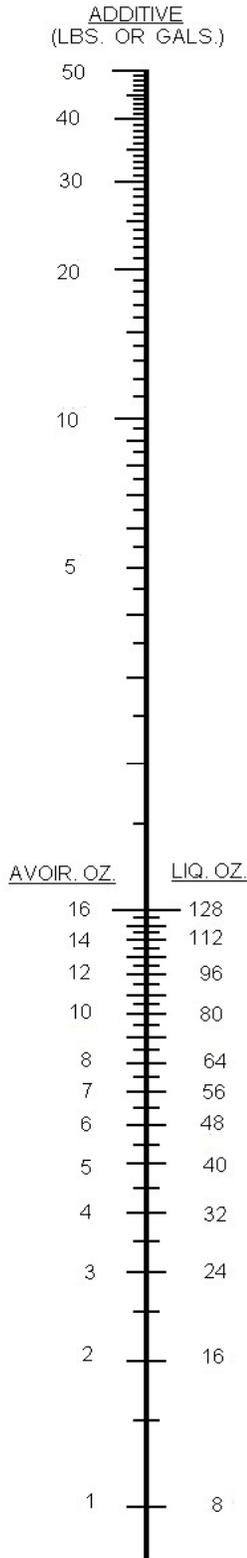
5-10 FORM FDA 482c NOTICE OF INSPECTION – REQUEST FOR RECORDS

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.
	6. NUMBER AND STREET			p.m.
	7. CITY AND STATE & ZIP CODE		8. PHONE # & AREA CODE	
<p>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 1.361³.</p>				
9. SIGNATURE (<i>Food and Drug Administration Employee(s)</i>)		10. TYPE OR PRINT NAME AND TITLE (<i>FDA Employee(s)</i>)		
<p>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:</p> <p>¹Sec. 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.</p> <p>²Sec. 414(a) RECORDS INSPECTION. - (1) ADULTERATED FOOD. - If the Secretary has a reasonable belief that an article of food, and any other</p>		<p>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.</p> <p>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.</p>		

5-11 FOOD ADDITIVE NOMOGRAPH I

FOOD ADDITIVES NOMOGRAPH I

1. Additive and batch weight known. Apply a straight edge to appropriate points on outside columns. Read ppm and/or percent additive where straight edge intersects central column.
2. Tolerance and batch weight known. Apply a straight edge to appropriate points on central and right-hand columns. Read the amount of additive in lbs. or gals. where straight edge intersects the left-hand column.

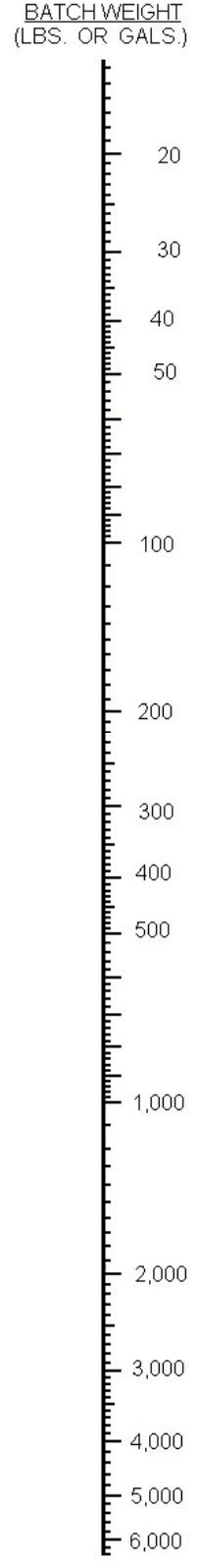
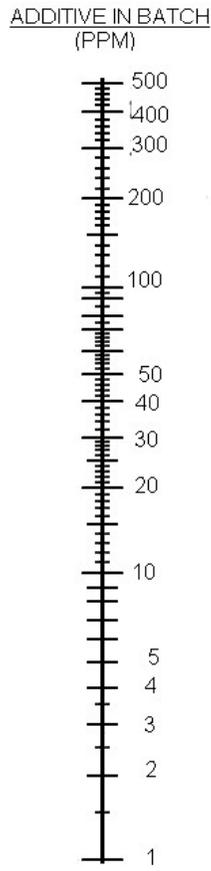
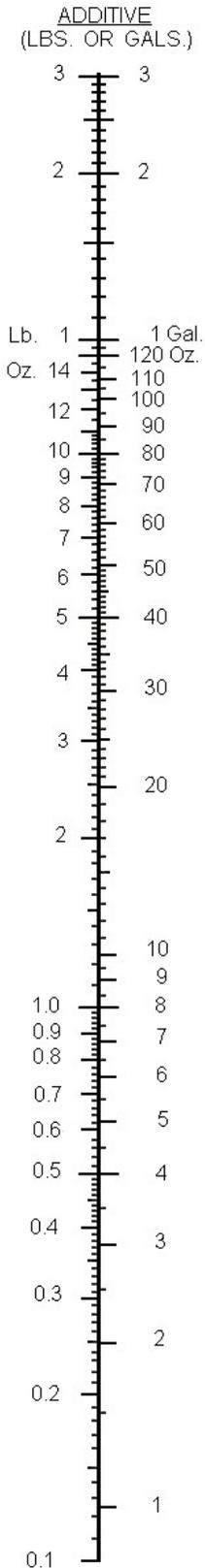


For more precise determination of additives in the 1-500 ppm range, use Nomograph II

5-11 FOOD ADDITIVE NOMOGRAPH II

FOOD ADDITIVES NOMOGRAPH II

1. Additive and batch weight known. Apply a straight edge to appropriate points on outside columns. Read ppm and/or percent additive where straight edge intersects central column.
2. Tolerance and batch weight known. Apply a straight edge to appropriate points on central and right-hand columns. Read the amount of additive in lbs. or gals. where straight edge intersects the left-hand column.



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 SUBSTANTIALLY EQUIVALENT MEDICAL DEVICES

Operation	Submit 510(k)	Register	List	COMPLY W/GMP
1. Manufacture and distribute device	YES: 807.81(a)	YES 807.20(a)	YES 807.20(a)	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
3a. Contract manufacturer who meets the definition of finished device manufacturer per 21 CFR 820.3(l).	NO	YES 807.20(a)(2)	YES 807.20(a)(2)	YES
3b. Contract manufacturer who does not meet the definition of finished device manufacturer per 21 CFR 820.3(l) (e.g., component manufacturer, subassembler)	NO	NO	NO	NO
4. Manufacturer modifies device or new intended use and distribute	NO: preamble no. 17 & 18 FR 8/23/77 YES: 807.81(a)(3) with signif. change in device or use	YES 807.20(a)	YES 807.20(a)	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
6. Specification initiator and distribute only	YES: 807.81(a)	YES: 807.20(a)(1)	YES: 807.20(a)(1)	YES: 820.181, etc.
7. Specification consultant only; no distribution	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 820.3(w), 820.3(o) and Preamble Comment 28, FR 52610
9. Relabeler or repacker: distribute under own name	NO: 807.85(b): no change to device or existing labeling and another person has a cleared premarket notification application	NO	NO	NO
10. 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
11. Kit assembler changes intended use (801.4) of prepackaged/prelabeled devices	YES: 807.81(a)	YES: 807.20(a)(3)	YES: 807.20(a)(3)	YES: 820.120, 820.130, etc.
12. Kit assembler changes prepackaged/prelabeled devices	NO: if no significant change to labeling or device: otherwise YES: 807.81(a)(3)(i)	YES: 807.20(a)(3)	YES: 807.20(a)(3)	YES
13. Manuf. Accessory, component and package & label for health purpose to end user.	YES: 807.81(a)	YES: 807.20(a)(6)	YES: 807.20(a)(6)	YES
14. Manuf. Components & dist. Only to finished device mfr.	NO: 807.81(a)	NO: 807.65(a)	NO	Use as guide: 820.1
15. Contract mfr. Of subassembly or component (see no. 13, accessory)	NO	NO	NO	Primary mfr. must see that GMP is met 21 CFR 820.50
16. Contract packager or labeler	NO	YES	YES	Yes 820.2(a)(1) 820.3(o)
17. 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
18. Manufacture custom device (domestic or foreign)	NO: 807.85(a)(1)&(2)	YES 807.20(a)	YES 807.20(a)	YES: also see 520(b); 520(f)
19. 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
20. Foreign manufacturers and all foreign establishments	YES: 807.81	YES, 807.40(a)	YES 807.40(a)	YES
21. 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: 807.3(d), 820.198, 820.100, 820.200, etc.
22. Installer-mfr.'s agent	NO	NO	NO	YES: 820.170
23. Installer-user	NO	NO	NO	NO: for x-ray see 1020.30(d) report
24. Device being investigated under ide	Exempt: 812.1(a)	NO	NO: 807.40(c)	Exempt per 812.1(a), except for Design Control per 820.30
25. 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
26. Reprocessor of single use device	YES	YES: 807.20(a)(4)	YES: 807.20(a)(4)	YES
27. Foreign exporter of device (device manufactured in foreign country)	YES: (original manufacturer's 510(k) maybe used)	YES: 807.40 (a)	YES: 807.40 (a)	YES 820.1(a)(2) YES

5-14 eNSpect PROFILE - COMSTAT

PROFILING A FIRM'S CGMP/QS COMPLIANCE STATUS

Table 5-14.1	Quick Reference Guide	5-14.3.11	Remark Status Field
Table 5-14.2	Example of a Maintain Profiles Screen	5-14.3.12	Remarks Field
5-14.1	Introduction	5-14.3.13	Out-of-Business Firm
5-14.2	Purpose	5-14.3.14	Firm Merge
5-14.3	Instructions	5-14.3.15	Troubleshooting
5-14.3.1	Pre-Inspection Preparation	5-14.4	Contact Information
5-14.3.2	Firm's Operations	5-14.5	Data Quality Assurance Projects
5-14.3.3	Maintain Profiles Screen	5-14.6	Establishment Profile Criteria
5-14.3.4	Previous Inspection Profile	Table 5-14.6.1	Device, Biologic, Drug, and Veterinary Establishments TO Profile
5-14.3.5	Firm information	Table 5-14.6.2	Establishment and Operations NOT to Profile.
5-14.3.6	Inspection Coverage of Profile Class Codes	5-14.6.3	Pre-Approval Inspection Profile Classes and Codes
5-14.3.7	Discontinue and Delete Buttons	5-14.7	Profile Class Codes
5-14.3.8	CGMP Inspection and Other Toggle Buttons	5-14.7.1	Biologics
5-14.3.9	Initial, In Review, and Final	Table 5-14.7.1.1	Devices
5-14.3.10	Final Profile Status	Table 5-14.7.1.2	Drugs and Veterinary
5-14.3.10.1	Other Status	Table 5-14.7.1.3	Special Veterinary
5-14.3.10.2	Acceptable Status	Table 5-14.7.1.4	
5-14.3.10.3	Unacceptable Status		

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 ORA Production 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 ORA/OISM/DSS/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](mailto: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 ORA 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"

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.

5-14.6.3 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 systems should be treated like any other QS 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)).

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 <i>Remarks</i> 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 <i>Remarks</i> 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 <i>Remarks</i> 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

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 FROM PLANT/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

Table 5-14.7.1.3 Drugs and Veterinary

DRUGS	
Profile Class Code	Definitions
ADM	AEROSOL DISPENSED MEDICATION
AMT	ADVANCED MANUFACTURING TECHNOLOGIES (including 3D printing, continuous drug manufacturing)

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

5-16 FACTS REIMBURSABLE CHECK BOX

Screenshot showing location of Reimbursable check box:

The screenshot shows a software window titled "Inspection Accomplishment Hours". The window is divided into two main sections. The top section, labeled "Operation", contains several input fields: "Operation Code" (12 - Domestic Inspection), "Work Subject / Title" (MN Seafood FY 05), "Assignment Status" (In Progress), "Status Date" (07/27/2005), and "Performing Org." (MIN-GRP6). A "Reimbursable:" checkbox is located to the right of the "Status Date" field, and a black arrow points to it. The bottom section, labeled "Assignees Accomplishment Hours", contains a table with columns: "Lead", "Employee", "Position", "Hours", "PAC", "Est", "Process", and "Hours". The first row is checked and contains the name "Rogers, Sidney H", position "INV", and "MIN-DO". To the right of the table are "Add", "Delete", and "Duplicate" buttons. A "Total Hours:" field is located at the bottom right of the table area.

Lead	Employee	Position	Hours	PAC	Est	Process	Hours
Invstgr	Name	Class	Credited To		Type		
<input checked="" type="checkbox"/>	Rogers, Sidney H	INV	MIN-DO				
<input type="checkbox"/>							
<input type="checkbox"/>							
<input type="checkbox"/>							
<input type="checkbox"/>							
<input type="checkbox"/>							

5-17 FORM FDA 4056 - PRODUCE FARM INSPECTION OBSERVATIONS



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration



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	FEI NUMBER	
LAST NAME, FIRST NAME, MIDDLE INITIAL AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED (Most responsible individual present) TO:			
FARM NAME (include business name, if different)			
OWNER/OPERATOR			
FARM MAILING ADDRESS		FARM PHYSICAL LOCATION, IF DIFFERENT FROM MAILING ADDRESS (e.g., location identifiers such as GPS coordinates)	
TYPE OF INSPECTION: <input type="checkbox"/> Initial <input type="checkbox"/> Routine <input type="checkbox"/> Follow-up <input type="checkbox"/> For-cause <input type="checkbox"/> Other (please specify)		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.

Representatives of the regulatory agency should record their observations on this form as clearly and specifically as possible and should order their observations by significance within each area (most important first). In some cases, an observation may relate to more than one topic area. Representatives of the regulatory agency should record observations in the topic area listed below that, in the representatives' judgment, is the most appropriate topic. Not all topic areas may be applicable in every situation. In addition, 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.

Representatives of the regulatory agency should discuss all observations with the management of the farm or their representative as they are observed, or on a daily basis, to minimize surprises, errors, and misunderstandings when this form is issued. Discussion should include those observations which may be written on the form and those that will only be discussed with management during the closeout meeting. This form should be issued during the exit conference of all produce inspections, including when no observations have been recorded.

The farm may use this opportunity to ask questions about the observations or to request clarification. If the farm has implemented, or plans to implement, corrective action in response to an observation, this may be discussed with the representatives of the regulatory agency during the inspection. Representatives of the regulatory agency should annotate the form, as applicable, with any completed or promised corrections discussed during the inspection. FDA representatives are encouraged to verify the farm's completed corrective actions during the inspection as long as the verification does not unreasonably extend the duration of the inspection. Inclusion of annotations regarding corrective actions does not signify any conclusion by the regulatory agency regarding the sufficiency of the actions.

FARM NAME *(include business name, if different)*

DATE(S) OF INSPECTION

FEI NUMBER

If you have any questions, please contact the regulatory agency at the phone number and address above.

Representatives of the regulatory agency should record observations consistent with procedures established for conduct of inspections, including additional instructions that appear in Chapter 5 of the IOM, available at <https://www.fda.gov/ICECI/Inspections/IOM>.

REPORTABLE OBSERVATIONS MADE DURING THE INSPECTION

Representatives of the regulatory agency should check one of the following options. As noted above, 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.

- 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.

Personnel Qualifications and Training (21 CFR Part 112, Subpart C)

1. §§ 112.21 and 112.22: Qualifications and training for personnel who handle (contact) covered produce or food contact surfaces

- Observation Corrective action taken

Description:

[Light blue shaded area for description]

2. § 112.23: Assignment or identification of supervisors

- Observation Corrective action taken

Description:

[Light blue shaded area for description]

3. § 112.30: Record-keeping

- Observation Corrective action taken

Description:

[Light blue shaded area for description]

Health and Hygiene (21 CFR Part 112, Subpart D)

4. § 112.31: Measures to prevent ill or infected persons from contaminating covered produce with microorganisms of public health significance

- Observation Corrective action taken

Description:

[Light blue shaded area for description]

5. § 112.32: Hygienic practices of personnel

- Observation Corrective action taken

Description:

[Light blue shaded area for description]

FARM NAME (include business name, if different)

DATE(S) OF INSPECTION

FEI NUMBER

6. § 112.33: Measures to prevent visitors from contaminating covered produce and food contact surfaces with microorganisms of public health significance

Observation Corrective action taken

Description:

[Redacted description area]

Agricultural Water (21 CFR Part 112, Subpart E)

7. § 112.41: Quality of agricultural water

Observation Corrective action taken

Description:

[Redacted description area]

8. § 112.42: Agricultural water sources, water distribution system, and pooling of water

Observation Corrective action taken

Description:

[Redacted description area]

9. § 112.43: Treating agricultural water

Observation Corrective action taken

Description:

[Redacted description area]

10. § 112.44: Microbial quality criteria applicable to agricultural water used for certain intended uses

Observation Corrective action taken

Description:

[Redacted description area]

11. § 112.45: Corrective measures if agricultural water does not meet requirements of § 112.41 or § 112.44.

Observation Corrective action taken

Description:

[Redacted description area]

12. §§ 112.46 and 112.47: Testing agricultural water that is subject to the requirements of § 112.44.

Observation Corrective action taken

Description:

[Redacted description area]

13. § 112.48: Water that is used during harvest, packing, and holding activities

Observation Corrective action taken

Description:

[Redacted description area]

14. § 112.50: Record-keeping

Observation Corrective action taken

Description:

[Redacted description area]

FARM NAME (include business name, if different)

DATE(S) OF INSPECTION

FEI NUMBER

Biological Soil Amendments of Animal Origin and Human Waste (21 CFR Part 112, Subpart F)

15. § 112.52: Handling, conveyance, and storage of biological soil amendments of animal origin

Observation Corrective action taken

Description:

[Redacted description area]

16. § 112.53: Use of human waste

Observation Corrective action taken

Description:

[Redacted description area]

17. §§ 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

Observation Corrective action taken

Description:

[Redacted description area]

18. § 112.60: Record-keeping

Observation Corrective action taken

Description:

[Redacted description area]

Domesticated and Wild Animals (21 CFR Part 112, Subpart I)

19. § 112.83: Measures related to grazing animals, working animals, or animal intrusion

Observation Corrective action taken

Description:

[Redacted description area]

Growing, Harvesting, Packing, and Holding Activities (21 CFR Part 112, Subpart K)

20. § 112.111: Measures related to growing, harvesting, packing, or holding both covered and excluded produce

Observation Corrective action taken

Description:

[Redacted description area]

21. § 112.112: Measures to be taken immediately prior to and during harvest activities

Observation Corrective action taken

Description:

[Redacted description area]

22. § 112.113: Handling harvested covered produce

Observation Corrective action taken

Description:

[Redacted description area]

FARM NAME (include business name, if different)

DATE(S) OF INSPECTION

FEI NUMBER

23. § 112.114: Disposition of dropped covered produce

Observation Corrective action taken

Description:

[Redacted description area]

24. § 112.115: Measures related to packaging covered produce

Observation Corrective action taken

Description:

[Redacted description area]

25. § 112.116: Measures related to food-packing (including food-packaging) material

Observation Corrective action taken

Description:

[Redacted description area]

Equipment, Tools, Buildings, and Sanitation (21 CFR Part 112, Subpart L)

26. § 112.123: Equipment and tools

Observation Corrective action taken

Description:

[Redacted description area]

27. § 112.124: Instruments and controls used to measure, regulate, or record

Observation Corrective action taken

Description:

[Redacted description area]

28. § 112.125: Equipment used in the transport of covered produce

Observation Corrective action taken

Description:

[Redacted description area]

29. § 112.126: Buildings

Observation Corrective action taken

Description:

[Redacted description area]

30. § 112.127: Domesticated animals in and around a fully-enclosed building

Observation Corrective action taken

Description:

[Redacted description area]

31. § 112.128: Pest control in buildings

Observation Corrective action taken

Description:

[Redacted description area]

FARM NAME (include business name, if different)

DATE(S) OF INSPECTION	FEI NUMBER
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32. § 112.129: Toilet facilities
 Observation Corrective action taken
 Description:
 [Redacted]

33. § 112.130: Hand-washing facilities
 Observation Corrective action taken
 Description:
 [Redacted]

34. § 112.131: Control and disposal of sewage
 Observation Corrective action taken
 Description:
 [Redacted]

35. § 112.132: Control and disposal of trash, litter, and waste
 Observation Corrective action taken
 Description:
 [Redacted]

36. § 112.133: Plumbing
 Observation Corrective action taken
 Description:
 [Redacted]

37. § 112.134: Control of animal excreta and litter from domesticated animals
 Observation Corrective action taken
 Description:
 [Redacted]

38. § 112.140: Record-keeping
 Observation Corrective action taken
 Description:
 [Redacted]

Sprouts (21 CFR Part 112, Subpart M)
 Check here if entity does not engage in growing, harvesting, packing, and/or holding of sprouts

39. § 112.142: Seeds or beans used to grow sprouts
 Observation Corrective action taken
 Description:
 [Redacted]

40. § 112.143(a): Fully-enclosed buildings
 Observation Corrective action taken
 Description:
 [Redacted]

FARM NAME (include business name, if different)

DATE(S) OF INSPECTION	FEI NUMBER
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41. § 112.143(b): Cleaning and sanitizing food-contact surfaces

Observation Corrective action taken

Description:

[Redacted description area]

42. §§ 112.144(a), 112.145, and 112.148: Environmental monitoring for *Listeria* species or *L. monocytogenes* (written environmental monitoring plan, collection and testing, corrective actions)

Observation Corrective action taken

Description:

[Redacted description area]

43. §§ 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)

Observation Corrective action taken

Description:

[Redacted description area]

44. § 112.150: Record-keeping

Observation Corrective action taken

Description:

[Redacted description area]

Records (21 CFR Part 112, Subpart O)

45. § 112.181 - 112.187: General record-keeping

Observation Corrective action taken

Description:

[Redacted description area]

Other Observations

46. Other

Observation Corrective action taken

Description:

[Redacted description area]

FDA REPRESENTATIVE SIGNATURE	FDA REPRESENTATIVE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
[Redacted signature]	[Redacted name and title]	[Redacted date]

FARM NAME *(include business name, if different)*

DATE(S) OF INSPECTION

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Continuation Sheet

Additional Observations and/or Comments

Large light blue area for entering additional observations and/or comments.

Continue

FARM NAME *(include business name, if different)*

DATE(S) OF INSPECTION	FEI NUMBER
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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.