Chapter 5
ADMINISTRATIVE ACTIONS

NOTE: The district compliance officer (or, the center CSO/Scientist, if the action was center-initiated) assigned to the administrative action should diligently pursue and actively monitor the progress of the case through the Agency review process to its conclusion. The Office of Enforcement (Division of Compliance Management and Operations) can assist in situations where significant delays are experienced or assistance is needed to resolve technical, scientific, or policy issues. (Also, see section on ***Ad Hoc*** Committees in Chapter 10.) For actions resulting from a Current Good Manufacturing Practice (CGMP) or Quality System (QS) inspection of a domestic or foreign drug, biologics, or medical device facility, the firm's profile status information in the Field Accomplishment and Compliance Tracking System (FACTS) should be appropriately updated at each stage in the review process. (See "Firm Profile Updates in FACTS" in Chapter 4 for more information.)

This chapter contains the following sections.

5-1 CITATIONS

5-1-1 Purpose

This section describes the Food and Drug Administration's (FDA) procedures for issuing Section 305 Notices (Citations).

5-1-2 Legal Authority

FDA issues Citations under Section 305 of the Federal Food, Drug, and Cosmetic Act (the Act), which states:

"Before any violation of this Act is reported by the Secretary to any United States attorney for institution of a criminal proceeding, the person against whom such proceeding is contemplated shall be given appropriate notice and an opportunity to present his views, either orally or in writing, with regard to such contemplated proceeding."

21 CFR 7.84 provides requirements about the issuance of such notice and opportunity.

NOTE: Citation is to be used only when a prosecution recommendation is contemplated. Do not use a Citation for warning purposes.

5-1-3 Citation Under Multiple Laws

On occasion, the same or related conduct that violates the Act may also constitute a violation of one or more other federal laws, such as the licensing provisions for biologics under the Public Health Service Act (42 U.S.C. Section 262), 18 U.S.C. Section 1001 (Fraud and False Statements), and 18 U.S.C. Section 371 (Conspiracy to commit offense or to defraud United States).

In such a case, identify the section of each law under which action is contemplated, and the specific actions considered to violate that law.

5-1-4 Criteria For Citation

The basic criteria for consideration of citation are as follows:

A violation of the law has been established and the agency has evidence in its possession to support the case in court.

The violation is significant in terms of consumer protection.

Except in cases involving a health hazard, fraud, or extremely gross violations, prior warning must have been given to the firm and each individual involved. This prior warning may be in the form of conferences, previous meetings, letters or discussions of FDA 483s at the conclusion of inspections or previous court actions. See Chapter 10 for a discussion of Prior Notice. In instances where the prior warning was in the form of letters or a Section 305 Notice involving past violations, copies must have been directed to each individual to be cited. NOTE: Additional, more specific criteria in many areas may be found in Compliance Policy Guides (CPG) and the Compliance Program Guidance Manual (CPGM).

5-1-5 Determining The Need For Citation

The district compliance branch is responsible for deciding whether citation is warranted. The compliance officer assigned to the case should ensure that all samples and other evidence have been considered. The search for other samples and evidence may include:

1. Searching the Field Accomplishments and Compliance Tracking System (FACTS) for further information on the firm;

2. Checking with the laboratory to find out if there are other samples that are in-process and need to be analyzed;

3. Checking the collection report (C/R) on the initial sample to ensure that all related samples are attached; and,

4. Checking outstanding sample assignments in FACTS.

If there are other samples to be analyzed or the establishment inspection report has not been completed, and seizure has not yet been considered, you may wish to defer action until the entire case can be considered at one time. In such instances, discuss the matter with investigations branch and/or the laboratory to expedite processing of the report or the samples.

Conduct a thorough review of the evidence. For example, review the firm's regulatory history to determine who was responsible for the violations and whether prior warning has been given. Review inspection reports to ensure that any inspectional observations that are inconsistent with analytical results are addressed. Ensure that reserve samples are available, where required. In labeling violations, search the file to determine whether the firm has revised the labeling since the shipment of the samples in question.

A citation may be based solely on establishment inspection evidence. A minimum of two documentary samples covering violative products is desirable.

NOTE: Under normal circumstances, notice and an opportunity to present information and views will always be given before violations are reported for criminal prosecution. However, there are certain circumstances under which notice and opportunity need not be provided. Notice and opportunity need not be given when there is reason to believe that alerting the prospective defendants by a Section 305 Notice may result in the destruction of evidence, or cause the proposed defendants to flee to avoid prosecution. (21 CFR 7.84(a)(2)). In addition, notice and opportunity need not be given when further investigation by the Department of Justice is contemplated. (21 CFR 7.84(a)(3)).

Such situations are infrequent and should be approved on a case-by-case basis. Submit the facts to the center and request concurrence from the center, OE, and OCC when you do not believe providing notice and an opportunity for presentation of views is appropriate.

5-1-6 Time Frames

The following time frames apply to citations:

1. Field: 15 working days after analysis of most recent sample involved in case.
2. Center: 15 working days after receipt of the recommendation.

There may be good reasons for exceeding these timeframes in a particular case. For example, analytical procedures may be lengthy, or there may be a need to obtain assistance from other districts to establish responsibility. Document the reasons for delays in the case file.

5-1-7 Field Office Citation Procedures

1. ***Prior Consultation With OCI***

   The Office of Criminal Investigations (OCI) is responsible for reviewing all matters in FDA for which a criminal investigation is recommended, and is the focal point for all criminal matters.

   FDA personnel must refer all criminal matters, regardless of their complexity or breadth, to OCI. This includes criminal search warrants, misdemeanor prosecutions, and citations.

   District management must communicate with its local OCI office before pursuing any criminal matter. This communication is absolutely essential to preclude potential interference with other on-going criminal investigations and to prevent confusion among the components of the Office of Chief Counsel and the Department of Justice that are responsible for handling FDA’s criminal cases. During this communication, OCI is to be provided with all of the facts of the potential case and any additional information that is

relevant to, or could impact, the case in any way. OCI will decide promptly whether or not it is interested in pursuing the case and will communicate that decision to the district.

If OCI chooses not to pursue a criminal matter, the district office, after considering the reasons for the declination, is at liberty to proceed with the case in accordance with the procedures in this chapter.

2. ***Authorization To Cite***

Citation may issue either on a direct basis or after the submission of a recommendation to the appropriate center and receipt of concurrence to issue the Section 305 Notice.

It is incumbent upon the office issuing the Section 305 Notice to ensure that the firm and each individual to be cited have received prior warning, unless such warning is not required.

a. Direct Citation
   CPGs give field offices authority to issue Section 305 Notices in cases where specific criteria are met. Most of these guidelines involve filth violations or noncompliance with standards. Check the manual each time the district office believes citation is the action of choice to preclude submitting unnecessary recommendations to a center.

b. Citation Recommendation
   Where the district office does not have direct citation authority, it should submit a citation recommendation to the appropriate center for approval.

   The recommendation should include the full background of the case, the history of notification, and the facts supporting the violation(s) for which prosecution is being considered. Include the names and responsibilities of each individual to be cited, the proposed charges, and the supporting samples. Submit any labels, worksheets, and pertinent inspection reports. Identify and discuss any issues, concerns, discrepancies, or other problems with the case. The recommendation package should be well-organized, tabbed, and indexed. The recommendation should identify the location of supporting information it discusses. Interstate (IS) documentation remains the responsibility of the districts and need not be submitted. However, the center may request IS documentation if there's a special need to review it.

c. Citation Recommendation After or Concurrently with Seizure
   When the district follows a seizure action with a citation recommendation based on the same underlying violations, it is acceptable to submit a memorandum that references information in the seizure recommendation, provided that the center has all of the labeling and other documents necessary to consider the citation.

   When the district office is recommending citation at the same time it is recommending seizure, flag the recommendation memorandum as "Seizure and Citation Recommendation."

5-1-8 Determination Of Citees

1. ***Corporations, Partnerships, and Associations***
   Corporations, partnerships, and associations are "persons" under the Act, and may be prosecuted as separate legal entities. They should always be included in the citation.

2. ***Individuals***
   In every case, carefully consider citing individuals. Prior warning is a prerequisite except where the violation involves a danger to health, fraud, or where the violation is extremely gross.

   It is FDA policy to cite officers of corporations and members of partnerships and associations, when the available evidence establishes that the individual stood in a "responsible relationship" to the violation. As the U.S. Supreme Court stated in U.S. v. Park: "The Act imposes not only a positive duty to seek out and remedy violations when they occur but also, and primarily, a duty to implement measures that will insure that violations will not occur."

   Persons who have the power and authority, and therefore the responsibility, to carry out these duties and fail to do so, are logical candidates for citation. Obtain the type of information needed to demonstrate responsibility from observations reported by the investigators, through correspondence and/or memoranda of conferences with the individuals, or through other means. In addition, if there is a need, obtain information from officers and individuals located at a parent plant, as well as persons at the inspected plant.

5-1-9 Setting Date For Meeting

If the firm and individuals to be cited are located within a reasonable proximity of the office in which the meeting is to be held, schedule the meeting for approximately 10 days after issuing the Section 305 Notice. If the citees must travel extensive distances or wish to have a corporate attorney in attendance, or the violations involved are complex, schedule the meeting approximately 20 days after issuing the Section 305 Notice.

When there are multiple citees, schedule a separate meeting for any citee who requests one in writing. The meeting may be held at a separate time on the same date or on a separate date. The citee must submit the request to the office that issued the Section 305 Notice, and the request must be received at least three working days before the date set in the notice.

5-1-10 Preparation Of Citation Documents

1. ***Section 305 Notice (Exhibit 5-1)***

   Insert the district address under the printed heading "Food and Drug Administration." Under the caption at the right, "In reply refer to," insert the key or file reference sample number for the action, and "et. al." if there are several samples involved. If there is only one product or class of products, such as "drugs," bakery products," etc., identify the product directly below the reference sample number. The complete list of samples will appear on the Charge Sheet along with the respective products. See Exhibits 5-2 and 5-3 for examples of charge sheets.

Enter the date that Notice issues directly above the rectangle on "Section 305 Notice" or centered under the city and state of the district's address.

In the space for addressee, insert the name and address of the firm or sole owner cited (primary citee). When the citation also names responsible individuals, address it in the following manner:

Standard Pharmaceutical Co.
and Mr. Henry Jones
and Mr. John Doe
125 Main Street
Canton, Ohio 28531

(Do not show titles of individuals listed as citees.)

In the body of the Notice, following the phrase "with respect to the following," enter clear, concise statements identifying the specific interstate shipment and product for each sample on which citation is issuing. In each statement include the name of the product, sufficient quotation from the label to identify the brand, size, etc., the date of shipment, where the shipment originated, and where and to whom it was consigned. When there is more than one sample, show sample numbers in parenthesis following the description of each shipment. If there is insufficient space on the form to enter the samples and shipments involved, enter the notation "See Page 2" conspicuously in the body of the Notice and continue the additional information regarding the samples on a separate page captioned as follows: "Page 2 - Section 305 Notice".

NOTE: When charging violations involving items other than shipments, include a concise factual statement of the violations (see Exhibits).

Following the words, "A meeting has been scheduled for," insert the day, date, specific time and location of the meeting. Add any other information that may facilitate the citee's appearance in parentheses following this statement (e.g., availability of parking near the building).

Type the name of the Compliance Officer who will conduct the meeting at the bottom of the form, and have that individual sign the copies mailed to the firm and each individual cited.

If individuals have been cited along with the firm, show distribution on all copies of the Notice under the parenthetical statement: "(IMPORTANT: NOTE ALL ENCLOSURES CAREFULLY)" such as: 1 cc to Mr. John Doe and to Mr. Robert Roe each with Charge Sheet and Information Sheet.

2. ***Charge Sheet (Form FDA 1854) (Exhibit 5-2)***

Use Form FDA 1854. Under the title, list each sample and product in ascending numerical order. If the list of samples is long, arrange it in two columns.

Under the heading "PROHIBITED ACT" state the section(s) of the law(s) violated and the statutory description from the law. In charges involving Title 18 or Title 42, cite those laws.

At the left of the sheet, following the above paragraph type the word "CHARGES". If only one sample and charge are involved, enter the statement "The article is violative in that" followed by the non-legal description of the violation. In the case of multiple charges, enter the statement: "The article is violative in the following respects:" and list each charge separately, numbered as "1," "2," "3," etc.

When a number of samples and charges are involved, use the statement "The articles are violative in the following respects:" and list the charges as described above. Show the sample numbers involved at the left of each charge.

State the charges in “lay language.” There is no need to reference specific sections of the Act (other than the "Prohibited Act") or the regulations. Exhibit 5-3 contains examples of charges.

3. ***Legal Status Sheet (Form FDA 454) (Exhibit 5-4)***

Enter the sample numbers involved in the citation in the upper right hand side of the form following the caption "Sample No."; and the date(s) of the alleged violations over the "(Date)" caption following line "A." If more than two dates are involved, show the earliest and latest dates only; for example "3/3/94 thru 4/12/94." The district office makes no other entries.

4. ***Information Sheet (Form FDA 466a) (Exhibit 5-5)***

This form describes the purpose and nature of the meeting. It is not necessary to type any information on the form; however, it is mandatory that a form accompany the Section 305 Notice sent to each individual cited.

5-1-11 Distribution Of Citation Documents

1. ***Distribute the Section 305 Notice, Charge Sheet, Legal Status Sheet, and Information Sheet as follows****:*

   a. Send a signed, original copy of the Section 305 Notice, a Charge Sheet, an Information Sheet, and a Legal Status Sheet to the primary citee (generally the firm).

   b. Send a signed copy of the Section 305 Notice, a copy of the Charge Sheet, and an Information Sheet, to each of the other citees, if it is a joint citation.

   c. Forward one copy of the Section 305 Notice, together with one copy of the Charge Sheet, to the factory file, the reading file, and, if applicable, to the district resident post.

   d. Retain three copies of the Section 305 Notice and the Charge Sheet in the District Sample File for use when making a recommendation for disposition of the charges.

2. ***Mailing Instructions***

Mail the Section 305 Notice in a regular, letter size envelope with the typed name and address of the citee. Do not use window envelopes. When individuals are cited along with a firm, circle or underline their names on their respective copies and mail each

citee's copy in a separate envelope. Where the interests of the individual citees may be at odds, you may send the individual notices to the home addresses of the citees.

Send the Section 305 Notice by certified mail with return receipt requested.

3. ***Postponement Of Meetings***

   Districts may grant a reasonable postponement of a meeting upon written request by a citee or person representing a citee (see exception below). The length of the postponement will depend on particular circumstances, but should avoid excessive delay. Confirm the new date by a letter to the citee or representative who requested the postponement. Provide an information file copy to the center.

   Exception: If an office in headquarters directed that the meeting be scheduled within a certain time frame, do not agree to postponements without first consulting with that office.

5-1-12 Transfer Of Meeting

Occasionally citees will request a transfer of the scheduled meeting to another city in the district area, to another district office, or to Washington headquarters. The citee also has the option of answering by other means when personal appearance at the district headquarters is impractical.

1. ***Transfer Within District Area***

   Do not grant requests for transfer of the meeting to another city in the district area. The cost to the public of holding the meeting in another city outweighs any benefit or convenience to the citee.

2. ***Transfer to Another District***

   A request to transfer a meeting to another district may be granted if reasonable grounds are presented, the request is addressed to the office that issued the Section 305 Notice, and the request is received in that office at least 3 working days prior to the date set in the notice. (See 21 CFR 7.84(e)). However, before granting the request to transfer the meeting, check with the district involved to make sure it can handle the meeting.

   Once the request is granted, verify the transfer by letter to the citee. Send two copies of the letter to the new district with these attachments:

   a. complete file on the samples involved

   b. pertinent Establishment Inspection Reports (EIR's)

   c. a FACTS printout of firm's record, if pertinent to the case

   The home district should establish a temporary jacket as a record of the transfer.

   The transferee district will reschedule the meeting promptly and advise accordingly. This may be done by letter with reference to the original Section 305 Notice and to the letter approving transfer from the original district. Forward copies to the home district.

After the meeting, send the Record and any exhibits to the home district along with the original files.

Prepare a skeleton sample jacket containing a copy of the Record, transcripts (if any), and copies of any collateral correspondence that may have issued on the case.

3. ***Transfer to Headquarters***

   Discourage requests by citees, before or during the meeting, to transfer the meeting to headquarters.

   If, however, the citee insists that the meeting be held at headquarters, refer the request to the center involved. If granted, the center will inform the citee and home district of the new date set for the meeting. The district should then promptly forward the case file to the center for review and use during the meeting. The center will return the case file with the Record to the home district for disposition of the charges.

5-1-13 Correspondence With Attorneys

Attorneys representing clients who received a Section 305 Notice will often correspond with the district compliance officer regarding the Section 305 Notice. Because the issuance of a Section 305 Notice is confidential and generally not releasable to the public until all potential criminal matters are resolved, district compliance officers are responsible for ensuring that representatives of the citee provide appropriate documentation regarding their authorization (see 21 CFR 7.84(g)).

It is not necessary to send citees copies of correspondence from their attorneys. However, when a citee is identified as having received a copy of the citee's attorney's correspondence, and we have responded to that correspondence, you may wish to send the citee a copy of our response.

5-1-14 Drug Advertising Citations

Due to the specialized nature of medical advertising, the Division of Drug Marketing, Advertising and Communications (DDMAC), Center for Drug Evaluation and Research (CDER) is the primary reviewer of drug advertisements. With few exceptions, DDMAC will initiate citations based on violative drug advertisements.

After determining that an advertisement is violative and that citation is warranted, DDMAC may initiate a request for samples to support an action. Samples that are obtained are routed to the home district of the responsible firm.

DDMAC will prepare citation instructions for issuance by the appropriate district. The instructions will specify whether the meeting is to be held at the district office or at headquarters. In most cases, meetings are held at headquarters.

The district will issue the Section 305 Notice in the normal manner, with a copy to DDMAC.

Following the meeting, DDMAC will make a decision on the disposition of the charges and notify the district of that decision.

5-2 SECTION 305 MEETING

5-2-1 Purpose

This section summarizes the authority, policies, and procedures pertaining to the opportunity, under Section 305 of the Act, for a person to present their views before criminal prosecution is recommended to a United States Attorney.

5-2-2 Authority

The Secretary of Health and Human Services delegates broad authority to the Commissioner of Food and Drugs under 21 CFR 5.10, and, unless specifically prohibited, gives the Commissioner the authority to redelegate this authority. District Directors, Regional Food and Drug Directors, and Directors and Deputy Directors of the centers, are authorized under 21 CFR 5.28(a), to designate officials to hold hearings under section 305 of the Act. A Compliance Officer has authority to hold Section 305 meetings by such designation.

21 CFR 7.85 provides requirements about the conduct of such meetings.

5-2-3 Preparation

Except in unusual circumstances, the Compliance Officer who holds the meeting is the individual who issued the Section 305 Notice. As there is normally a time lapse between the issuance of the Section 305 Notice and the meeting date, the Compliance Officer should review the case immediately prior to the meeting. The Compliance Officer will need to be completely familiar with the charges, the law and regulations, and fully understand any analytical results and methodology that are part of the case (if necessary, through discussion with the analyst).

The Compliance Officer should assemble any necessary references, such as the Act, regulations, official compendia, etc. The Compliance Officer may also wish to mark or photocopy pertinent information in the files to avoid searches for data during the meeting. Such information may include records relating to samples, EIRs, and FDA 483s, and documents relating to prior warnings to the firm or individuals in the form of citations, seizures, prosecutions, office interviews, letters, etc. To avoid the need to reread all of the material, it is best to organize this information at the time of the initial review, when preparing the Section 305 Notice.

5-2-4 Respondents' Request For Special Information

Respondents, their attorneys, and others occasionally attempt to obtain detailed information concerning the government's case. Such requests constitute requests for information under the Freedom of Information Act (FOIA). Point out that under the FOIA, they must submit requests in writing to the Director of FDA's Division of FOI. Refer the requester to http://www.FDA.Gov/RegulatoryInformation/foi/default.htm, and mention that the request must be processed according to law and FDA's procedures. For example, FDA's Associate Commissioner for Public Affairs might determine that some or all of the information about FDA's case may be withheld from disclosure under 21 C.F.R. 20.62 (pre-decisional information, attorney work product, etc.) and/or 21 C.F.R. 20.64 (open investigatory, personal privacy, confidential source, etc.).

NOTE: If a respondent requests a portion of a sample, follow the procedures set forth in 21 CFR 2.10(d) and 2.10(c).

5-2-5 Conducting The 305 Meeting

Respondents are occasionally quite upset due to the receipt of the Section 305 Notice and may tend to be discourteous or argumentative. The 305 meeting is not a debate and nothing can be gained by the Compliance Officer losing objectivity or by the respondent becoming abusive. The Compliance Officer should politely point out that the proceedings are not a trial but rather an opportunity for the respondents to give their side of the story and discuss any mitigating circumstances, corrective actions taken or planned, etc., and that FDA will consider this information when deciding whether or not to forward the case to the Department of Justice for the institution of criminal proceedings.

The Compliance Officer should strive for continuity and relevancy. Some respondents may digress into time-consuming, irrelevant or repetitious discussion unless there is a diplomatic effort to focus upon relevant matters. Listed below is a suggested routine format for achieving orderly progress during the meeting:

1. ***Identification Of Respondents***

   After the respondents have been introduced and seated, make notes showing the name, address, position, and business connection of each respondent. The notes are for ready reference during the meeting and useful during the dictation of the Record.

2. ***Failure Of Respondent To Appear***

   Frequently, a cited individual does not attend the meeting. Determine if anyone present purports to represent such respondent and enter any responses into the record.

   Designated representative(s) must have a signed written statement of authorization for each respondent for whom he/she has authority to act. If a representative appears without written authorization, the meeting may proceed with respect to any respondent for whom the representative appears, only if the Compliance Officer first verifies by telephone, or other appropriate means, the authenticity of the representative's authority (21 CFR 7.84(g)).

3. ***Attendance By Individuals Not Cited***

   Occasionally, an individual who was not named in the Section 305 Notice will appear and, during the course of the meeting, it will become apparent that the person shares the responsibility for the violation. In such instances, request a short delay and have the legal clerk prepare a supplemental Section 305 Notice including the individual's name, present it to him/her, and proceed with the meeting.

   Respondents may arrive at a meeting accompanied by many adherents. When this situation occurs, the Compliance Officer should have each person identify themselves by name, state their relationship to the respondent, and, for the record, state that they are attending on behalf of the respondent. The Compliance Officer should then announce to the group that the meeting is not open to the public, that it concerns only the respondent, and that the only legitimate business other persons have in being there is that they are there at the request of, and on behalf of, the respondent; otherwise, they may not be present. Afterwards, the Compliance Officer will hear comments from all

persons remaining present. If these actions are not taken, the respondent may claim that FDA deprived him/her of his/her rights to fully respond and explain.

4. ***More Than One Respondent***

   Requests for separate meetings should be in writing and should be received at least three working days before the date set in the notice (21 CFR 7.84(e)). However, if there is more than one respondent, advise the respondents in advance that they are entitled to separate meetings if they so wish.

5. ***Legal Status Sheet, Form FDA 454***

   Ask for the Legal Status Sheet. The respondent may complete the sheet before or at the meeting. However, you may not demand completion or submittal of the sheet since there is no legal requirement that respondents furnish the sheet.

6. ***Explain The Purpose Of The Meeting And The Charges***

   Although the Information Sheet (Form FDA 466a), which accompanies the Section 305 Notice and Charge Sheet, contains information concerning the reason for the notice, the Compliance Officer should reiterate the purpose of the notice prior to the discussion of the charges and advise the respondents that:

   a. The meeting is being held in accordance with Section 305 of the Act to give them an opportunity to present any facts they believe are relevant prior to the FDA making its decision whether to recommend prosecution to the Department of Justice; and,

   b. The purpose of the meeting is not to resolve conclusively whether violations occurred, and therefore FDA will not present either witnesses or evidence at the meeting.

   The Compliance Officer should briefly state the information in the FDA's possession, which indicates that violations of the Act (and other laws, if pertinent) occurred and that the individuals listed in the Section 305 Notice were responsible, either through their actions or their failure to take action. This may be by reference to the pertinent inspections, FDA 483s, warning letters etc., to provide a brief summary of the relevant time and acts. Request that the respondents follow their copies of the Section 305 Notice and Charge Sheet as the Compliance Officer either reads verbatim or summarizes the pertinent information concerning the shipment or receipt of each product and the charges pertaining to it, or the acts that constitute violations.

   The Compliance Officer should ask the respondents whether they understand the charges. If the response is negative, answer any questions to ensure that the respondent understands the basis of the allegations. If the respondent indicates that the shipping or receiving dates are incorrect, clarify the discrepancies. If they indicate that they will make no admissions with regard to the shipment or receipt of the products, do not pursue the matter.

7. ***Miranda Warning***

   In the past, there were questions regarding whether the Compliance Officer needs to give the "Miranda Warnings" prior to conducting a Section 305 meeting. They are not to be given.

In Miranda v. Arizona, the court ruled that when an individual is taken into custody or otherwise deprived of his freedom and subjected to questioning, the person must be notified of his right to remain silent, that anything he says may be used against him, and that he has the right to an attorney. This warning does not apply to Section 305 meetings because a respondent to a Section 305 Notice is not "taken into custody or otherwise deprived of his freedom." In addition, even though not required, FDA notifies the respondents (Form FDA 466a) that they are not compelled to answer and that an attorney may represent them. In 1976, in Beckwith v. United States, the Supreme Court held that even when the investigation has "focused" on an individual, he is not entitled to Miranda warnings unless he is in custody. In Oregon v. Mathiason, decided in January 1977, the Supreme Court held that a meeting at which the individual was free to leave did not require Miranda warnings.

8. ***Respondents' Statement***

After discussing the purpose for the meeting and the charges, the Compliance Officer should invite the respondents to state their views with respect to the alleged violations. Take notes regarding the various points covered by the respondents to ensure that pertinent comments are not inadvertently omitted when the summary is dictated.

Occasionally respondents appearing at a meeting present a prepared written response. In such instances the Compliance Officer should, if practical, read the written response aloud while the respondents follow their copies. The Compliance Officer should ask questions regarding any points that need clarification. In the dictation of the meeting summary, refer to the written response, which will be attached to the record as an exhibit, indicate that it was read aloud in the presence of the respondents, and include in the dictation only information concerning the points discussed for clarification.

Each respondent may present any information bearing upon the issues. This may consist of proposed or revised labeling, letters, laboratory data, sanitation contracts, etc. Identify each exhibit submitted by respondents at the meeting with the related sample number, date received, and the Compliance Officer’s initials. Place the identification at the top right hand corner of the exhibit, if it is possible to do so without obscuring any material.

Respondents may request that the Compliance Officer comment on the adequacy of the proposed corrections. Unless headquarters provided specific instruction, refrain from commenting, and explain that comments may be provided after careful consideration of the submitted material and that it may involve headquarters review. Advise the respondents that the information will be included in the record as an exhibit.

9. ***Ensure Scope Of Respondents' Responsibility***

Usually respondents demonstrate their responsibilities while expressing their views with respect to the alleged violations. Normally, they express responsibilities in the form of comments such as "I hired extra men for sanitation" or "I ordered the destruction of the merchandise" etc.

If there are any doubts about the responsibility of any of the respondents, ask questions

to ensure that you are not including individuals in a criminal proceeding who lack the authority to detect, prevent or correct violations. For example, ask who had the authority to change pest control firms or consulting laboratories, who hires or discharges employees for sanitation or quality control work, who directs labeling changes, and who expends monies for structural repairs and the purchase of new equipment, etc.

In addition to the responsibility of those who appear, the Compliance Officer may need to make inquiries regarding the responsibilities of an individual listed in the Section 305 Notice who does not appear. This could be particularly important in cases where officials of a company at a location other than the one inspected have been cited, but do not appear at the meeting.

10. ***Guaranties***

Unless a respondent voluntarily includes as part of his presentation a guaranty related to the violations, explore thoroughly the question of whether one exists. Otherwise, the respondent may overlook the fact that he/she had a guaranty, until he/she or his/her attorney eventually presents it as a defense at trial.

If a respondent requests information regarding guaranties so that he/she may obtain them in the future, furnish a copy of 21 CFR 7.13.

If the respondent presents a guaranty at the meeting, do not comment upon its validity. Tell the respondents that the validity of the guarantee will be reviewed after the meeting.

11. ***Summary***

At the conclusion of the meeting, the Compliance Officer will dictate an accurate summary of the meeting in the presence of the respondents, or at their option, immediately after their departure. The respondents, for a variety of reasons, may wish to leave the meeting before the summary is dictated, and should be afforded that option. In that event, a draft copy of the summary should be forwarded to the respondents, requesting their comments within 10 days, and explaining that without benefit of comment the record will stand as drafted. In the event respondents remain during the dictation, they should be offered an opportunity to provide additional comments or corrections. Inform the respondents that if they disagree with, or wish to clarify, any of the statements they may do so after dictation of the summary.

If respondents undertake to have long or irrelevant statements included in the dictated summary, tactfully suggest that they may wish to submit a statement after the meeting, and that the statement will be included as an attachment to the Record. (21 CFR 7.85(g)).

a. Required Statements
The Summary should always contain statements to the effect that:

i. The purpose of the meeting was discussed with the respondents and they understood that it was being held pursuant to Section 305 of the Act;

ii. The charges were discussed with the respondents and they understood them;

iii. The respondents indicated that the shipments had been made, or received, as alleged. (If not admitted, or they have reservations, this information should be included);

iv. Information concerning the statements each respondent made concerning his scope of authority (responsibility) at the firm;

v. The respondents were asked if they had any corrections or comments to make (followed by their statements or a comment in the record that they had none);

vi. Copies of the Summary will be forwarded to the respondents; and,

vii. (In the final section of the record) that the Summary was dictated in the presence of the respondents and when asked if they felt that the dictation accurately and fairly summarized the discussion they indicated that it did (or did not in the following respect). If the respondents elected not to remain during the dictation of the summary, the final section of the draft should reflect that fact.

A copy of the typed summary should be provided to each respondent, and should be accompanied by a cover letter, which states that the firm and individuals have an opportunity to make any additions or corrections in writing within 10 days after receipt.

b. Addendum to the Summary

Occasionally after the respondents have left the premises, the Compliance Officer will realize that significant information was omitted from the Summary. In such a case, an addendum to the Summary should be dictated and mailed to the respondents along with the Summary dictated in their presence. A cover letter should accompany the Summary and addendum pointing out the inadvertent omission. Request a letter from the respondents within 10 days indicating that the additional information had been discussed as recorded in the addendum.

A respondent may request that the meeting be reopened in order to submit new information for the record. Such a request must be timely, in writing, state the nature of the new information, the reason it was not previously available at the time of the original meeting and why the information cannot be submitted in documentary form. If the district concludes that the meeting should be reopened to receive the new information, it may do so.

On occasion, respondents will request an additional meeting at headquarters to discuss the matter further. Such meetings are an extension of the Section 305 meeting and are governed by the procedures of this chapter.

c. Verbatim Transcript of Meeting

The respondent has the right to a verbatim transcript, at his expense. If exercising this right, the respondent must provide the necessary person or equipment to make the transcript. The respondent must submit a copy of such

transcription to the district at no cost with an opportunity to make corrections and obtain agreement as to its accuracy. Under these circumstances, the Compliance Officer need dictate only a brief in-house summary after departure of the respondents, explaining the circumstances under which the verbatim transcript was made, who was present, etc. In this case, FDA does not prepare a "Summary".

The Compliance Officer may also order the meeting transcribed at FDA's expense. In this case, a copy of the transcription is provided to each respondent (21 CFR 7.85(e)).

d. Handling of Electronic Recording

If the meeting statement has been recorded, after transcribing, appropriately identify the recording medium with the date of the meeting, the name of firm cited, the sample numbers, and the transcriber's name. File the recording in the lead sample jacket and retain it until the 10-day period for review by the respondent has expired, then remove and destroy, or erase the recording.

e. Preparation of Summary

i. Method of Preparation

- Prepare the summary as a separate document, using the format in Exhibit 5-6 as an example.
- Include the following statement at the bottom of the copy provided to each respondent:

  "Copy of this Summary (or transcript) furnished to (respondent)."
- Include the transmittal letter advising respondents of the 10-day period for additions or corrections.

ii. Number of Copies - Make sufficient copies for the following distribution:

- Original + 1 copy for center (hold for submission with case)
- One copy for district case file
- One copy for district establishment file on firm
- One copy for Resident Investigator, if desired
- One copy for district reading file
- One copy for each respondent

12. ***Multi-Session Meetings***

The intent of the regulations is to limit multi-session meetings. Requests for changes in time and place of the meeting must be made in accordance with 21 CFR 7.84(e). New evidence may be submitted in accordance with 21 CFR 7.85(g). Nevertheless, a

respondent may appear for a meeting, but claim he/she has further evidence to submit. If the request is reasonable, recess the meeting until a mutually agreeable date. Prepare only one Record covering both meetings.

When the respondent merely requests an opportunity to submit supplemental documentary evidence without further personal appearance, he/she may do as provided in 21 CFR 7.85(g). Mark additional information and/or documentation that is received within ten calendar days after respondents' received their copy of the summary or transcription of the meeting as an exhibit and add it to the Record.

13. ***Response By Mail***

Frequently, respondents elect to respond in writing in lieu of making a personal appearance. It is not necessary to acknowledge receipt of a written response. However, it may be desirable to acknowledge a written response when you also need to clarify some point of misunderstanding or oversight on the part of the respondent.

Hold correspondence to a minimum to avoid "holding a meeting by mail."

5-2-6 Procedures After Meeting

After the meeting (or written response, if any), a decision must be made as to disposition of the charges for each sample involved. The charges are disposed of by one or a combination of the following actions: Permanent Abeyance, Temporary Abeyance, or Prosecution.

1. ***Reporting Permanent Abeyance And Temporary Abeyance Cases***

The district should process cases designated as in abeyance within seven days after the meeting, with notification to the appropriate center, as described below.

a. Permanent Abeyance

Prepare a memorandum to the appropriate center(s) compliance office, headed "PA after CITATION" which provides the reason for placing the case in permanent abeyance (PA) and the planned district follow-up. Attachments should include a copy of the Section 305 Notice endorsed "PA (date and initials)", a copy of the Charge Sheet, a copy of the Summary, and any relevant information. Hold all copies the above documents in the district case file.

Forward a copy of the memorandum to the center(s), an endorsed "PA (date and initials)" copy of the Section 305 Notice, and a copy of the Charge Sheet to the district establishment file.

The Home District's Compliance Branch should update the Sample Disposition record(s) in FACTS with the appropriate information about the status of the samples.

b. Temporary Abeyance

Prepare assignments for necessary follow-up and forward copies to the appropriate center(s) compliance office. Hold the file in the District Compliance Branch. A case in TA is not considered closed.

2. ***Notification Of Non-Prosecution***

When the Agency makes a final determination that prosecution will not be recommended for any of the persons named in a notice (i.e., the case is closed), the district that issued the 305 Notice will advise each person in writing of that fact (21 CFR 7.85(h)(1)).

After the Agency decides to decline prosecution, that decision must be communicated to the office (generally a district office) that originated the citation recommendation to ensure that notification of non-prosecution issues in accordance with regulations. The FDA unit to which the recommendation was made, e.g., center, OE, OCC, is responsible for issuance of the declination to the originating office/district. Upon receipt of the declination, and absent a request for reconsideration of the recommendation, the originating office/district should issue the notification of non-prosecution within 10 working days.

When it is determined that one of several persons named in a notice will not be included in a recommendation for criminal prosecution, the Office of Chief Counsel (OCC) will determine when that person will be notified (21 CFR 7.85(h)(2)). The Office of Chief Counsel will notify the district of this fact, and the district will issue the letter. The latter procedure applies when the Department of Justice declines to proceed with the entire case (21 CFR 7.85(h)(3)) or declines to proceed against an individual (21 CFR 7.85(h)(4)). See Exhibit 5-7 for the model letter to use.

5-3 ADMINISTRATIVE DETENTION OF FOODS

5-3-1 Purpose

This section provides the procedures and defines the responsibilities for the various operations related to the Administrative Detention of articles of food.

5-3-2 Background

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (“the Bioterrorism Act”) (Public Law 107-188) was signed into law on June 12, 2002. The Bioterrorism Act includes a provision, Section 303, which amended Section 304 of the Federal Food, Drug, and Cosmetic Act (the Act) by adding subsection (h) to authorize administrative detention of food. Section 304(h) of the Act provides that an officer or qualified employee of FDA may order the detention of any article of food that is found during an inspection, examination, or investigation under the Act if the officer or qualified employee has credible evidence or information indicating that the article of food presents a threat of serious adverse health consequences or death to humans or animals. Section 303 of the Bioterrorism Act also amended the Act by adding Subsection (bb) to Section 301, making it a prohibited act to move an article of food in violation of a detention order or to remove or alter any mark or label required by a detention order that identifies an article of food as detained.

Regulations have been established in 21 CFR Part 1, Subpart K, for administrative detention of foods. Administrative detention is intended to protect the public by preventing movement in commerce of food until FDA has had time to consider the appropriate action to be taken and,

when appropriate, to initiate a seizure or injunction action. Administrative detention of food requires prior approval of the district director or official senior to the district director of the district where the detained article of food is located. The period of the detention must be for a reasonable period, not to exceed 20 days. However, the period of detention may be extended up to a total of 30 days, if necessary to provide sufficient time to institute a seizure or injunction action.

Any person who would be entitled to claim the detained article of food, if seized, may appeal the administrative detention and may request a hearing on the appeal. The appeal and request for a hearing must be submitted to the district director of the district that issued the detention order. The hearing must be held within two (2) calendar days after the appeal is filed. The decision to affirm or revoke the detention must be made within five (5) calendar days after the appeal is filed.

1. ***References***

   The regulatory authority for administrative detention of foods and associated operations appears in sections 304(h) and 201(x) of the Act, and in 21 CFR 1.377-1.406, 21 CFR Part 16, 21 CFR 10.19, and 21 CFR 10.45. Investigations Operations Manual (IOM) Subchapter 2.7 Detention Activities contains the instructions for implementing the detention authority.

5-3-3 Issuing and Terminating Detention Orders

1. ***Basis for Detention***

   An FDA employee, or State or local officer or employee commissioned by FDA as an officer of the Department, may order a detention as part of his/her function of inspecting, examining, or investigating an article of food. The detention order must be based on credible evidence or information indicating that the article of food presents a threat of serious adverse health consequences or death to humans or animals. (21 CFR 1.378)

2. ***Approval of Detention Order by the District Director***
   The FDA district director in whose district the article of food is located, or an FDA official senior to such director (hereinafter termed “District Director”), must approve the detention order. If prior written approval is not feasible, prior oral approval must be obtained and confirmed in writing as soon as possible. (21 CFR 1.391)

   Prior to approving the detention order, the “District Director” should ensure that there is appropriate scientific support for the determination that the article of food presents a threat of serious adverse health consequences or death to humans or animals. The district should initiate this process by notifying FDA’s Emergency Operations Center (EOC) at 301-443-1240. EOC will coordinate the emergency response activities associated with an article of food that may present a threat of serious adverse health consequences or death to humans or animals and will notify the appropriate center (CFSAN and/or CVM) and ORA offices, either verbally or in writing.

   CFSAN or CVM, as appropriate, should determine whether the food presents a threat of serious adverse health consequences or death to humans or animals and verbally provide that determination to the district and EOC. The center should subsequently provide written documentation of the determination, including documentation necessary

to support subsequent legal action.

3. ***Center Notification***

As soon as possible after contacting EOC regarding the threat of serious adverse health consequences or death to humans or animals, the district should notify the appropriate center compliance contact of the impending legal action to discuss available evidence, to determine with the center what, if any, additional evidence should be obtained to support the case, and to work with the center to expedite the recommendation.

a. Compliance Contacts:

i. Food for Humans: Director, Division of Enforcement, Office of Compliance (HFS-605), Center for Food Safety and Applied Nutrition, 301-436-2417

ii. Food for Animals: Director, Division of Compliance, Office of Surveillance and Compliance (HFV-200), Center for Veterinary Medicine, 240-276-9200.

4. ***Issuing the Detention Order***

The detention order is issued in writing, in the form of a Detention Notice (Form FDA 2289). The detention order must be signed and dated by the FDA employee (usually an investigator) or commissioned officer who has credible evidence or information indicating that the article of food presents a threat of serious adverse health consequences or death to humans or animals.

FDA must issue the detention order to the owner, operator, or agent in charge of the place where the article of food is located. If this individual is not the owner of the article of food, FDA must provide a copy of the detention order to the owner, if the owner's identity can be readily determined. Copies that cannot be hand delivered by an investigator must be sent expeditiously, usually by overnight delivery, with documentation of receipt of delivery.

If the article of food is detained in a vehicle or other carrier used to transport the detained article, FDA must provide a copy of the detention order to the shipper of record, the owner and operator of the vehicle or other carrier, and the owner of the food, if their identities can be readily determined. Copies that cannot be hand delivered by an investigator must be sent expeditiously, usually by overnight delivery, with documentation of receipt of delivery.

5. ***Detention Notice and Detention Tags – Forms***

Section 2.7.2.3 of the IOM provides instructions for completing the Detention Notice (Form FDA 2289). Section 2.7.2.4 provides instructions for completing the Detention Tag (Form FDA 2290), which should be affixed to the article of food subject to the detention order. If necessary, a label other than the Detention Tag may be used to identify the detained article of food, providing the label includes the information required in 21 CFR 1.382.

The detention order frames the issues for any appeal, including any informal hearing that may result from the detention. Therefore, the information on the order concerning the reason for detention is important.

The detention order must contain a brief, general statement of the reasons for the detention. There is no requirement that the order include all of the reasons for believing that the article of food presents a threat of serious adverse health consequences or death to humans or animals. The reasons used in the detention order do not limit the charges that may be included in a subsequent legal action. If the detention is based on classified information, this information must not be provided in the detention order.

6. ***Length of Detention***

The article of food initially should be detained for 20 calendar days, unless the district believes that additional time will be required to institute a seizure or injunction. In such cases, the detention should be made for 30 calendar days at the time the order is issued.

If the article of food is detained for 20 days and a seizure or injunction cannot be instituted against the article of food within that time frame, the detention can be extended to a total of 30 days. If a detention is extended from 20 to 30 days, FDA will issue another detention order and place new tags or labels on the product. The entire detention period may not exceed 30 days.

7. ***Movement, Use, etc. of a Detained Article of Food***

An article of food subject to a detention order may not be delivered under the execution of a bond. Notwithstanding Section 801(b) of the Act, while any article of food is subject to a detention order under Section 304(h) of the Act, it may not be further delivered to any of its importers, owners, or consignees. This does not preclude movement at FDA's direction of imported food to a secure facility under an appropriate Customs Bond when that bond is required by U.S. Customs and Border Protection law and regulation.

The detained article of food must be held in the location and under the conditions specified by FDA in the detention order. The movement of an article of food in violation of a detention order is a prohibited act under Section 301(bb) of the Act.

Except as noted below, no person may transfer a detained article of food within or from the place where it has been ordered detained, or from the place to which it was removed, until the detention order is terminated by the “District Director” or the detention period expires, whichever occurs first.

a. The “District Director” may approve, in writing, a request to modify a detention order to permit movement of a detained article of food for any of the following purposes:

    i. To destroy the article of food;

    ii. To move the detained article of food to a secure facility under the terms of a detention order (see below);

iii. To maintain or preserve the integrity or quality of the article of food; or

iv. For any other purpose that the "District Director" believes is appropriate in the case.

The required tags or labels must accompany the detained article during and after movement, and must remain with the article of food until FDA terminates the detention order or the detention period expires, whichever occurs first, unless otherwise permitted by the "District Director" who approves the modification of a detention order.

If FDA approves a request for modification of a detention order to allow the food to be moved, the article may be transferred but remains under detention before, during, and after the transfer. The letter allowing the transfer should reiterate this. A detained article of food may not be transferred without FDA supervision unless FDA has declined in writing to supervise the transfer. If FDA has declined in writing to supervise the transfer of a detained article, the person who received the detention order, or his representative, must immediately notify the "District Director" who approved the modification of the detention order that the article of food has reached its new location, and the specific location of the detained article within the new location. Such notification must be in writing, and may be in the form of a fax, e-mail, or other form as agreed to by the "District Director."

8. ***Movement to a Secure Facility at FDA's Request***

If, after a food is detained, FDA determines that removal to a secure facility is necessary, the article of food must be removed to a secure facility at the expense of the owner or claimant. The investigator who issued the initial detention order or other qualified official will issue a modified detention order, indicating the location to where the food must be moved. A detained article of food remains under detention before, during, and after movement to a secure facility. FDA will also state in the detention order any conditions of transportation applicable to the detained article.

As noted above, the detained article of food must not be moved to the secure facility until the FDA modifies the detention order.

9. ***Legal Actions against Detained Food, Including Perishable Food***

The district should expedite the preparation of a legal action recommendation to obtain control over the detained food, particularly perishable food. This will most often be through a seizure action.

If FDA initiates a seizure action against a perishable food, as defined in 21 CFR 1.377, that has been detained, we are required by 21 CFR 1.383 to send the seizure recommendation to the Department of Justice (DOJ) within 4 calendar days of issuing the detention order, unless there are extenuating circumstances. Extenuating circumstances include (but are not limited to) instances where the results of confirmatory testing or other evidentiary development requires more than 4 calendar days to complete. If the fourth calendar day is not a working day, the Office of Chief Counsel (OCC) should advise DOJ on the last working day before the deadline of its plans to recommend a seizure and will send the seizure as soon as practicable on the first working day after the non-work day.

All recommendations for legal action against detained food should be flagged to indicate they involve product that is under detention, include the date the detention expires (and, for perishable food, the deadline for sending the recommendation to DOJ), and be delivered to the responsible center, Division of Compliance Management and Operations (DCMO) (for seizures only), and OCC by the most expeditious means, which may include hand-carrying or electronically. Overnight delivery service may be used if the food is nonperishable and deadlines can still be met.

The center, DCMO, and OCC will review the recommendation concurrently. The center compliance office, DCMO, and OCC should expedite their reviews if the legal action is to be instituted prior to expiration of the detention.

When the action is a seizure, the district is responsible for coordination with the U.S. Attorney's office and the Marshal's Service, to facilitate the prompt filing of the complaint and seizure of the food. The district also is responsible for immediately providing oral or e-mail notice of the accomplishment of the seizure to the appropriate center compliance office, DCMO, OCC, and the presiding officer of any in-process appeal of a detention order.

When FDA institutes a seizure or injunction action regarding the article of food involved in the detention order, the process for the appeal of a detention order terminates. (21 CFR 1.402(c))

10. ***Termination of Detention Orders***

If FDA terminates a detention order or the detention period expires, the “District Director” will issue a detention termination notice releasing the article of food to any person who received the detention order or that person’s representative and will remove, or authorize in writing the removal of, the required tags or labels. While the regulation does not give a time frame for FDA to issue the termination notice, we expect that we will normally be able to issue the termination notice to the person who received the detention order within one calendar day of the decision to terminate the detention order.

a. FDA will terminate a detention order when one of the following occurs:

    i. FDA determines that the food does not present a threat of serious adverse health consequences.

    ii. FDA approves voluntary destruction and the destruction is accomplished.

    iii. The detention order is appealed and the presiding officer revokes the detention order.

    iv. The detention period expires. If FDA fails to issue a detention termination notice and the detention period expires, the detention is deemed to be terminated.

The “District Director” issues a Detention Termination Notice (Form FDA 2291) to the person(s) who received the Detention Notice, or his representative(s) and, if movement

of the food occurred prior to the termination, to the person possessing the food. The notice may be issued in person or by mail. If the termination notice is issued by mail, request that the Detention Tags (Form FDA 2290) be returned. If the termination notice is issued in person, see Section 2.7.2.5 of the IOM for instructions.

11. ***Responsibilities For Issuing And Terminating Detention Orders***

a. District Responsibilities; The district is responsible for:

i. Notifying the appropriate center as soon as it becomes aware of a situation where administrative detention may be appropriate.

ii. Ensuring legal and scientific support from the senior compliance official of the appropriate center before issuing a detention order.

iii. Issuing the detention order.

iv. Notifying the Director, DCMO, the senior compliance official or designee of the appropriate center, and OCC by phone or e-mail of the detention and supplying them with a copy of the detention order by the most expeditious means available (fax, express mail, e-mail, etc.) immediately after issuance.

v. Approving and monitoring the movement of detained food.

vi. Notifying the Regional Food and Drug Director (RFDD) that the district issued a detention order. NOTE: The RFDD should not become involved in decisions relating to issuing or monitoring the detention order. The RFDD may be the presiding officer at a hearing, if requested, and so must avoid participating in the investigation or action that is the subject of the hearing, and must be free from bias or prejudice (21 CFR 16.42(b)).

vii. Pursuing, with appropriate speed, the follow-up legal action.

viii. When warranted, issuing a Detention Termination Notice (Form FDA 2291) in a timely manner.

b. Center Responsibilities; The center is responsible for:

i. Providing a prompt response to the district's request for a determination on whether the article of food presents a threat of serious adverse health consequences or death to humans or animals. The center should expeditiously indicate its decision concurrently to the district and EOC by phone, fax, or e-mail.

ii. Providing written documentation of the determination on whether the article of food presents a threat of serious adverse health consequences or death to humans or animals, including documentation necessary to support the subsequent legal action.

iii. Working with the district Compliance Office to identify evidence needed to support the legal case.

iv. Notifying DCMO and OCC about the administrative detention and the legal action.

v. Promptly notifying the district and OCC of any issues or center concerns that need to be resolved, prior to providing support for the legal action.

vi. Expeditiously reviewing the legal action recommendation and providing expert witnesses and other support, as appropriate, for the legal action.

vii. Coordinating the legal action with DCMO and OCC.

c. RFDD Responsibilities

Although the RFDD should be informed about an impending administrative detention, the RFDD should refrain from becoming involved in decisions relating to issuing or monitoring the detention order. After the detention order has been issued, the RFDD must insulate himself/herself from all aspects of the detention except those relating to his/her responsibilities as a presiding officer for the hearing, if requested.

5-3-4 Appeal of a Detention Order

1. ***Appeal and Hearing***

Any person who would be entitled to be a claimant for the article of food, if seized under the Act, may appeal a detention order. The appeal must be submitted in writing, to the district director, in whose district the detained article of food is located, at the mailing address, e-mail address, or fax number identified in the detention order. The appeal must include a verified statement identifying the appellant's ownership or proprietary interest in the detained article of food, in accordance with Supplemental Admiralty Rule C of the Federal Rules of Civil Procedure.

If the detention order is appealed, the agency must provide the appellant with an opportunity to request an informal hearing. The request for a hearing must be in writing, must be included in the request for an appeal, and must conform to the time frames specified below. The agency has the authority to deny a hearing when the appeal raises no genuine and substantial issue of fact and FDA is entitled to judgment as a matter of law. If the district director, in consultation with OCC, determines that a hearing is not justified, written notice of the determination will be given to the parties explaining the reason for denial.

2. ***Time Frames***

a. Perishable food - The appeal must be filed within 2 calendar days of receipt of the detention order.

b. Nonperishable food - The appeal must be filed within 10 calendar days of receipt of the detention order. However, if the appeal includes a request for a hearing, the notice of intent to request a hearing must be filed within 4 calendar days of receipt of the detention order, or the hearing will not be granted.

The date of filing the appeal will be the date the submission is received by the district

office.

If a hearing is requested, and FDA grants the request, the hearing must be held within 2 calendar days after the date the appeal is filed. The decision to affirm or revoke the detention must be made within five (5) calendar days after the appeal is filed.

The appeal process terminates if FDA institutes a seizure or injunction action regarding the article of food involved in the detention order. (21 CFR 1.402(c)).

A summary of these timeframes is presented in Exhibits 5-8 and 5-9 "Timeframes for Administrative Detention of Food."

3. ***Presiding Officer***

The presiding officer for an appeal and an informal hearing must be an RFDD or another FDA official senior to an FDA district director. (21 CFR 1.404) Generally, the RFDD of the region where the detained article of food is located will serve as the presiding officer. If that individual is not able to serve as the presiding officer, he or she is responsible for arranging to have an RFDD from another region serve as the presiding officer. If an RFDD is not available, the Director, Office of Enforcement (OE), ORA will serve as the presiding officer.

4. ***Communications between Parties to the Hearing and the Presiding Officer***

Parties to the hearing should avoid any off-the-record communication with the presiding officer. If any communication of this type occurs, it must be reduced to writing and made part of the administrative record of the hearing. The other party must be provided with a copy of the letter or memorandum of the communication and must be provided an opportunity to respond (21 CFR 16.44(b)).

The person who writes a letter or memorandum of meeting between a participant in the hearing and the presiding officer must send a copy to all of the participants (21 CFR 16.44(c)).

5. ***Appeal Processing Responsibilities***

   a. District Responsibilities
   Preparation for an appeal should begin when the district decides to detain an article of food.

      i. When the district receives an appeal, the district director:

         - Dates and time stamps the appeal and notifies the appellant of receipt of the appeal.

           If the appeal has not been filed within the established time frame, the appeal is not valid and the detention remains in place until it is terminated.

           If it is determined that the appeal does not demonstrate ownership or proprietary interest as required in 21 CFR

1.402(b), the appeal is not valid. OCC may be consulted on this issue. At the discretion of the district director, if sufficient time is available, the district may notify the appellant of the requirement to provide written demonstration of ownership or proprietary interest and allow the appellant to re-file the appeal with the required information. The re-filing must be accomplished within the applicable timeframe.

If the appeal does not clearly specify that a hearing is requested, a hearing will not be granted.

- Notifies, orally or by email, the center, DCMO, OCC, and the RFDD of the appeal immediately and forwards a copy of the appeal to them as soon as possible by fax or electronically. Requests assistance of the center and OCC for completing the next item.

ii. When the appeal includes a request for a hearing:

- Prepare a general summary of the information that will be presented by FDA at the hearing in support of the detention order ("general summary") and a comprehensive statement of the basis for the detention order ("comprehensive statement"), in accordance with 21 CFR 16.24(f).

  EXCEPTION: When a detention order is based on classified information, 21 CFR 16.24(f) does not apply, and the district should consult with OCC to determine whether the presiding officer can give the appellant notice of the general nature of the information consistently with safeguarding the information and its source. (21 CFR 1.403(e) and 1.406)

  The detention order (Detention Notice) may serve as the comprehensive statement only if the reason for detention is described in sufficient detail. See Exhibits 5-10 and 5-11 for an example of a general summary and a comprehensive statement, respectively.

  Except when the detention is based on classified information, forward the general summary and the comprehensive statement to the appellant (21 CFR 16.24(f) and Section 201(x)(3) of the Act), the presiding officer, center, and OCC representatives to the hearing. Send the documents immediately so that they arrive as soon as possible, but at least one day prior to the hearing. If the detention is based on classified information, do not forward any information (or statements) to the appellant without the concurrence of OCC.

- At least one day before the hearing, provide the appellant, presiding officer, center, and OCC representatives to the

hearing, written notice of, or copies of, if they could not reasonably be expected to obtain copies, any published articles or written information to be presented at or relied on at the hearing (21 CFR 16.24 (g)).

iii. When the appeal does not include a request for a hearing:

- Forward all the information that supports the detention to the presiding officer. This includes the referenced general summary and comprehensive statement and any additional information provided by the appellant. The information should arrive no later than the third calendar day after the appeal is filed, so that the information can be reviewed and a decision rendered within 5 calendar days after the date the appeal is filed.

b. Presiding Officer Responsibilities

i. When notified of an appeal, and a hearing is requested, the presiding officer should:

- Orally contact the parties as soon as possible and set a date for a hearing to be held within two (2) calendar days after the date the appeal is filed. The hearing normally takes place at the district office where the goods are located.

- Provide all parties with written notification of the time, date, and location of the hearing.

- Provide the appellant with oral and written notification (see form letter as Exhibit 5-12):

1. of those portions of 21 CFR Part 16 that are excluded or modified under 21 CFR 1.403 and waived or modified for hearings on appeal of administrative detentions (see "Informal Hearing on Appeal of a Detention Order.");

2. that the informal hearing is not a public hearing per 21 CFR 16.60(a), in order to protect investigatory records compiled for law enforcement purposes that are not available for public disclosure under 21 CFR 20.64, or trade secrets and confidential commercial information that is not available for public disclosure under 21 CFR 20.61;

3. that the appellant should provide, at the hearing, a brief summary of any lengthy documents for presentation at the hearing (e.g., volumes of computer printouts);

4. that the appellant should provide the district director written notice of, or a copy of (if the district director could not reasonably be expected to obtain a copy), any published articles or written information for presentation at or relied on

at the hearing, at least 1 day before the hearing, if feasible, as required by 21 CFR 16.24(g); and notification

5. of the requirements under 21 CFR 16.44(c) (see "Communications between Parties to the Hearing and the Presiding Officer.")

ii. When notified of an appeal, and *no hearing is requested* , the presiding officer should orally notify the:

- parties that they should submit information supporting their positions as soon as possible, and no later than the third calendar day after the appeal is filed, so that the information can be reviewed and a decision issued within 5 calendar days after the date the appeal is filed.
- appellant of the requirement under 21 CFR 16.44(c) (see "Communications between Parties to the Hearing and the Presiding Officer," above.)

iii. When advice of the OCC is needed, the presiding officer should contact the Deputy Chief Counsel for Litigation.

c. OCC Responsibilities; OCC is responsible for:

i. Assigning an OCC attorney to review information on the detention order and to represent the district during any appeal and hearing;

ii. Expediting review of information provided by the district;

iii. Determining whether the district and the presiding officer require legal counsel; and,

iv. Working with the district to prepare for any hearing and appeal.

d. Center Responsibilities The center is responsible for providing:

i. scientific, technical, and policy support to the district; and,

ii. representatives to the hearing, if necessary.

e. DCMO Responsibilities; DCMO is responsible for ensuring that all:

i. agency and OCC components are notified of and prepared for a hearing; and,

ii. documentation from the district relating to the detention and hearing is provided to the center compliance office and OCC.

5-3-5 Informal Hearing on Appeal of a Detention Order

1. ***Background***

Section 304(h)(4) of the Act requires the Secretary to provide the appellant with an opportunity for an "informal hearing." Section 201(x) of the Act defines this term. 21 CFR 1.403 requires that FDA conduct the hearing in accordance with 21 CFR Part 16, Regulatory Hearing before the Food and Drug Administration, with the waivers and modifications noted below. 21 CFR 16.5(b) advises that Part 16 procedures apply to the extent that they are supplementary to, and not in conflict with, the other procedures specified in a regulation that provides a person with an opportunity for a hearing. 21 CFR 10.19 and 21 CFR 16.60(h) give the presiding officer the authority to suspend, modify, or waive provisions under Part 16.

2. ***Waivers and Modifications to 21 CFR Part 16***

If FDA grants a request for an informal hearing on an appeal of a detention order, FDA must conduct the hearing in accordance with 21 CFR Part 16, except that:

a. The detention order under 21 CFR 1.393, rather than the notice under 21 CFR 16.22(a), provides notice of opportunity for the hearing and is part of the administrative record of the regulatory hearing under 21 CFR 16.80(a);

b. A request for a hearing must be addressed to the FDA district director in whose district the article of food involved is located;

c. The provision in 21 CFR 16.22(b), providing that a person not be given less than 3 working days after receipt of notice to request a hearing, does not apply;

d. The provision in 21 CFR 16.24(e), stating that a hearing may not be required to be held at a time less than 2 working days after receipt of the request for a hearing, does not apply;

e. 21 CFR 1.406, rather than 21 CFR 16.24(f), describes the statement that will be provided to an appellant where a detention order is based on classified information;

f. 21 CFR 1.404, rather than 21 CFR 16.42(a), describes the FDA employees, e.g., Regional Food and Drug Directors or other officials senior to a district director, who preside at hearings;

g. The presiding officer may require that the hearing be completed within 1 calendar day, as appropriate;

h. 21 CFR 16.60(e) and (f) do not apply to the hearing. The presiding officer must prepare a written report of the hearing. All written material presented at the hearing will be attached to the report. The presiding officer must include as part of the report of the hearing a finding on the credibility of witnesses (other than expert witnesses) whenever credibility is a material issue, and must include a proposed decision, with a statement of reasons. The hearing participant may review and comment on the presiding officer's report within 4 hours of issuance of the report. The presiding officer will then issue the final agency decision;

i. 21 CFR 16.80(a)(4) does not apply to the hearing. The presiding officer's report of the hearing and any comments on the report by the hearing participant under 21 CFR 1.403(h) are part of the administrative record;

j. No party shall have the right under 21 CFR 16.119 to petition the Commissioner of Food and Drugs for reconsideration or a stay of the presiding officer's final agency decision; and,

k. If FDA grants a request for an informal hearing on an appeal of a detention order, the hearing must be conducted as a regulatory hearing pursuant to regulation in accordance with 21 CFR Part 16, except that 21 CFR 16.95(b) does not apply to the hearing. With respect to the regulatory hearing on an appeal of a detention order, the administrative record of the hearing specified in 21 CFR 16.80(a)(1), (a)(2), (a)(3), and (a)(5), and 1.403(i) constitutes the exclusive record for the presiding officer's final decision on an administrative detention. For purposes of judicial review under 21 CFR 10.45, the record of the administrative proceeding consists of the record of the hearing and the presiding officer's final decision.

21 CFR 16.60(b), which provides that all parties may confront and conduct reasonable cross-examination of any person (except for the presiding officer and counsel for the parties) who makes any statement on the matter at the hearing, is modified. Reasonable questions will be allowed instead. Reference Congressional intent: House of Representatives Report no. 94-853. Also, see 21 CFR 16.5 and 16.60(h).

3. ***Conducting the Hearing***

The presiding officer should inform the parties of the applicable modifications to 21 CFR Part 16 “Regulatory Hearing Before the Food and Drug Administration,” as provided for in the administrative detention regulation (21 CFR 1.403). The presiding officer will explain that the purpose of the hearing is to determine whether FDA, at the time of the detention and as charged in the detention order, had credible evidence or information indicating that the article of food presents a threat of serious adverse health consequences or death to humans or animals.

The FDA representative(s) must explain the bases for the detention and answer reasonable questions from the appellant.

The appellant may present relevant information to support his/her position that the article should not be subject to detention.

Both parties may conduct reasonable questioning of the other (section 201(x)(4) of the Act; 21 CFR 16.60(b), as modified herein).

The presiding officer will ensure that the material presented and the questions asked are relevant to the issue of the hearing.

The appellant may request that a transcript of the hearing be taken. However, the appellant must pay the cost of the transcript and furnish the presiding officer a copy for the record. FDA also may request a transcript of the hearing, in which case the costs are borne by the government.

The appellant may obtain a copy of the government transcript by submitting a request under the Freedom of Information Act (FOIA). 21 CFR Part 20 applies to the release of the transcript.

The presiding officer should notify the parties that his/her decision will not await transcription or correction of the transcripts so ordered.

4. ***Responsibilities For The Hearing:***

   a. Center Responsibilities
   The center will provide documents, witnesses, or office representatives for the hearing if requested by the district or the OCC attorney counseling the district.

   b. OCC Responsibilities
   OCC will provide counsel for the district and/or the presiding officer, as appropriate, for the hearing.

   c. District and Presiding Officer Responsibilities
   The section "Conducting the Hearing" includes individual responsibilities of the district and the presiding officer.

5-3-6 Issuing the Decision on an Appeal and Requirements After a Hearing on an Appeal of a Detention Order

1. ***Confirming or Revoking the Detention Order***

   If the agency can demonstrate it has credible evidence or information indicating that the article of food presents a threat of serious adverse health consequences or death to humans or animals, the presiding officer will affirm the detention order. If not, the presiding officer will revoke the detention order.

2. ***Time Period for Rendering Decision***

   The presiding officer must issue a final decision confirming or revoking the detention order within five calendar days after the appeal is filed. If the presiding officer fails to confirm or terminate the detention order within the five calendar day period, the detention order is deemed terminated.

3. ***Issuance of the Order***

   The decision should be issued in the form of an order. If classified information was used to support the detention, then any confirmation of the detention must state whether it is based in whole or in part on that classified information, but will not reveal the classified information. (See Exhibit 5-13 for model order, to be used when no hearing is held, or when the order cannot be consolidated with the Written Report of the Hearing because the report cannot be completed within the timeframe for issuing the order.)

   The appellant should be orally notified of the order immediately. A copy of the order should then be mailed to the appellant to ensure overnight delivery and documentation of receipt of delivery (e.g., FedEx or certified mail, return receipt requested). The center, DCMO, and OCC should be notified of the decision as soon as possible.

4. ***Additional Requirements After a Hearing***

a. Written Report of Hearing and Opportunity for Comment
The presiding officer must issue a written report of the hearing that includes a proposed decision confirming or revoking the detention by noon on the fifth calendar day after the appeal is filed. The report must include a finding on the credibility of witnesses (other than expert witnesses) whenever credibility is a material issue, and must include a proposed decision confirming or revoking the detention, with a statement of reasons. All written material presented at the hearing must be attached to the report.

The hearing participants must be given a four hour opportunity to submit comments on the report.

The presiding officer must issue the final order on the detention within the five calendar day time period after the appeal is filed. The completion of the written report of the hearing should not delay the order. Normally, the order is consolidated with the written report of the hearing. However, when the presiding officer needs additional time to complete the written report of the hearing, the report is separate from and will shortly follow the order.

b. Administrative Record of the Hearing
The presiding officer should prepare the Administrative Record of the Hearing, which consists of the following items (21 CFR 1.403(k)):

i. The notice of opportunity for hearing and the response (e.g., the detention order that indicates the opportunity for a hearing and the request for hearing or appeal without a request for a hearing);

ii. All written information and views submitted to the presiding officer in conjunction with the hearing;

iii. Any transcript of the hearing;

iv. All letters and memoranda of meetings and communications between participants and the presiding officer referred to in 21 CFR 16.44(c); and,

v. The presiding officer's written report of the hearing and any comments on the report, including comments on the proposed decision, by the hearing participant under 21 CFR 1.403(h).

The original Administrative Record of the Hearing should be filed with the firm's official file at the district office after completion of the report. A copy should be forwarded to the involved center compliance office for its information. A copy of the record should be sent to and maintained by the office of the presiding officer, if requested.

5. ***FOIA Requests***

   21 CFR Part 20 applies to all requests for documents involved in administrative detentions.

5-4 DETENTION OF FOODS – OTHER STATUTORY AUTHORITY

5-4-1 Purpose

This section contains the procedures for exercising FDA's authority to detain meat, poultry and egg products as delegated to FDA under the provisions of the Federal Meat Inspection Act (MIA), the Poultry Products Inspection Act (PPIA) and the Egg Products Inspection Act (EPIA).

For the purpose of this section only, the following definitions apply:

1. ***Meat And Meat Products***

   The carcasses of cattle, sheep, swine, goats, horses, other equines, parts of such carcasses, and products made wholly or in part from such carcasses.

2. ***Poultry And Poultry Products*** –

   The carcasses of domesticated birds, parts of such carcasses, and products made wholly or in part from such carcasses.

   EXCEPTION - In the case of both meat and poultry products, certain products are exempted from the above referenced Acts by USDA because they contain a relatively small portion of meat or poultry or historically have not been considered meat or poultry products.

3. ***Eggs***

   The shell eggs of the domesticated chicken, turkey, duck, goose or guinea.

4. ***Egg Products***

   Dried, frozen or liquid eggs, with or without added ingredients, except products exempted by USDA because they contain a relatively small proportion of eggs or historically have not been considered egg products.

5-4-2 Authority

The Federal Meat Inspection Act (MIA) as amended by Public Law (P.L.) 90-201 and Sections 19 and 20(b) of the Poultry Products Inspection Act (PPIA) as amended by P.L. 90-492 and Sections 19 and 23(d) of the Egg Products Inspection Act (EPIA) provide certain detention powers.

The detention authority under the MIA and the PPIA provide that FDA representatives may detain articles subject to these acts if they are outside a USDA inspected plant and there is reason to believe that the products are adulterated or misbranded under the Federal Food, Drug, and Cosmetic Act (the Act).

The detention authority under the EPIA provides that FDA representatives may detain products subject to that act if the products are found outside a USDA inspected plant and there is reason to believe that the products are in violation of the EPIA.

NOTE: Interstate Commerce is not a requirement for FDA jurisdiction over eggs and egg products because authority is based on violation of the Egg Products Inspection Act rather than the Federal Food, Drug, and Cosmetic Act (the Act).

The detention process is another regulatory tool to achieve compliance with the Act. It should be considered when such products are encountered during regular district operations, on assignment, or as a follow-up to complaints. This procedure becomes most appropriate when no immediate arrangements can be made for local or state authority to take control of the product, and/or it appears that the product will not be held voluntarily.

5-4-3 Criteria For Effecting And Terminating Detentions

Use the following procedures in detention situations:

1. Exercise Of Detention Authority

a. Meat and Poultry Products
Detentions may be made when all of the following criteria are met:

i. The article meets the jurisdictional requirement of interstate commerce in Section 304 of the Act and the article is in commercial channels;

ii. The article is located in an establishment that does not have USDA meat or poultry inspection service;

iii. The article is intended for human food or could readily be diverted into use for human food;

iv. The article is adulterated or significantly misbranded under the Act. (NOTE: Detentions based solely on misbranding or on adulteration involving Section 402(b) of the Act must be cleared by the Center for Food Safety and Applied Nutrition (CFSAN) before detention.); and,

v. The respective USDA, Food Safety Inspection Service District Office has been notified and the action is coordinated with that office.

b. Eggs and Egg Products
Detentions may be made when all of the following criteria are met:

i. The article is in commercial channels. (NOTE: Interstate commerce is not a requirement for jurisdiction under the Egg Products Inspection Act.);

ii. The article is located in an establishment that does not have USDA egg products inspection service;

iii. The article is intended for human food or could readily be diverted into use for human food; and,

iv. There is reason to believe the article is in violation of the Egg Products Inspection Act.

2. Termination Of A Detention Action

Detention should be continued until one of the following criteria is met:

a. State, county or municipal authorities have exercised jurisdiction and control of the article; or, in the case of meat or poultry, USDA has assumed control;

b. It has been determined that there is no significant violation of the Federal Food, Drug, and Cosmetic Act, or the Egg Products Inspection Act, and the USDA has been notified that we intend to terminate the detention action;

c. The detained article has been denatured, destroyed or reconditioned under appropriate supervision;

d. The detention period of 20 consecutive days, counting the day the detention was executed as the first day, has expired; or,

e. Seizure has been accomplished.

NOTE: Forward seizure recommendation as soon as possible after detention is accomplished, because the detention cannot be reinstated after the 20 day detention period expires.

3. Procedures

The IOM, Chapter 2, subchapter 2.7- Detention Activities contains specific inspectional instructions including initial reporting requirements, detention initiation, reconditioning, and termination.

5-5 ADMINISTRATIVE DETENTION OF DEVICES

5-5-1 Purpose

This section provides the procedures and defines responsibilities for the Administrative Detention of Devices.

5-5-2 Detention of Devices

1. ***Background***

Section 304(g) of the Act authorizes the FDA to detain devices intended for human use for a period of up to 30 calendar days if, during an inspection, the FDA has reason to believe the devices are adulterated or misbranded. The intent of administrative detention is to protect the public by preventing distribution or use of violative devices until FDA has had time to consider the appropriate action to take and, where appropriate, to initiate a regulatory action. The action of choice, in most cases, is a seizure. Detention of devices requires prior approval from the district director in which the devices are located and the concurrence of the appropriate center‘s director for compliance.

Any person entitled to claim the devices, if seizure occurred, may appeal the detention and may request a hearing on the appeal. The decision to affirm or revoke the detention must occur within five (5) working days of receipt of the appeal if there is no request for a hearing or if the request for a hearing is within 5 working days after filing the appeal. If requesting the hearing for a date more than 5 working days after receiving the appeal, the decision must occur within 5 working days after the conclusion of the hearing.

The Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH) are responsible for administering the medical device amendments.

2. ***References***

The regulatory authority for administrative detention and associated operations appears in Sections 304(g) and 201(x) of the Act, and in 21 CFR 800.55, 21 CFR Part 16, 21 CFR 5.47, and 21 CFR 10.19. The IOM Chapter 2, Subchapter 2.7, Detention Activities contains the instructions for implementing the detention authority.

3. ***Detention Policy***

This enforcement tool should be considered when there is likelihood that the device(s) will be moved or distributed before seizure can be accomplished. Whenever possible, state embargoes should be used instead of administrative detention because the latter can be resource intensive.

If the district director concludes that the person in possession of the device(s) will voluntarily hold the product, will provide assurance that integrity and security will be maintained over the devices on hand, and agrees to correct the violation(s) prior to shipment, there is no need to detain the goods.

At a minimum, prior to approving the detention order, the district director contacts the senior compliance official in the appropriate center to ensure that the Agency supports an administrative detention based on the violations observed. This ensures that the Agency considers recent policy developments or changes not yet communicated to the field. In addition, the district director notifies headquarters of the impending seizure recommendation.

Contacts are:

Director, Office of Compliance (HFZ-300), CDRH (301) 594-4692 or, if a biological device:

Director, Office of Compliance and Biologics Quality (HFM-600), CBER (301) 827-6190.

Concurrence is by telephone. The field or headquarters does not require written concurrence except for cause, for example, for issues of science, policy, or law involving precedent or questionable facts.

a. Approval of Detention Order By The District Director

The district director approves a detention order, before issuance, either orally or in writing. If the approval is oral, it should be placed in writing as soon as possible.

b. Detention Order Issuance

An investigator or other authorized agent signs the order. Issue the order in writing to the owner, operator, agent, or other responsible person in charge of the place where the device is located.

When issuing the order, the FDA investigator informs the owner, agent or other responsible person that they have the opportunity to appeal and have a hearing on the detention as noted on the order. If the order is not issued to the owner or agent of the owner of the device, then the district sends, as soon as possible, copies of the detention order and 21 CFR 800.55(g)(1)& (2) to the owner, via certified mail return receipt requested.

c. Form of Order

Issue the detention order on Form FDA 2289 Detention Notice.

Section 2.7.2.3 of the IOM contains instructions for completion of the form.

The detention order frames the issues for appeal or informal hearing, which may result from the detention. Therefore, the information on the order concerning the reason for detention is very important.

There is no requirement that the order include all of the reasons for believing that the product is adulterated or misbranded. Only list the more significant violations. However, if a violation is not identified in the order, it may not be relied on to support the detention. State the charge in the order in factual, non-statutory language. For example, if the investigator finds a sterile, individually packaged syringe with holes along the seams of the packaging, black greasy spots on the needle, and the label lacks the Zip Code of the manufacturer, describe the apparent violation in the reason for detention as "there is reason to believe the device is:

Adulterated per Section 501(a)(2)(A) of the Act because there are holes in the package and black spots on the needles. The firm prepared, packed, or held the product under insanitary conditions whereby it may have been rendered injurious to health.

Misbranded per Section 502(a) because the label states that it is sterile and the integrity of the package is compromised by holes. The labeling is false or misleading."

Note: Use a "continuation sheet" if all of the charges will not fit on the form.

Note: Charges used in the detention order do not necessarily limit the charges

that may be identified in a subsequent complaint filed in court.

d. Length of Detention

According to statute, a detention is for 20 calendar days unless the district believes that additional time is required to accomplish a legal action. In such cases, the detention is for 30 calendar days at the time of issuing the order. When extending a detention from 20 to 30 days, issue another detention order and place new tags on the devices.

By statute, the detention cannot last for longer than 30 calendar days.

e. Movement, Use, etc. of Detained Devices

Except as noted below, without the written permission of the Agency, detained devices cannot be moved, used, altered, or tampered with in any manner. Therefore, if possible, the investigator should segregate the detained devices from other devices or products at the time of the detention so they remain undisturbed.

With the approval of the district director, the investigator who detained the devices or any other responsible district official may authorize, in writing, the movement of detained material. Whoever moves the devices must immediately notify (orally) the authorizing official of the new location.

The only exception to the prohibition on movement without written permission is when the goods are not in final form for shipment and the manufacturer wants to complete work on them. The manufacturer may move them within the facility where detained to complete manufacture, but must orally notify FDA of the movement as it occurs. When completing manufacturing, the manufacturer must immediately segregate the detained devices from other products and orally notify FDA of their new location.

However, the manufacturer may not move the devices from the establishment without prior written approval of the district director as referenced above.

Note: 21 CFR 800.55(h)(2) prohibits further movement even within the establishment without FDA approval.

f. Legal Actions Against Detained Devices

The district should expedite the preparation and processing of a seizure recommendation involving the detained devices. The recommendation should be flagged to indicate that it involves detained devices and show the date the detention expires, and should be forwarded to the responsible center by overnight delivery service.

The center compliance office, ORA, and OCC should likewise expedite their reviews to accomplish the legal action prior to expiration of the detention. If the detention expires prior to the seizure, the person who owns the devices may

move the goods and the violative product may find its way into commercial distribution.

The district is responsible for monitoring the length of the detention and the progress of the recommendation. If a 20-day detention expires prior to accomplishing the legal action, the district should extend the detention for an additional 10 days.

The district is responsible for coordination with the U.S. Attorney's office and the Marshal's Service, ensuring prompt filing of the complaint, and seizure of the goods.

The district is also responsible for immediately providing oral notice to the appropriate center compliance office, OCC, and the presiding officer of the accomplishment of the seizure or of any appeal of a detention order.

g. Recordkeeping Requirements

At the time of issuance of a detention order, or as soon as possible thereafter, the district informs the owner, operator, or agent in charge of the establishment where the devices are detained of their responsibility to establish and maintain records as required by 21 CFR 800.55(k).

h. Termination of Detention Orders

i. The reasons for termination of Detention orders:

- FDA determines that the device(s) is (are) not violative.
- FDA approves voluntary destruction or compliance by reconditioning or other means (e.g., relabeling).
- FDA revokes the detention on appeal.
- FDA accomplishes a regulatory action against the product. Actual seizure or entry of TRO or an order by consent or otherwise of preliminary injunction is necessary. The filing of a complaint does not necessarily terminate a detention order.
- The detention period expires.

The district director, within whose district the devices are detained, must approve termination of detention orders. Approval is oral or written, and if oral, confirmation is in writing. The district issues the Detention Termination Notice (Form FDA 2291) to the person(s) who received the Detention Notice, or his representative and, if movement of the devices occurred prior to the termination, to the person possessing the devices. Issuance of the notice is in person or by mail. If the termination notice is issued by mail, request that the Detention Tags (Form FDA 2290) be returned. If the termination notice is issued in person, see IOM 2.7.2.5 for instructions. Per 21 CFR 800.55(k)(2), the district issues a statement

advising the owners, operators, or agents in charge to keep the records concerning the detention for the remainder of the two year period from the date of detention or such shorter period as FDA directs.

4. ***Responsibilities for Issuing and Terminating Detention Orders***

a. District Responsibilities As referenced above, the district is responsible for:

i. Ensuring support from the senior compliance official of the appropriate center before issuing a detention order.

ii. Issuing the detention order.

iii. Notifying the Director of the Division of Compliance Management and Operations (DCMO) by phone of the detention and supplying that person with a copy of the detention order by the most expeditious means available (fax, express mail, etc.) immediately after issuance.

iv. Approving and monitoring the movement of detained devices.

v. Notifying the regional director that the district issued a detention order. NOTE: Keep the Regional Food and Drug Director (RFDD) insulated from detention proceedings after the detention is in place in order to avoid even the appearance of bias or prejudice.

vi. Pursuing the follow-up legal action as discussed under the heading, "Legal Actions Against Detained Devices."

b. Center Compliance Office Responsibilities

District contact with the center, for concurrence, is a routine procedure. If the director of compliance for the center will not support a proposed detention, do not issue the order. Communication of the director's decision to the district is by phone, e-mail, or other expedited communication. Generally, a formal submission of documents supporting detention is not necessary.

The compliance office will quickly review any information provided by the district, through DCMO, alert the district, DCMO, and OCC of any problems, and forward to the district all requested documents. The compliance office will provide expert witnesses and other support, as appropriate.

c. Office of Chief Counsel Responsibilities

OCC will quickly review any information provided by the district, and through DCMO, alert the district, the center office, and DCMO, of any problems, prior to the detention being put in place.

The Deputy CC for Litigation or the Deputy CC for Regulations and Hearings shall make staff assignments in OCC and notify the center and DCMO of the attorney assigned to the case. OCC will begin preliminary preparations for any appeal. OCC will determine whether the district and the RFDD require legal counsel.

d. DCMO Responsibilities

Upon notification that a detention has been affected or a subsequent appeal received by the district:

DCMO will immediately notify the center compliance office and OCC, and deliver to them copies of the detention order, request for hearing, and other supporting documents. DCMO will coordinate the detention to ensure that all Agency and OCC components receive notification and prepare for a hearing in a timely manner.

e. RFDD Responsibilities

The RFDD must insulate himself/herself, after the detention is in place, from all aspects of a detention except those relating to his/her responsibilities as a presiding officer. Responsibilities at that time are in the next section, "Appeal of a Detention Order."

5-5-3 Appeal Of A Detention Order

1. ***General Information***

a. Background

Section 304(g) of the Act permits anyone who is entitled to claim the goods, if seized, to appeal a detention order.

If appealing the detention, Section 304(g) requires that the Agency afford the appellant with an opportunity for an informal hearing. If the appellant does not request an informal hearing, the decision to affirm or revoke the detention must be rendered within 5 working days after the filing of the appeal. The appellant may request the holding of an informal hearing either within 5 working days after filing the appeal or at a later date, but not later than 20 calendar days after receipt of the detention order (21 CFR 800.55(g)(1)). If the appellant requests a hearing within 5 working days after filing the appeal, the presiding officer holds the hearing and renders a decision within 5 working days of the filing of the appeal. In the event of a request for a delayed hearing, the scheduling of the hearing must occur after the fifth working day following the appeal, and a decision must be issued within 5 working days of the hearing's conclusion.

Regardless of the scheduling of the hearing, there is no extension past the 30-calendar day detention period without the consent of the appellant. (The provision for extension of the detention found in 21 CFR 800.55(g)(6) is incorrect and should not be followed.)

b. Time to Appeal

The regulations allow an appellant 5 working days from the receipt of the detention order (which also serves as a notice of opportunity for a hearing) to appeal the detention, with or without a request for an informal hearing. The

appeal must be in writing, must be addressed to the district director of the district office within whose area the goods are detained, and must contain a statement asserting that interest (e.g., ownership) in the detained goods would qualify the appellant to claim the goods if they were to be seized. The postmark on the appeal letter will determine the date of the appeal.

The district director will allow 1 day of additional time for the receipt of an appeal request. Allow additional time if the appellant shows that it was impossible to appeal earlier.

c. Presiding and Deciding Official

The RFDD for the region where the district is located and in which the goods were detained must be the presiding and deciding official unless he/she disqualifies him/herself (21 CFR 800.55(g)(4), 21 CFR 16.40 and 16.42, and 21 CFR 5.47). In the event of disqualification, the RFDD will immediately arrange for another RFDD to preside and provide immediate notification of any such change to the district director and the appellant.

Communications Between Parties to the Hearing And the Presiding Officer
Avoid any off-the-record communication between parties to the hearing and the presiding officer. If any such communication occurs, reduce it to writing and make it a part of the record. The presiding officer must supply a copy of any memoranda of such communication, which would affect his or her decision, to the other party, giving them an opportunity to respond (21 CFR 16.44(b)).

The person who originates any written communication between a participant in the hearing and the presiding officer must send a copy of any such communication to all of the participants (21 CFR 16.44(c)).

2. ***Appeal Processing Responsibilities***

a. District Responsibilities

Preparation for an appeal should begin when the district decides to detain a device(s), in case a hearing is requested within 5 working days of the filing of the appeal.

i. When the district receives an appeal, the director:

- Dates and time stamps the appeal, and notifies the appellant of receipt of the appeal. If the appeal does not specify that a hearing is or is not requested, does not demonstrate ownership or proprietary interest as required in 21 CFR 800.55(g)(1) and (2), or does not specify the time period within which to hold a hearing (see “Appeal of a Detention Order- Background"), contact the appellant and clarify this information. Make any declaration of ownership or proprietary interest in writing.

- Orally notifies the RFDD and the Director, DCMO of the appeal

immediately and forwards a copy of the appeal to them as soon as possible. Requests assistance of OCC and the appropriate center for completing the next item.

ii. When the appeal includes a request for a hearing:

- Prepare (1) a general summary of the information that supports the detention and (2) a comprehensive statement of the basis for the action. The Detention Order (notice) may serve as the comprehensive statement only if the reason for detention is described in sufficient detail. See Exhibits 5-14 and 5-15 for an example of a general summary and a comprehensive statement respectively. See Exhibit 5-16 for examples of reasons detailed enough for the FDA 2289 to serve as a comprehensive statement.

- Forward the general summary and comprehensive statement to the appellant (21 CFR 16.24(f) and Section 201(x)(3) of the Act), the RFDD, and any office and OCC representatives to the hearing. Send the documents immediately so that they arrive as soon as possible, but at least 1 day prior to the hearing.

- At least 1 day before the hearing, provide the appellant, the RFDD, and any office and OCC representatives to the hearing, written notice of, or copies of, if they could not reasonably be expected to obtain copies, any published articles or written information to be presented at or relied on at the hearing (21 CFR 16.24 (g)).

iii. When the appeal does not include a request for a hearing, the district forwards all the information that supports the detention to the RFDD acting as the deciding official. The district includes the referenced general summary and comprehensive statement and any additional information provided by the appellant. It must arrive within sufficient time to be reviewed and for a decision to be rendered within 5 working days after receipt of the appeal.

b. Presiding RFDD Responsibility

When notified of an appeal, the RFDD

i. If a hearing is requested,

- Orally contact the parties as soon as possible. Depending on the time period within which the appellant requests a hearing, either set a hearing date and time to allow for a decision within 5 working days after the date of receipt of the appeal by the district, or set a hearing date and time later than 5 working days after receipt of the appeal by the district, but not later than 20 calendar days after issuance of the detention order. The hearing normally takes place at the district office where the goods are

located.

- Provide all parties with written notification of the time, date, and location of the hearing.
- Provide the appellant with oral and written notification (see form letter as Exhibit 5-17) of the following:

i. Notification of those portions of 21 CFR Part 16 that are excluded or modified under 21 CFR 800.55(g)(3) and waived or modified for hearings on appeal of administrative detentions (see "Informal Hearing on Appeal of a Detention Order.")

ii. Notification that the informal hearing is not a public hearing per 21 CFR 16.60(a), in order to protect investigatory records compiled for law enforcement purposes that are not available for public disclosure under 21 CFR 20.64, or trade secret material under 21 CFR 20.61.

iii. Notification that the appellant should provide, at the hearing, a brief summary of any lengthy documents for presentation at the hearing (e.g., volumes of computer printouts).

iv. Notification that if feasible, at least 1 day before the hearing, the appellant should provide the district director written notice of, or a copy of (if the district director could not reasonably be expected to obtain a copy), any published articles or written information for presentation at or relied on at the hearing as required by 21 CFR 16.24(g).

v. Notification of the requirements under 21 CFR 16.44(c) (see "Communications Between Parties to the Hearing and the Presiding Officer.")

ii. If an appeal is made but no hearing is requested, the presiding officer must immediately orally notify the parties to submit information supporting their positions as soon as possible so that the information can be reviewed and a decision reached within 5 working days of the receipt of the appeal. We will accept additional information submitted prior to the decision. The presiding officer orally notifies the appellant of the requirement under 21 CFR 16.44(c) (see "Communications Between Parties to the Hearing and the Presiding Officer.")

When advice of the CC is needed, contact the Deputy CC for Litigation.

5-5-4 Informal Hearing On Appeal Of A Detention Order

Section 304(g) of the Act states that upon appeal of a detention order, the Agency will afford the appellant with an opportunity for an "informal hearing." Section 201(x) of the Act defines an informal hearing and lists specific provisions. 21 CFR 800.55(g)(3) provides that 21 CFR Part 16, Regulatory Hearing, establishes the procedures for conducting the informal hearing. 21

CFR 16.5 of the regulations advises that Part 16 procedures apply to the extent that they are supplementary to, and not in conflict with, other procedures specified for the hearing. 21 CFR 16.60(h) gives the presiding officer the power to suspend, modify, or waive provisions under Part 16.

1. ***Waivers, Modifications, Etc. To 21 CFR Part 16***

   21 CFR 800.55(g)(3) waives the following sections of 21 CFR Part 16:

   a. §16.22(a) concerning the issuance of a separate notice of opportunity for hearing because the detention notice FDA 2289 serves that function under 21 CFR 800.55(g)(3)(i).

   b. §16.22(b) concerning the forwarding of the appeal to the presiding officer because 21 CFR 800.55 (g)(1) requires sending the appeal to the district director.

   c. §16.24(e) concerning not permitting the hearing to be held within 2 days of the receipt of the appeal because time constraints cannot allow for such a restriction.

   d. §16.42(a) regarding those persons who may act as the presiding officer because 21 CFR 800.55(g)(4) only allows RFDDs to be presiding officers.

   The presiding officer has the authority to waive, suspend, or modify any of the provisions under Part 16 (21 CFR 10.19 and 21 CFR 16.60(h)). The presiding officer must waive the following other provisions:

   a. §16.60(f) which requires the hearing officer to make a recommended decision with statement of reasons to the deciding official because the RFDD performs both functions.

   b. §16.95(b)(1) & (2) which state that the Administrative Record of a Regulatory Hearing (21 CFR 16.80(a)(1)-(5)) is the exclusive record and basis for the decision, are modified as follows: FDA bases the decision, in most cases, on all information presented to the presiding officer prior to or during the hearing. The decision is not to be based on the following information or documents, if they are not received or completed by the presiding officer within the time necessary for the presiding officer to review or complete them prior to making the decision as required by the Act or regulation:

      i. Information and views submitted to the presiding officer after the hearing are not part of the official record unless the presiding officer permits post-hearing submissions and submittal of information occurs within the period specified by the presiding officer (21 CFR 16.80(a)(2)).

      ii. Any transcript of the hearing (21 CFR 16.80(a)(3)).

      iii. The presiding officer's report of the hearing and comments on the report under 21 CFR 16.60(e) and 16.80(a)(4).

   FDA waives that part of 21 CFR 16.60(b) which provides that all parties may confront and conduct reasonable cross-examination of any person (except for the presiding

officer and counsel for the parties) who makes any statement on the matter at the hearing. There is an allowance for reasonable questions instead. Reference Congressional intent: House of Representatives Report no. 94-853. Also, see 21 CFR 16.5 and 16.60(h).

2. ***Responsibilities for the Hearing***

   a. CENTER Responsibilities
   The center will provide documents, witnesses, or office representatives for the hearing if requested by the district or the OCC attorney counseling the district.

   b. Office Of Chief Counsel Responsibilities
   OCC will provide for the district and/or the presiding officer, as appropriate, for the hearing.

   c. District And Presiding RFDD Responsibilities
   The section “Conducting the Hearing” includes individual responsibilities of the district and the presiding RFDD.

3. ***Conducting The Hearing – General Procedures/Responsibilities***

   At the onset, the presiding officer reminds the parties of the modifications to Part 16 that apply and explain the purpose or issue of the hearing. The issue at the hearing is whether FDA had reason to believe the devices were adulterated or misbranded at the time of the detention and as charged in the detention order. The issue is not whether the law has been violated. That question is properly left to the court trial, if one is held.

   The FDA representative(s) is present to explain the bases for the detention and answer reasonable questions from the appellant.

   The appellant then presents relevant information and reasons why he believes the Agency did not have reason to detain the product.

   The FDA representatives may then ask reasonable questions (see Section 201(x)(4) of the Act).

   The presiding officer ensures that the material presented and the questions asked are relevant to the issue of the hearing.

   The appellant may request a transcript of the hearing. However, the appellant must pay the cost of it and furnish the presiding officer a copy for the record. The Agency can also request a transcript of the hearing and the costs are borne by the government.

   If the appellant wishes a copy of the government transcript, he/she may obtain it via a Freedom of Information (FOI) Act request. 21 CFR Part 20 applies to the release of the transcript.

   The presiding officer notifies the parties that his decision will not await transcription or correction of the transcripts so ordered.

5-5-5 Requirements After A Hearing On Appeal Of A Detention Order

1. ***Presiding RFDD Responsibility***

   a. Confirming or Revoking the Detention Order

      i. Time Period for Rendering Decision

      As referenced in "Appeal of a Detention Order - Background," the presiding officer must by order, confirm or revoke the detention order within 5 working days of the receipt of the appeal by the district director, if there is no hearing requested or if the appellant requests a hearing within 5 working days. However, if the appellant requests a hearing later than the referenced 5 working day time frame, but not later than 20 calendar days after issuance of the detention order, then the presiding officer must, by order, confirm or revoke the detention order within 5 working days after the close of the hearing (21 CFR 800.55(g)(5) and (6)). The detention may not be extended past the otherwise applicable 30-day period (see "Appeal of a Detention Order - Background") without the consent of the appellant.

      ii. Basis for Rendering Decision

      If the Agency can show that it had a reason to believe that the devices were adulterated or misbranded at the time of the detention under one or more of the charges in the detention order, the presiding officer will affirm the detention order. If not, the presiding officer will revoke the detention order.

      iii. Issuance of the Order

      The decision is issued in the form of an order. (See Exhibit 5-18 for model order.) The parties to the appeal should be orally notified of the order immediately. Copies of the order should then be mailed to them via certified mail return receipt requested.

      FDA must order the decision rendered on the detention within the above time frames; however, the completion of the written decision and report of the hearing (discussed below) cannot delay the order. Normally, the order is consolidated with the written decision and report of the hearing. However, there are cases when the Agency needs additional time to complete the written decision and report of the hearing. In that case, it is separate from and will shortly follow the order.

   b. Written Decision and Report of Hearing

   The presiding officer must prepare a written decision to include the reasons and basis for his decision (§ 16.95(b)(2)). The written decision must include the report of the hearing required by Section 201(x)(5) of the Act and 21 CFR 16.60(e). All written material submitted during the hearing must be attached to the written decision and report of the hearing (Section 201(x)(5) of the Act and 21 CFR 16.60(e)). Any transcripts of the hearing must be included.

Whenever time permits, the participants will be given the opportunity to review and comment on the written decision and report of the hearing. However, the presiding officer should set a time limit for the participants to comment. (As previously noted, whenever possible, the written decision and report of the hearing should be issued with the order as a single document).

c. Administrative Record of the Hearing

The presiding officer must prepare the Administrative Record of the Hearing, which consists of the following items:

i. The detention order and the appeal.

ii. All written information and views submitted to the presiding officer in conjunction with the hearing.

iii. Any transcript of the hearing.

iv. The presiding officer's written decision, report of the hearing, order, and any comments on the written decision or report of the hearing permitted under Section 201(y) of the Act and 21 CFR 16.60(e).

v. All letters and memoranda of meetings and communications between participants and the presiding officer referred to in 21 CFR 16.44(c).

File the original Administrative Record of the Hearing with the firm’s official file at the district office after completion of the report. A copy should be forwarded to the center involved for its information. A copy should be maintained in the office of the RFDD that held the hearing.

2. ***FOI Requests***

21 CFR Part 20 applies to all requests for documents involved in administrative detentions

5-6 LICENSE REVOCATION OR SUSPENSION

5-6-1 Purpose

This section contains procedures for revoking and suspending biologic licenses issued under the Public Health Service Act. These procedures are applicable to actions recommended by the field or by CBER.

"Revocation" is the cancellation of a license and the withdrawal of the authorization to introduce or deliver for introduction into interstate commerce, biological products, at either the request of the manufacturer or when grounds exist for the Agency to initiate such an action.

"Suspension" is a summary action taken by the Agency and may be an initial or intermediate step in the revocation process. Suspension provides for the immediate withdrawal of the authorization to introduce or deliver for introduction, biological products into interstate commerce when the Commissioner has reasonable grounds to believe that any of the grounds for revocation exist and that by reason thereof there is a danger to health.

5-6-2 General

Licenses issued for the manufacture of specific biologic products under the provisions of Section 351(a) of the PHS Act, may be: 1) revoked upon request of the licensee or by initiative of the Commissioner when sufficient grounds exist; or 2) suspended if one or more of the grounds for revocation exists and presents a danger to health (see 21 CFR 601.5 and 601.6).

CBER's Office of Compliance and Biologics Quality (OCBQ), Division of Case Management (DCM) reviews recommendations for license revocation and suspension proposed by the field offices or the appropriate unit within CBER. If DCM concurs with the recommendation, it is forwarded to the Office of Chief Counsel (OCC) for review. If OCC concurs, the recommendation and action letter are sent to the Director, CBER for concurrence and signature. Pursuant to SMG 1410.203, the Commissioner has delegated the authority to issue notices of revocation and suspension to the Director and Deputy Director, CBER.

OCBQ ensures that recommendations for license revocation or suspension are supported with evidence of violations of the applicable statutes and regulations. License suspensions and revocations are significant enforcement actions with possible far-reaching consequences. As such, it is important to consider the impact that the action may have on product supply as part of the Agency's review of a proposed license suspension or revocation action.

When the license relates to multiple locations, revocation may be limited to one or more of the locations, if inspectional findings support that approach.

In the absence of willful noncompliance or a history of violations of a significant nature, the district or CBER inspection review unit considers issuing a Warning Letter or conducting a meeting with the firm, rather than recommending revocation as a first choice remedy.

Part V of the Compliance Program Guides for inspections of CBER-regulated products contains information on deviations that may warrant regulatory or administrative action. These inspection programs are located at: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ComplianceActivities/Enforcement/CompliancePrograms/default.htm.

5-6-3 General Considerations For Revocation

The Agency may consider revocation of a biologic license when any of the conditions specified in 21 CFR 601.5 exist. In establishing that the grounds for revocation in 21 CFR 601.5 are met, the recommending unit considers the two courses of action provided in the regulations: 1) notice of intent to revoke with the possibility of demonstrating or achieving compliance, or 2) in cases involving willfulness, notice of FDA's intention to move directly to revocation without providing an opportunity to demonstrate or achieve compliance.

1. ***Notice of Intent to Revoke***

   Inspectional findings must demonstrate a current history of repeated or continuous significant deviations that represent a breakdown of process controls, rather than isolated incidents. Ordinarily, a demonstration of prior warning to the firm is via Warning Letter and/or a meeting or other contact with the firm before consideration of license revocation. If a past Warning Letter issued and one or more non-violative inspection(s) follows it, a recommendation for license revocation based on current significant deficiencies must document whether the deficiencies are of a continuing nature and

how the current inspection relates to any previous inspection which resulted in the Warning Letter or other communication with the firm that provided the firm notice of such deficiencies. Issuance of a Warning letter in the past may not preclude issuance of an additional Warning Letter, especially if the nature and cause of the violation have changed. For example, a firm issued a Warning Letter three years ago for viral marker testing violations may warrant issuance of another Warning Letter or other action, rather than proceeding to license revocation, if the current inspection shows violations in different areas of the operation or manufacturing practices, e.g., computer validation.

In addition, FDA may proceed to revocation upon suspension of a license, as provided by 21 CFR 601.6(b).

Upon issuance of a "Notice of Intent to Revoke" letter (except in cases involving willfulness), we provide the licensee an opportunity to demonstrate or achieve compliance before instituting proceedings for revocation of the license.

2. ***Direct Revocation***

   FDA may proceed directly to revocation in cases involving willful conduct.

   Willful conduct is established by showing that an individual: 1) knowingly committed a prohibited act, such as records falsification or concealment; or 2) acted with careless disregard of the regulatory requirements, as exemplified by repeatedly failing to correct violations. In cases involving willfulness, FDA ordinarily does not provide the licensee with the opportunity to demonstrate or achieve compliance, in accordance with 21 CFR 601.5(b). In all cases, FDA notifies the licensee of the opportunity to request a hearing pursuant to 21 CFR 12.21(b).

5-6-4 Issues Not Supporting License Revocation

CBER ordinarily will not support license revocation when the following issues are the basis for the recommendation to revoke:

1. ***Biological Product Deviation Reports***

   Biological product deviation reports, in and of themselves, ordinarily may not form the basis for a license revocation unless the firm failed to recognize the error, failed to investigate and properly document the investigation, and/or failed to implement corrective action to prevent its recurrence, or failed to notify FDA if so required under 21 CFR 600.14. In addition, in order to meet the grounds for license revocation, the deviation must be of such a nature or extent as to represent a firm's failure to establish or maintain control over one or more of the systems employed for the manufacture of biological products.

2. ***Isolated Incidents***

   Isolated occurrences do not ordinarily establish grounds for license revocation, unless there is documentation to demonstrate that the occurrences represent a pattern of violative activity.

3. ***Past Violations***

Violations that occurred prior to the current FDA inspection (and for which implementation of appropriate corrective action prevents reoccurrence) ordinarily do not form the basis for license revocation. However, FDA must document previous violations even with correction, or no repeats, because they may demonstrate a pattern or history of non-compliance. If violations persist, such a pattern is pertinent to a future decision to proceed to revocation.

5-6-5 Revocation Procedures

If the inspection review unit is considering revocation as an enforcement option, contact CBER, DCM, during the inspection or soon after issuance of the FDA 483. Discussions with CBER prior to submission of a recommendation will facilitate the processing of the recommendation.

If the inspection review unit believes license revocation is appropriate, that office submits a recommendation to DCM for revocation with supporting documentation. Include the district director's concurrence on recommendations for revocation. In addition to forwarding documentation of the violations, the recommending unit submits a detailed summary of the firm's inspectional and compliance history over the past five years. The recommending unit also assesses the impact of license revocation on the supply of the biological products involved. The initial CBER contact is DCM, HFM-610, (301) 827-6201, FAX: (301) 594-0940.

CBER assigns a consumer safety officer from HFM-610 to each revocation recommendation. If using express delivery, send to:

Food and Drug Administration
Center for Biologics Evaluation & Research
Attn: Division of Case Management (HFM-610)
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448

CBER personnel review the information received and determine whether the inspectional findings support revocation of the firm's license.

If CBER does not concur with the revocation recommendation, it communicates its decision to the recommending unit. CBER sends a memorandum confirming the reasons for the disapproval and provides other enforcement options, if appropriate.

If CBER concurs with the district's recommendation, it prepares an Action Memorandum with supporting documentation to the Director, CBER, and a letter notifying the licensee of the Agency's intention to initiate proceedings to revoke the license. This package is forwarded to the Office of Chief Counsel (OCC) for review (see RPM Chapter 4, Exhibit 4-1). If OCC concurs, the recommendation and action letter are sent to the Director, CBER for concurrence and signature. Recommendations that CBER has initiated are also routed to the Director of CBER for clearance. Prior to doing so, however, the CBER initiating office contacts the appropriate district office to advise the district of the action proposed by CBER.

After the Director signs the letter, the Director, DCM verbally advises the most responsible person at the firm of the Agency's intention to revoke the license. DCM then transmits a copy of the letter to the firm via facsimile and mails the original letter as Certified/Return Receipt Requested.

CBER's OCBQ advises the district office and/or recommending unit within CBER of the action concurrently. In addition, they transmit copies of the Action Memorandum and the revocation letter to the recommending unit via facsimile or electronic mail.

Both CBER and the recommending unit review the establishment's response to the letter of revocation expeditiously. The recommending unit provides CBER with its conclusions and comments regarding the adequacy of the firm's response.

The Agency usually gives an establishment the opportunity to demonstrate or achieve compliance. If the establishment has not waived its opportunity for a hearing by voluntarily requesting revocation, CBER's OCBQ and the firm continue to correspond until all corrective actions appear satisfactory. CBER will distribute copies of all correspondence between CBER and the firm to the recommending unit for review. When the recommending unit and CBER's OCBQ agree that all corrective actions appear satisfactory, CBER will ask the district office to conduct a follow up inspection expeditiously.

The district will advise CBER of the approximate date of reinspection and notify CBER by telephone or electronically of its findings and recommendation. Afterwards, the district sends a written recommendation either to move toward revocation or to discontinue proceedings for license revocation.

In some instances, the firm may have made significant progress in demonstrating or achieving compliance, but after review of the FDA 483 and the firm's response(s), the district and/or CBER may view a limited follow-up inspection as necessary prior to making a final determination on the matter of revocation.

Following reinspection, if CBER and the district determine that the firm demonstrated or achieved compliance, CBER will notify the firm of this determination.

In cases involving willfulness, ordinarily the establishment has 10 days from the date of the revocation letter to waive the opportunity for hearing by requesting voluntary revocation in writing. If the establishment does not waive the opportunity for a hearing by surrendering the license within the ten-day time frame, DCM forwards a request to the Division of Regulations and Policy, HFM-17, to prepare the Federal Register Notice of Opportunity for Hearing.

FDA publishes the Notice of Opportunity for Hearing on a proposal to revoke a license in the Federal Register together with an explanation of the grounds for the proposed action. A person subject to the notice has 30 days after its issuance to request a hearing. There is no extension of the 30-day period. A request for hearing must set forth specific facts showing that there is a genuine and substantial issue of fact that justifies a hearing, and may not rely upon mere allegations or denials.

5-6-6 General Considerations For Suspension

Pursuant to 21 CFR 601.6, the Commissioner may suspend a license if the Commissioner has reasonable grounds to believe that any of the grounds for revocation exist and that by reason thereof there is a danger to health. Investigators obtain documentary evidence to support revocation and danger to health, and CBER conducts an evaluation of the danger to health.

Once CBER determines that a danger to health exists, the recommending unit immediately contacts the appropriate state health authorities. In addition, the district considers legal actions such as injunction or seizure, particularly if a given state health department lacks regulatory

authority over intrastate operations or if the license suspension does not result in immediate corrective action. The recommending unit provides CBER with any information obtained regarding the state health department authority and the likelihood it may take regulatory action based on FDA's findings.

If a blood establishment is involved, the recommending unit determines the approximate number of annual collections and the percentage of blood products distributed in interstate commerce. The recommending unit, together with CBER, examines supply issues and considers contacting the large national blood organizations to ensure that a license suspension will not adversely affect the public health.

As in the case of revocation, when there are multiple locations encompassed by one license, suspension may be limited to one or more of the locations, if inspectional findings warrant that approach.

5-6-7 Suspension Procedures

If the inspecting unit believes a danger to health exists, it should contact CBER's DCM, HFM-610, 301-827-6201 immediately, during the inspection, and provide specific, substantive information relating to the grounds for suspension. It must not wait until the conclusion of the inspection to make contact. At that time, DCM assigns a consumer safety officer from HFM-610 to the suspension recommendation who will work with the investigators in case development.

The inspecting unit should transmit a copy of the FDA 483 (draft or final copy) as quickly as possible to DCM by facsimile, electronic mail, or express delivery, along with any additional requested preliminary information and/or documentation. To avoid delay, do not send supporting documentation through the regular mail system if other means of transmission are available. If using overnight express delivery, send to:

Food and Drug Administration
Center for Biologics Evaluation & Research
Attn: Division of Case Management (HFM-610)
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448

DCM will consult, as necessary, with the appropriate scientific/medical staff to determine if a danger to health exists. If a danger to health exists, the inspecting office will be advised and should submit a recommendation in a brief memorandum that includes the basis of the recommendation. Transmit the recommendation by facsimile (301 594-0940) or by electronic mail. Recommendations for suspension are given a high priority and supervisors are to act promptly. Recommendations for suspension should have the concurrence of the district director. The district will make every effort to expedite the submission of a recommendation to CBER to suspend operations under license at an establishment whose practices present an imminent danger to health.

Frequently DCM may concur with a suspension recommendation after receiving the FDA 483 but before receiving the Establishment Inspection Report (EIR). In cases involving complex issues, DCM may need to review the completed EIR before reaching a decision. In either event, write the EIR promptly and forward by express mail service to DCM.

Depending upon the products involved, CBER may ask the recommending unit to obtain a complete inventory of the products on the firm's premises.

If DCM concurs with the suspension recommendation, it will prepare an Action Memorandum and a letter of suspension within three working days of receipt of the recommendation. Documents will be sent to OCC for review as soon as available (see RPM Chapter 4, Exhibit 4-1). Upon OCC concurrence, the Director, CBER, who notes the date and time of signature, signs the Action Memorandum and letter of suspension. The Director, OCBQ or DCM will immediately telephone the firm and advise it of the suspension of its biologics license. DCM will then send the letter to the firm by facsimile and certified mail.

CBER may concurrently advise the recommending unit of FDA's action. In some situations, CBER may arrange to transmit a copy of the suspension letter to the district for hand delivery to the firm.

If CBER does not concur with a suspension recommendation, it communicates its decision to the recommending unit. DCM will prepare a memorandum explaining the reasons for the disapproval. If CBER disagrees with the suspension recommendation based on the absence of a danger to health, and any of the conditions specified in 21 CFR 601.5(b) exist, DCM considers whether it is appropriate to revoke the license or send a Warning Letter and will discuss these options with the recommending unit.

DCM and the recommending unit concurrently review the reply to a letter of suspension and continue to correspond with the firm until both agree that all corrective actions appear satisfactory. At this point, DCM notifies the firm, ordinarily by telephone (later confirmed by letter), that limited operations may resume for the purpose of a reinspection to determine that the corrective actions implemented are effective. CBER requests that the district office conduct a follow up inspection expeditiously, generally within 30 days of resumption of limited operations.

The district office advises CBER of the approximate date of reinspection. As soon as possible upon its conclusion, the district notifies CBER by telephone of its findings and recommendation (CBER contact is DCM, HFM-610, 301-827-6201). The district follows-up by sending a written recommendation on the last day of the inspection or shortly thereafter. If issuing a FDA 483, the district forwards a copy of the firm's response, if any, to CBER. In addition, the district sends a written copy of the establishment inspection report to CBER as quickly as possible to support continued suspension, revocation or reinstatement.

In some instances the firm may have made significant progress in achieving compliance, but after review of the FDA 483 and the firm's response(s), the district and/or CBER may view a limited follow-up inspection as necessary prior to making a final determination as to whether to recommend reinstatement of the license.

If the follow-up inspection indicates inadequate corrective actions and continued deviations, the district obtains additional documentation and notifies CBER as soon as possible. CBER decides whether to allow the firm to continue in limited operations or to cease all operations. In addition, CBER considers the possibility of proceeding toward license revocation.

If the firm is achieving compliance, CBER prepares an Action Memorandum and letter of reinstatement for the signature of the Director, CBER. After the letter is signed, the Director OCBQ or DCM telephones the firm and advises it that the Agency has lifted the suspension of

the firm's activities and they may now ship products collected or manufactured since the date they resumed limited operations. Also, DCM advises the district by telephone and sends a copy of the reinstatement letter, which, if appropriate, may contain instructions to the firm for filing a request to use products in inventory at the time of suspension.

On a case-by-case basis, CBER evaluates written requests for release of products in inventory at the time of suspension. Communicate in writing all decisions regarding the disposition of products to the firm (copy to the district). CBER may request that the district monitor the disposition of the inventory.

Send copies of all correspondence, verbal and written communications, and EIRs relating to suspensions of operations under license, to the attention of:

Food and Drug Administration
Center for Biologics Evaluation & Research
1401 Rockville Pike, Suite 200N
Rockville, Maryland 20852-1448
ATTN: Division of Case Management, HFM-610

5-7 ORDERS OF RETENTION, RECALL, DESTRUCTION AND CESSATION OF MANUFACTURING RELATED TO HUMAN CELL, TISSUE AND CELLULAR AND TISSUE-BASED PRODUCTS (HCT/Ps)

5-7-1 Purpose

This section contains procedures for issuing an Order of Retention, Recall, Destruction and Cessation of Manufacturing (Order) related to human cell, tissue, and cellular and tissue-based products (HCT/Ps) pursuant to 21 CFR Part 1271.440, promulgated under section 361 of the Public Health Service Act (PHS Act) [42 U.S.C. 264].

5-7-2 Background

In February 1997, FDA proposed a new, comprehensive approach to the regulation of human cells, tissues, and cellular and tissue-based products (HCT/Ps). FDA proposed a tiered, risk based approach under which some HCT/Ps would be regulated only under Section 361 of the PHS Act and the newly proposed regulations in order to prevent the introduction, transmission, and spread of communicable diseases. Other HCT/Ps would also be regulated as drugs, devices, and/or biological products.

Since that time, the agency has published multiple regulations to fully implement this approach. In January 2001, we issued regulations to create a new, unified system for registering HCT/P establishments and for listing their HCT/Ps (66 FR 5447). In May 2004, FDA issued regulations requiring most cell and tissue donors to be tested and screened for risk factors for, and clinical evidence of, relevant communicable disease agents and diseases (69 FR 29786). In November 2004, FDA issued regulations requiring HCT/P establishments to follow current good tissue practice (CGTP), which governs the methods used in, and the facilities and controls used for, the manufacture of HCT/Ps; recordkeeping; and the establishment of a quality program. The CGTP regulations also contain certain labeling and reporting requirements, as well as inspection and enforcement provisions (69 FR 68612). These regulations apply to HCT/Ps recovered on or after May 25, 2005. HCT/Ps that were recovered before this effective date are subject to 21 CFR Part 1270, and subparts A and B of

Part 1271, as appropriate.

HCT/Ps that meet all of the criteria set forth in 21 CFR 1271.10(a) are subject to regulation solely under 21 CFR Part 1271 and section 361 of the PHS Act, so no premarket approval is required. HCT/Ps that do not meet all of the criteria in 21 CFR 1271.10(a) are regulated also as drugs, devices, and/or biological products.

Part 1271 contains six subparts:

Subpart A of Part 1271 – scope, purpose, and definitions
Subpart B of Part 1271 - registration
Subpart C of Part 1271 - screening and testing of donors to determine eligibility
Subpart D of Part 1271 - provisions on CGTP
Subpart E of Part 1271 - certain labeling and reporting requirements
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 HCT/Ps regulated solely under section 361 of the PHS Act and Part 1271, as well as 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 regulated solely under section 361 of the PHS Act and Part 1271. However, with the exception of two provisions (Sec. Sec. 1271.150(c) and 1271.155), subparts D and E are not being implemented for reproductive HCT/Ps.

21 CFR 1271.440 authorizes FDA to issue Orders of Retention, Recall, Destruction, and Cessation of Manufacturing in certain circumstances. Such an order is intended for use in situations when needed to prevent the introduction, transmission, or spread of communicable diseases, and applies only to those HCT/Ps regulated solely under section 361 of the PHS Act and Part 1271.

5-7-3 General Considerations

The agency may consider an Order of Retention, Recall, Destruction, or Cessation of Manufacturing when any of the conditions specified in 21 CFR 1271.440(a) exist. Under this provision, an Order may be justified when the agency finds that there are reasonable grounds to believe that an HCT/P is a violative HCT/P because:

1. The HCT/P was manufactured in violation of the regulations in Part 1271 and, therefore, the conditions of manufacture of the HCT/P do not provide adequate protections against the risk of communicable disease transmission; or

2. The HCT/P is infected or contaminated so as to be a source of dangerous infection to humans; or

3. An establishment is in violation of the regulations in Part 1271 and, therefore does not provide adequate protections against the risks of communicable disease transmission.

Based upon one or more of the above findings, the agency may order the retention, recall, and/or destruction of the violative HCT/P; take possession of and/or destroy the violative

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

NOTE: FDA will not issue an order for the destruction of reproductive HCT/Ps, nor will FDA carry out such destruction itself (21 CFR 1271.440(f)).

5-7-4 Procedures for Orders of Retention, Recall, or Destruction of HCT/Ps

An Order of Retention, Recall, or Destruction of HCT/Ps may be appropriate in situations where there are significant concerns regarding the source or violative nature of the HCT/P, the adequacy of the screening and/or testing, or a failure of the establishment to fulfill stated commitments to gain control over violative HCT/Ps.

As soon as practicable after the possibility of issuing an Order of Retention, Recall, or Destruction is first identified, the district should contact the Chief, Blood and Tissue Compliance Branch(BTCB)/ Division of Case Management (DCM), in CBER's Office of Compliance and Biologics Quality. It is important to make this initial contact during the inspection if possible; do not wait until the conclusion of the inspection to contact CBER. Discussions with CBER prior to submission of a recommendation will facilitate the processing of the recommendation.

The district should upload a copy of the FDA 483 (draft or final) into CMS along with any additional, preliminary information and/or documentation as quickly as possible and should notify (BTCB)/ DCM, for example by electronic mail. BTCB/DCM, will notify CBER's Office of Cellular, Tissue, and Gene Therapies (OCTGT) and the Office of Chief Counsel (OCC) of the potential for an Order as appropriate.

If the district believes an Order of Retention, Recall, or Destruction is appropriate, complete documentation of the violative conditions should be collected, including an inventory of products on the premises as well as those products distributed (including names and addresses of consignees and HCT/Ps shipped to consignees) as of the last day of the inspection.

The district prepares and submits a written recommendation for an Order of Retention, Recall, or Destruction to CBER. Include the district director's concurrence with recommendations for Orders. Transmit the Order recommendation, FDA 483, and all supporting documentation via MARCS-CMS or, where needed, by electronic mail.

All districts should identify Order recommendations as high priorities and make every effort to expedite submissions of the documents described above. BTCB/DCM reviews the information received, also as a high priority, and determines whether the inspectional findings support the issuance of an Order of Retention, Recall, or Destruction.

CBER may concur with issuance of an Order after reviewing the FDA 483 and supporting documentation, but before receiving the Establishment Inspection Report (EIR), if the violations are serious and if there are not adequate protections against risks of communicable disease transmission. It is essential that the district completes the EIR expeditiously and forwards it, along with the exhibits and additional supporting documentation, by uploading it into MARCS-CMS. In cases involving complex issues, CBER may need to review the completed EIR before deciding whether to concur with the recommendation to issue an Order.

BTCB/DCM transmits the FDA 483 and other available supporting documentation as needed

to the Division of Human Tissues (DHT), OCTGT. If one or more of the conditions in 21 CFR 1271.440(a) (as described above in section 5-7-2) are present, DHT will confirm this in writing, signed by the Director, DHT (or designee).

If CBER concurs with the Order recommendation, and OCTGT has confirmed that one or more of the conditions in 21 CFR 1271.440(a) are present, BTCB/DCM drafts the Order of Retention, Recall, or Destruction.

The draft Order, FDA 483, and supporting documentation are uploaded into MARCS-CMS for OCC review. If OCC concurs with the issuance of the Order, BTCB/DCM prepares the Order for signature by the CBER Center Director and delivers it to the Office of the Center Director for signature.

On the date that the Order is signed, the Director, OCBQ attempts to contact the HCT/P establishment by phone to notify the establishment that the Order is in effect. A copy of the order will be sent to the establishment by fax if possible, as soon as possible, after this call has taken place.

Also on the date the Order is signed, BTCB/DCM forwards the Order via overnight delivery to the district office for delivery to the HCT/P establishment. It is preferable to have the original, signed Order hand-delivered to the HCT/P establishment by an FDA investigator. If this is not practicable, the original signed order can be sent to the HCT/P establishment via overnight delivery.

If CBER does not concur with the Order recommendation, BTCB/DCM will notify the district regarding this decision by telephone or electronic mail, and forward a memorandum to the responsible district official explaining the reasons for non-concurrence and describing other potential regulatory actions, if appropriate.

If OCC does not concur with the Order recommendation, OCC will provide a written statement of its rationale to CBER, with a copy to the district office.

5-7-5 Follow-Up to Orders of Retention, Recall, or Destruction

The Order of Retention, Recall, or Destruction will ordinarily provide that the HCT/P be recalled and/or destroyed within five working days from the date of receipt of the Order. The district should promptly verify that the recall and/or destruction is carried out expeditiously, and the HCT/P establishment's action should be monitored or witnessed, as appropriate, by an FDA investigator. The district should manage recalls as provided for in Chapter 7. The Order will require the HCT/P establishment to notify its consignees to return or retain affected HCT/Ps in their inventories.

As an alternative to proceeding with recall and/or destruction, other arrangements for ensuring the proper disposition of the HCT/P may be agreed upon by the person receiving the written Order and FDA. Such arrangements may include, among other things, providing FDA with records or other written information that adequately ensures that the HCT/P has been recovered, processed, stored and distributed in compliance with the regulations and that, except as provided under 21 CFR 1271.60, 1271.65, and 1271.90, the donor of the cells or tissue for the HCT/P has been determined to be eligible. If the violative HCT/Ps can be reconditioned to become suitable for implantation, transplantation, infusion, or transfer into a human recipient as a result of these corrective actions, the establishment may be authorized to release the HCT/P for distribution.

If alternative arrangements are proposed by the HCT/P establishment, the district and CBER should review the proposal concurrently. The HCT/P establishment must retain the violative HCT/Ps in quarantine status until FDA agrees that the appropriate corrective actions have been implemented and adequate documentation has been provided to FDA to address the issues identified in the Order of Retention, Recall, or Destruction.

If FDA orders the destruction of HCT/Ps, it is the firm's responsibility to destroy all violative HCT/Ps and provide to FDA records documenting destruction. The district monitors the destruction of violative HCT/Ps and obtains destruction records. .

The regulations provide the agency with the authority to take possession of and/or destroy the violative HCT/Ps. The district must notify BTCB/DCM if it believes that taking possession of HCT/Ps may be appropriate. If CBER agrees that taking possession of HCT/Ps is appropriate in a particular situation, CBER will provide guidance on procedures for handling and destroying the HCT/Ps safely.

The district will schedule a follow-up inspection as appropriate. If the district observes continued deviations, it should contact BTCB/DCM during the inspection. The district and CBER will jointly consider what action to take.

5-7-6 Procedures for Orders of Cessation of Manufacturing

An Order of Cessation of Manufacturing may be appropriate in situations where there are significant concerns regarding one or more steps in the manufacture of HCT/Ps, or a failure of the establishment to fulfill stated commitments to gain control over or to bring the areas of manufacturing into compliance with the applicable regulations.

As soon as practicable after the possibility of issuing an Order of Cessation of Manufacturing is first identified, the district should contact the Chief, Blood and Tissue Compliance

Branch(BTCB)/Division of Case Management (DCM), in CBER's Office of Compliance and Biologics Quality. It is important to make this initial contact during the inspection if possible; do not wait until the conclusion of the inspection to contact CBER. Discussions with CBER prior to submission of a recommendation will facilitate the processing of the recommendation.

The district should transmit a copy of the FDA 483 (draft or final) as quickly as possible to BTCB/DCM by electronic mail, along with any additional, preliminary information and/or documentation. BTCB/DCM will notify CBER's Office of Cellular, Tissue, and Gene Therapies (OCTGT) and the Office of Chief Counsel (OCC) of the potential for an Order as appropriate.

If the district believes an Order of Cessation of Manufacturing is appropriate, complete documentation of the violative conditions should be collected, including an inventory of products on the premises as of the last day of the inspection.

An Order of Cessation of Manufacturing will be effective immediately if FDA determines there are reasonable grounds to believe there is a danger to health. BTCB/DCM will consult, as necessary, with the appropriate scientific/medical staff to determine whether there are reasonable grounds to believe that there is a danger to health. This evaluation will be documented by BTCB/DCM, working with appropriate scientific/medical staff. If a determination is made that a danger to health exists, the district will be advised immediately.

The district prepares and submits a written recommendation for issuance of an Order of Cessation of Manufacturing to CBER. Include the district director's concurrence with recommendations for Orders. Transmit the Order recommendation, FDA 483, and all supporting documentation via MARCS-CMS or, where needed, by electronic mail.

All districts should identify Order recommendations as high priorities and make every effort to expedite submissions of the documents described above. BTCB/DCM reviews the information received, also as a high priority, and determines whether the inspectional findings support the issuance of an Order of Cessation of Manufacturing.

CBER may concur with issuance of an Order after reviewing the FDA 483 and supporting documentation, but before receiving the Establishment Inspection Report (EIR) if the violations are serious and if there are not adequate protections against the risks of communicable disease transmission. It is essential that the district completes the EIR expeditiously and forwards it to BTCB/DCM, along with the exhibits and additional supporting documentation, by uploading it into MARCS-CMS. In cases involving complex issues, CBER may need to review the completed EIR before deciding whether to concur with the recommendation to issue an Order.

BTCB/DCM transmits the FDA 483 and other available supporting documentation as needed to the Division of Human Tissues (DHT), OCTGT. If one or more of the conditions in 21 CFR 1271.440(a) (as described above in section 5-7-2) are present, DHT will confirm this in writing, signed by the Director, DHT (or designee). If there are reasonable grounds to believe there is a danger to health, this must also be documented and signed by the Director, DHT (or designee).

If CBER concurs with the Order recommendation, and OCTGT has confirmed that one or more of the conditions in 21 CFR 1271.440(a) are present, BTCB/DCM drafts the Order of Cessation of Manufacturing.

The draft Order, FDA 483, and supporting documentation are uploaded into MARCS-CMS for OCC review. If OCC concurs with the issuance of the Order, BTCB/DCM prepares the Order for signature by the CBER Center Director and delivers it to the Office of the Center Director for signature.

On the date that the Order is signed, the Director, OCBQ attempts to contact the HCT/P establishment by phone to notify the establishment that the Order is in effect. A copy of the Order will be sent to the establishment by fax if possible, as soon as possible, after this call has taken place.

Also on the date the Order is signed, BTCB/DCM forwards the Order via overnight delivery to the district office for delivery to the HCT/P establishment. It is preferable to have the original, signed Order hand-delivered to the HCT/P establishment by an FDA investigator. If this is not practicable, the original signed order can be sent to the HCT/P establishment via overnight delivery.

If CBER does not concur with the Order recommendation, BTCB/DCM will notify the district regarding this decision by telephone or electronic mail, and forward a memorandum to the responsible district official explaining the reasons for non-concurrence and describing other potential regulatory actions, if appropriate.

If OCC does not concur with the Order recommendation, OCC will provide a written statement of its rationale to CBER, with a copy to the district office.

5-7-7 Follow Up to Orders of Cessation of Manufacturing

When FDA determines there are reasonable grounds to believe there is a danger to health, an Order of Cessation of Manufacturing is effective immediately. In other situations, the Order of Cessation of Manufacturing is effective after one of the following events, whichever is later: 1) passage of five working days from the establishment's receipt of the Order; or, 2) if the establishment requests a Part 16 hearing, a decision in the proceedings. . The Order will specify the regulations with which the HCT/P establishment must achieve compliance and will ordinarily specify the particular operations covered by the Order.The establishment is permitted to implement corrective actions in order to resume operations. However, the firm may not resume any operations subject to the Order without written authorization from FDA.

The district and CBER should concurrently review all correspondence received subsequent to issuance of an Order of Cessation concurrently. All meetings between the FDA and the Order recipient should include the appropriate district and CBER personnel.

5-7-8 Part 16 Hearing

The recipient of an Order may request a hearing by submitting a written request in accordance with 21 CFR Part 16 as described in the Order and in 21 CFR 1271.440(e). The recipient must make the request within five working days of receipt of a written Order of Retention, Recall, Destruction, and/or Cessation of Manufacturing, or within five working days of the agency's possession of an HCT/P. The HCT/P establishment may request additional time (beyond five working days) to consider whether to request a hearing. Reasonable requests for additional time will usually be granted. OCC, the FDA Office of the Ombudsman, and the district office should be notified promptly upon receipt of a Part 16 hearing request, and for a request for

additional time to request a hearing.

For an Order requiring destruction of HCT/Ps, a request for a Part 16 hearing places the portion of the Order requiring destruction of the violative tissue in abeyance, pending the outcome of the hearing. The portion of the Order requiring recall and retention of violative HCT/Ps, however, is not placed in abeyance or affected by the hearing request.

As described above, if an Order of Cessation of Manufacturing is not immediately in effect, it is effective after one of the following events, whichever is later: 1) passage of five working days from the establishment's receipt of the Order; or, 2) if the establishment requests a Part 16 hearing, a decision in the proceeding. If a Part 16 hearing is requested but denied, or if the Presiding Officer concludes after a Part 16 hearing that the Order was properly issued, the procedures in section 5-7-6 will be followed to notify the HCT/P establishment of the requirement to cease manufacturing.

5-8 CIVIL MONEY PENALTIES AND NO-TOBACCO-SALE ORDERS

5-8-1 Civil Money Penalty Authorities

The Civil Money Penalties (CMPs) included in this section are monetary penalties that are assessed by FDA for violations of the Federal Food, Drug, and Cosmetic Act (the Act) or the Public Health Service Act. Information on electronic products civil penalties under section 539(b) of the Act can be found in Chapter 6, section 6-6.

CMPs are authorized under the following sections of the Act and the Public Health Service Act. See 21 CFR 17.2 for the current maximum CMP amounts allowed.

1. Food

    a. Section 303(f)(2)(A) of the Act, 21 U.S.C. 333(f)(2)(A) – Authorizes CMPs against any person who introduces, or delivers for introduction, into interstate commerce an article of food that bears or contains a pesticide chemical residue that is unsafe within the meaning of section 408(a).

    Section 303(f)(2)(B) of the Act, 21 U.S.C. 333(f)(2)(B), states that a CMP cannot be assessed against any person who grew the article of food. That section also prohibits use of the seizure, injunction, or criminal authorities if a CMP is assessed.

2. Drugs

    a. Section 303(b)(2) of the Act, 21 U.S.C. 333(b)(2) – Authorizes CMPs against a manufacturer or distributor:

        i. if one of their representatives, during the course of their employment or association with the manufacturer or distributor, is convicted of selling, purchasing, or trading or offering to sell, purchase, or trade a prescription drug sample in violation of section 503(c)(1) and 301(t); or is convicted of violating any State law that prohibits the sale, purchase, or trade of a prescription drug sample subject to section 503(b), or the offer to sell, purchase, or trade such a prescription drug sample.

b. Section 303(b)(3) of the Act, 21 U.S.C. 333(b)(3) – Authorizes CMPs against a manufacturer or distributor:

    i. if they fail to report to the Secretary any convictions of their representatives for violations of section 503(c)(1) or a State law because of the sale, purchase, or trade of a prescription drug sample, or the offer to sell, purchase, or trade a prescription drug sample.

c. Section 303(f)(3)(A) of the Act, 21 U.S.C. 333(f)(3)(A) – Authorizes CMPs against any person who violates section 301(jj), 21 U.S.C. 331(jj), by:

    i. failing to submit the certification required by section 402(j)(5)(B) of the Public Health Service Act, 42 U.S.C. 282(j)(5)(B), when submitting certain human drug applications and submissions to FDA, or knowingly submitting a false certification;

    ii. failing to submit clinical trial information required by section 402(j) of the Public Health Service Act, 42 U.S.C. 282(j); or

    iii. submitting clinical trial information under section 402(j), 42 U.S.C. 282(j), that is false or misleading in any particular under section 402(j)(5)(D), 42 U.S.C. 282(j)(5)(D).

d. Section 303(f)(3)(B) of the Act, 21 U.S.C. 333(f)(3)(B) – Authorizes CMPs (in addition to those under section 303(f)(3)(A) above) if a violation of section 301(jj), 21 U.S.C. 331(jj), is not corrected within the 30-day period following notification under section 402(j)(5)(C)(ii), 42 U.S.C. 282(j)(5)(C)(ii), for each day of the violation after such period until the violation is corrected.

e. Section 303(f)(4)(A) of the Act, 21 U.S.C. 333(f)(4)(A) – Authorizes CMPs against any responsible person (defined in section 505-1, 21 U.S.C. 355-1) that violates a requirement of:

    i. Section 505(o), 21 U.S.C. 355(o) – Postmarket studies and clinical trials; labeling;

    ii. Section 505(p), 21 U.S.C. 355(p) – Risk evaluation and mitigation strategy; or

    iii. Section 505-1, 21 U.S.C. 355-1 – Risk evaluation and mitigation strategies.

f. Section 303(g)(1) of the Act, 21 U.S.C. 333(g)(1) – Authorizes CMPs against a person who is a holder of an approved new drug application for a prescription drug, or the holder of an approved biologics license application, if such person disseminates or causes another party to disseminate a direct-to-consumer advertisement that is false or misleading.

g. Section 307(a) of the Act, 21 U.S.C. 335b (a) – Authorizes CMPs against any person that:

    i. Knowingly made or caused to be made, to any officer, employee, or agent

of the Department of Health and Human Services ("DHHS personnel"), a false statement or misrepresentation of a material fact in connection with an abbreviated new drug application (ANDA);

ii. bribed or attempted to bribe or paid or attempted to pay an illegal gratuity to "DHHS personnel" in connection with an ANDA;

iii. destroyed, altered, removed, or secreted, or procured the destruction, alteration, removal, or secretion of any material document or other material evidence which was the property of or in the possession of DHHS for the purpose of interfering with DHHS's discharge of its responsibilities in connection with an ANDA;

iv. knowingly failed to disclose to an officer or employee of DHHS, a material fact relating to any drug subject to an ANDA, which such person had an obligation to disclose;

v. knowingly obstructed a DHHS investigation into any drug subject to an ANDA;

vi. has an approved or pending drug product application and has knowingly used in any capacity the services of a person who was debarred under section 306; or

vii. is debarred and, during the period of debarment, provided services in any capacity to a person that had an approved or pending drug product application.

3. Biologics

a. Section 303(f)(3)(A) of the Act, 21 U.S.C. 333(f)(3)(A) – Authorizes CMPs against any person who violates section 301 (jj), 21 U.S.C. 331 (jj), by:

i. failing to submit the certification required by section 402(j)(5)(B) of the Public Health Service Act, 42 U.S.C. 282(j)(5)(B), when submitting certain biological product applications and submissions to FDA, or knowingly submitting a false certification;

ii. failing to submit clinical trial information required by section 402(j) of the Public Health Service Act, 42 U.S.C. 282(j); or

iii. submitting clinical trial information under section 402(j), 42 U.S.C. 282(j), that is false or misleading in any particular under section 402(j)(5)(D), 42 U.S.C. 282(j)(5)(D).

b. Section 303(f)(3)(B) of the Act, 21 U.S.C. 333(f)(3)(B) – Authorizes CMPs (in addition to those under section 303(f)(3)(A) above) if a violation of section 301(jj), 21 U.S.C. 331(jj), is not corrected within the 30-day period following notification under section 402(j)(5)(C)(ii), 42 U.S.C. 282(j)(5)(C)(ii), for each day of the violation after such period until the violation is corrected.

c. Section 303(f)(4)(A) of the Act, 21 U.S.C. 333(f)(4)(A) – Authorizes CMPs

against any responsible person (defined in section 505-1, 21 U.S.C. 355-1) that violates a requirement of:

i. section 505(o), 21 U.S.C. 355(o) – Postmarket studies and clinical trials; labeling;

ii. section 505(p), 21 U.S.C. 355(p) – Risk evaluation and mitigation strategy; or

iii. section 505-1, 21 U.S.C. 355-1 – Risk evaluation and mitigation strategies.

d. Section 303(g)(1) of the Act, 21 U.S.C. 333(g)(1) – Authorizes CMPs against a person who is a holder of an approved new drug application for a prescription drug, or the holder of an approved biologics license application, if such person disseminates or causes another party to disseminate a direct-to-consumer advertisement that is false or misleading.

e. Section 351(d)(2) of the Public Health Service Act, 42 U.S.C. 262(d)(2) – Authorizes CMPs for any violation of an order issued by the Secretary to immediately recall a batch, lot, or other quantity of a licensed biological product that presents an imminent or substantial hazard to the public health.

f. Section 2128(b)(1) of the Public Health Service Act, 42 U.S.C. 300aa-28(b)(1) – Authorizes CMPs against any vaccine manufacturer who intentionally destroys, alters, falsifies, or conceals any record or report required by 42 U.S.C. 300aa-28(a)(1) or (2).

The penalty applies to the person who intentionally destroyed, altered, falsified, or concealed such record or report; to the person who directed that such record or report be destroyed, altered, falsified, or concealed; and to the vaccine manufacturer for which such person is an agent, employee, or representative. Each act of destruction, alteration, falsification, or concealment is treated as a separate occurrence.

4. Devices

a. Section 303(f)(3)(A) of the Act, 21 U.S.C. 333(f)(3)(A) – Authorizes CMPs against any person who violates section 301(jj), 21 U.S.C. 331 (jj), by:

i. failing to submit the certification required by section 402(j)(5)(B) of the Public Health Service Act, 42 U.S.C. 282(j)(5)(B), when submitting certain device applications and submissions to FDA, or knowingly submitting a false certification;

ii. failing to submit clinical trial information required by section 402(j) of the Public Health Service Act, 42 U.S.C. 282(j); or

iii. submitting clinical trial information under section 402(j), 42 U.S.C. 282(j), that is false or misleading in any particular under section 402(j)(5)(D), 42 U.S.C. 282(j)(5)(D).

b. Section 303(f)(3)(B) of the Act, 21 U.S.C. 333(f)(3)(B) – Authorizes CMPs (in addition to those under section 303(f)(3)(A) above) if a violation of section 301(jj), 21 U.S.C. 331(jj), is not corrected within the 30-day period following notification under section 402(j)(5)(C)(ii), 42 U.S.C. 282(j)(5)(C)(ii), for each day of the violation after such period until the violation is corrected.

c. Section 303(f)(1)(A) of the Act, 21 U.S.C. 333(f)(1)(A) [1] – Authorizes CMPs against any person who violates a requirement which relates to devices. Except that, in accordance with Section 303(f)(1)(B), CMPs do not apply to:

   i. any person who violates the requirements of section 519(a) (e.g., Medical Device Reporting), or section 520(f) (Quality System Regulation), unless the violations constitute a significant or knowing departure from the requirements, or a risk to public health;

   ii. any person who commits minor violations of section 519(e) (Device Tracking), or section 519(g) (only with respect to correction reports), if the person demonstrates substantial compliance with such section; or

   iii. violations of section 501(a)(2)(A) which involve one or more devices which are not defective.

   Note that a person accredited under section 704(g)(2) who is substantially not in compliance with the standards of accreditation under that section, or who poses a threat to public health or fails to act in a manner that is consistent with the purposes of that section, is considered to have violated a requirement of the Act that relates to devices.

5. Mammography Facilities

   a. Section 354(h)(3) of the Public Health Service Act, 42 U.S.C. 263b(h)(3) – Authorizes CMPs for:

      i. Failure to obtain a certificate as required by 42 U.S.C. 263b(b);

      ii. Each failure by a facility to substantially comply with, or each day on which a facility fails to substantially comply with, the quality standards established under 42 U.S.C. 263b(f), codified at 21 CFR Part 900, or the requirements of 42 U.S.C. 263b(d)(1)(B)(ii);

      iii. Each failure to notify a patient of risk as required pursuant to 42 U.S.C. 263b(h)(2); and

      iv. Each violation, or for each aiding and abetting in a violation of, any provision of, or regulation promulgated under, this section by an owner, operator, or any employee of a facility required to have a certificate.

[1] This section has been variously referred to as section 303(f) and 303(g) because of confusion at the time of legislative enactment in 1990. The explanatory notes to FDAAA of 2007 clarified that this section is now subsection (f).

6. Tobacco Products

   a. Section 303(f)(9) of the Act, 21 U.S.C. 333(f)(9)– Authorizes CMPs for violations of tobacco product requirements.

   b. Section 303(f)(9)(A) of the Act, 21 U.S.C. 333(f)(9)(A)– Authorizes CMPs against any person who violates a requirement of the Act which relates to tobacco products. Such person shall be liable to United States for a civil penalty in an amount not to exceed $15,000 for each such violation, and not to exceed $1,000,000 for all such violations adjudicated in a single proceeding.

   c. Section 303(f)(9)(B) of the Act, 21 U.S.C. 333(f)(9)(B) – Authorizes enhanced CMPs in an amount not to exceed $250,000 per violation, and not to exceed $1,000,000 for all such violations adjudicated in a single proceeding.

      i. if a person intentionally violates a requirement of:

         - Section 902(5) of the Act, 21 U.S.C. 387b(5), which deems a tobacco product to be adulterated if it is, or purports to be or is represented as, a tobacco product which is subject to a tobacco products standard established under section 907 unless such tobacco product is in all respects in conformity with such standard.

         - Section 902(6) of the Act, 21 U.S.C. 387b(6), which deems a tobacco product to be adulterated if (A) it is required by section 910(a) to have premarket review and does not have an order in effect under section 910(c)(1)(A)(i). or (B) it is in violation of an order under section 910(c)(1)(A).

         - Section 904 of the Act, 21 U.S.C. 387d, which requires each tobacco product manufacturer or importer, or agents thereof, to submit health information to the Secretary, as set forth in that section.

         - Section 908(c) of the Act, 21 U.S.C.387h(c), which requires the appropriate person (including the manufacturers, importers, distributors, or retailers of the tobacco product) to immediately cease distribution of such tobacco product if the Secretary finds that there is a reasonable probability that the product contains a manufacturing or other defect not ordinarily contained in tobacco products on the market that would cause serious, adverse health consequences or death.

         - Section 911(a) of the Act, 21 U.S.C.387k(a), which prohibits any person from introducing or delivering for introduction into interstate commerce any modified risk tobacco product unless an order issued pursuant to subsection 911(g) is effective with respect to such product.

      ii. if a person violates a requirement of:

- Section 911(g)(2)(C)(ii) of the Act, 21 U.S.C. 387k(g)(2)(C)(ii), which requires that an order under section 911(g) be conditioned on the applicant's agreement to conduct postmarket surveillance and studies and to submit to the Secretary the results of such surveillance and studies to determine the impact of the order on consumer perception, behavior, and health and to enable the Secretary to review the accuracy of the determinations upon which the order was based in accordance with a protocol approved by the Secretary.

- Section 911(i)(1) of the Act, 21 U.S.C. 387k(i)(1), which requires with respect to a tobacco product for which an applicant obtained an order under section 911(g)(1) that the applicant conduct postmarket surveillance and studies for such a tobacco product to determine the impact of the order issuance on consumer perception, behavior, and health, to enable the Secretary to review the accuracy of the determinations upon which the order was based, and to provide information that the Secretary determines is otherwise necessary regarding the use or health risks involving the tobacco product. The results of postmarket surveillance and studies must be submitted to the Secretary on an annual basis.

Tobacco Retailers

a. Section 103(q)(2)(A) of the Family Smoking Prevention and Tobacco Control Act, Public Law 111-31 ("Tobacco Control Act") 21 U.S.C. 333 note – Authorizes CMPs against tobacco retailers for violating restrictions promulgated under section 906(d) of the Act, including the regulations at 21 CFR Part 1140. This section provides reduced penalties for retailers with an approved training program. At this time, and until FDA issues regulations setting the standards for an approved training program, all applicable CMPs will proceed under the reduced penalty schedule.

b. Section 303(f)(8) of the Act, 21 U.S.C. 333(f)(8) – Authorizes imposition of a no-tobacco-sale order prohibiting the sale of tobacco products against a particular tobacco retail outlet that has committed "repeated violations" of restrictions promulgated under section 906(d) of the Act, including the regulations at 21 CFR Part 1140. (Section 103(q)(1)(A) of the Tobacco Control Act defines "repeated violation" as including at least 5 violations of particular requirements over a 36-month period at a particular retail outlet). A no-tobacco-sale order may be imposed with a CMP.

5-8-2 Reduction Of Civil Money Penalties For Small Entities

The Small Business Regulatory Enforcement Fairness Act of 1996 (SBREFA) (Public Law 10-121) was enacted on March 29, 1996, and seeks to improve the regulatory climate for small entities by, among other things, requiring agencies to establish small entity penalty reduction policies.

The Food and Drug Administration (FDA) has issued final guidance for the reduction of CMPs for small entities (penalty reduction guidance) as mandated by the SBREFA and the Presidential Memorandum of April 21, 1995 (60 FR 20621, April 26, 1995). This guidance can be obtained on FDA's internet site at
http://www.fda.gov/OHRMS/DOCKETS/98fr/010049gd.pdf

5-8-3 Civil Money Penalty Recommendations

When it is determined that Civil Money Penalty (CMP) is the appropriate course of action, the District's Compliance Officer should submit the recommendation package to the appropriate Center, except for tobacco retailers.

1. DISTRICT RESPONSIBILITIES
   The District recommends a Civil Money Penalty by transmitting to the Center, at a minimum, a cover memorandum recommending the action, a draft cover letter to respondents and a Complaint accompanied by the supporting evidence.

2. CENTER RESPONSIBILITIES
   The Center is responsible for the technical, regulatory, policy and scientific review of the District's Civil Money Penalty recommendation. Changes to proposed recommendations should be made only after discussion with the District's compliance staff.

Note: The Center for Tobacco Products (CTP) will initiate CMP actions against tobacco retailers.

Approved referrals transmitted to DCMO should include intact original case files organized as submitted from the District, the Center's proposed changes to respondent letters/Complaint and the Center's approval memorandum providing Center contact information, justification for imposition of civil money penalties and other information necessary to review and process the action.

3. DCMO RESPONSIBILITIES
   OE, Division of Compliance Management and Operations will review the appropriateness of the action and the adequacy of the draft cover letter to respondents and Complaint to ensure compliance with existing procedures, policies, regulations or statutes. Changes to proposed recommendations should be made only after discussion with the Center and the District's compliance staff.

   Approved recommendations to OCC should include DCMO's transmittal memorandum, DCMO's proposed changes to the respondent letters/Complaint and original materials submitted by the District and Center.

4. OFFICE OF CHIEF COUNSEL RESPONSIBILITIES
   OCC Approved recommendations will be processed in accordance with procedures outlined in 21 CFR Part 17; or, in the case of civil penalties authorized under section 307(a) of the Act, in accordance with the procedures in section 307(b) of the Act.

5-9 DISQUALIFICATION OF CLINICAL INVESTIGATORS

5-9-1 Purpose

This procedure describes the process, including timeframes, for initiating disqualification proceedings – from completion of the inspection to issuance of the Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE) to the clinical investigator. In addition, it includes the processes and timeframes for follow-up to a response to a NIDPOE, through issuance of a Notice of Opportunity for Hearing (NOOH).[2] This procedure is intended for use by center Bioresearch Monitoring (BIMO) Program Units, staff in the Office of the Commissioner (OC), the Office of Regulatory Affairs (ORA), and the Office of the Chief Counsel (OCC). Adherence to the procedures described in this chapter will assist the agency in achieving a uniform approach to the disqualification process.

5-9-2 Criteria for Initiating Disqualification Proceedings

Criteria for initiating disqualification proceedings are found at 21 CFR 312.70, 511.1(c), and 812.119 and are discussed in the clinical investigator CPGM, as noted in footnote 1. As discussed in the clinical investigator CPGM (7348.811, Part V. B.), a decision to initiate disqualification proceedings often starts with a decision to classify the Establishment Inspection Report (EIR) as Official Action Indicated (OAI).

5-9-3 Initiating the Disqualification Process

When a clinical investigator inspection reveals serious noncompliance, communication with the center is essential, as noted in the CPGM (7348.811 Part II, B.3.), since collection of appropriate supporting evidence is vital. In addition, this will allow the center to provide advance notice to OCC and other appropriate offices if it appears a recommendation for disqualification may be considered. It is also recommended that the district investigator contact the Bioresearch Monitoring Specialist in the Division of Compliance Policy (DCP) in the Office of Enforcement, ORA, who can provide assistance with the process and serve as an additional resource. The resulting EIR, with violations indexed to the supporting evidence and exhibits appropriately tabbed for easy reference, should be forwarded to the center BIMO Program Unit **within 30 days**[3] of completion of the inspection.

Because center BIMO Program Units need to expeditiously review inspectional findings that warrant initiation of disqualification proceedings, center BIMO Program Units should review and prioritize **within fourteen (14) days of receipt** all EIRs with a district office recommendation of OAI, with or without a recommendation for clinical investigator disqualification. Center BIMO Program Units should review and prioritize EIRs with RTC

---

[1] *Criteria for initiation of disqualification proceedings are included in the Compliance Program Guidance Manual (CPGM) (available at http://www.fda.gov/ICECI/EnforcementActions/BioresearchMonitoring/ucm133562.htm) for the inspection of clinical investigators, 7348.811, Part V. B. Procedures for the hearing process initiated by issuance of an NOOH are described in the FDA Staff Manual Guides (SMG), Volume IV – Agency Program Procedures, specifically SMG 7711 (available at http://www.fda.gov/AboutFDA/ReportsManualsForms/StaffManualGuides/ucm052928.htm)).*

[3] All timeframes are in **calendar** days unless specified otherwise.

(Refer to Center) designations within a similar timeframe to determine if any warrant an OAI designation and therefore possible initiation of disqualification proceedings. EIRs with district office recommendations other than OAI or RTC may also support initiation of disqualification proceedings. When a BIMO reviewer identifies such an EIR, the timeframes discussed below would apply.

Once the potential for initiating disqualification proceedings is identified, the assigned BIMO reviewer analyzes the inspectional findings and determines if the findings are supported by sufficient evidence of regulatory significance. The BIMO reviewer also determines if the district office has received any response to the Form FDA 483 and requests a copy of all responses. After reviewing all materials associated with the most recent inspection, as well as any information available in the center's inspectional files/databases, the BIMO reviewer drafts his/her rationale for or against initiation of disqualification proceedings. (Consultation with office/center regulatory personnel and/or OCC attorneys during this review may be warranted.) If initiation of disqualification proceedings is not deemed warranted, the BIMO reviewer prepares a document explaining that conclusion, for review by his/her supervisor, and initiates other appropriate actions. If initiation of disqualification proceedings is deemed warranted, the BIMO reviewer prepares appropriate documentation for the administrative record which will support all subsequent steps in the process. The portion of the administrative record supporting issuance of a NIDPOE, (hereafter referred to as the NIDPOE file) will include such documents as:

1. A chart and/or memo summarizing the significant inspectional findings and regulatory violations supporting the disqualification action;
2. A chronology/inspectional history of the clinical investigator;
3. A draft NIDPOE (see Exhibit 5-21 for sample); and
4. A draft Consent Agreement (see Exhibit 5-22 for sample)

The NIDPOE file should be appropriately indexed to facilitate review by center management, OCC, and ORA. For example, violations cited in the NIDPOE should be indexed to the supporting evidence supplied with the EIR. During preparation of the NIDPOE file, the BIMO Program Unit should alert all relevant center and agency offices that this file is in preparation to ensure timely review. Review of the NIDPOE file should proceed according to center-specific SOPs. The NIDPOE file should be ready for OCC review **within four (4) months from receipt of the EIR**. OCC should concur, with comments/suggested edits as necessary, or arrange for a discussion with appropriate center BIMO personnel if non-concurrence is considered, **within four (4) months** of receipt of the draft NIDPOE.

Upon receipt of OCC concurrence, the BIMO Program Unit incorporates any changes and/or additions to the NIDPOE letter and routes the entire NIDPOE file to the appropriate center official for signature of the NIDPOE. This signature should be affixed **within fourteen (14) days** of receipt of OCC concurrence. The NIDPOE file and signed NIDPOE are returned to the BIMO Program Unit. The BIMO Program Unit should issue the signed NIDPOE, with the consent agreement, to the clinical investigator within **1 working day of receipt** and distribute copies to the appropriate agency units, as described below.

The NIDPOE directs the clinical investigator to write or call the center, **within fifteen (15) working days**, to arrange for an informal conference or to indicate the intent to respond to the

allegations in writing. If the clinical investigator chooses to submit a written response, the NIDPOE directs him/her to respond **within 30 working days of receipt of the NIDPOE**.

5-9-4 Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE)

Delivery

A NIDPOE should be sent by certified mail (return receipt requested), or other method that documents transmission and receipt of delivery. If such delivery is unsuccessful, the center should contact the Director, Investigations Branch (DIB) in the appropriate district office and request that the NIDPOE be hand delivered by agency personnel. The Center will provide the district with addresses and alternative locations for delivery.

Distribution

The issuance of a NIDPOE is a significant regulatory action and appropriate agency units should be promptly advised of its issuance. These include:

GCF-1 (OCC)
HF-34 (GCPP)
HFC-130 (DFI)
HFC-230 (DCP/OE)

[*Center files and distribution*]

[*District Personnel, including the District Director; Director, Investigations Branch; and the district investigator(s)*]

HFD-45 (CDER/DSI)
HFM-664 (CBER BIMO group)
HFS-205 (CFSAN BIMO group)
HFV-234 (CVM BIMO group)
HFZ-310 (CDRH/DBM)

5-9-5 Consent Agreements

After issuance of the NIDPOE, the clinical investigator may choose to enter into a consent agreement with FDA. A finalized consent agreement between FDA and the clinical investigator terminates the administrative proceedings in this matter. The option of entering into a consent agreement with the agency is available at any time throughout the disqualification proceedings, up to the issuance of the Commissioner's Decision under 21 CFR 16.95 or issuance of a notification of disqualification under 21 CFR 312.70, 511.1(c), or 812.119. As noted above, a sample consent agreement is included in Exhibit 5-22.

5-9-6 Informal Conference with the Clinical Investigator

In the NIDPOE, the center will offer the investigator the opportunity to submit an explanation in writing, or at the investigator's option, in an informal conference. If the clinical investigator submits a written response, the regulations do not require the center to hold an informal

conference but the center may chose to do so. If an informal conference is requested, the center should schedule it as soon as possible, usually **within thirty (30) days** of the request. At the informal conference, the clinical investigator may be accompanied by a representative of his/her choosing and may provide documents for the record. A clinical investigator may submit written materials to FDA within 15 days after the informal conference.

At a minimum, FDA personnel attending the conference will include staff from the center BIMO Program Unit and counsel from OCC who reviewed the NIDPOE. FDA may also include other personnel with appropriate expertise or relevant experience with the case (e.g., a Medical Officer from the review team for the study involved, the FDA district investigator who conducted the inspection at the clinical investigator's site). The center should make arrangements for the informal conference, notify all pertinent parties of the specifics, and arrange to have the discussion transcribed for the administrative record. These informal meetings should be scheduled for up to two (2) hours. Because the meeting is informal, there is no prescribed format, but the meeting should address all allegations listed in the NIDPOE.

Following the informal conference, the center will provide a copy of the written transcript to the clinical investigator. The center, in consultation with OCC, should promptly review any new explanation or evidence provided by the clinical investigator. If it no longer appears that disqualification is warranted, alternatives such as a detailed corrective action plan may be considered. The center BIMO Program Unit should notify the clinical investigator in writing **within thirty (30) days** of the informal conference of this decision not to proceed with the disqualification and include the specifics of any such alternative corrective action plan.

If the clinical investigator's explanation is not accepted by the Center, disqualification is still warranted and the center should issue a Notice of Opportunity for Hearing (NOOH) to the clinical investigator.

5-9-7 The Notice of Opportunity for Hearing (NOOH)

If a clinical investigator fails to respond to a NIDPOE or the center determines that the clinical investigator's written or oral explanation is inadequate, the regulations provide that the clinical investigator be given an opportunity for a regulatory hearing under 21 CFR part 16 on the question of whether the investigator is entitled to receive investigational articles. Center BIMO Program Units should prepare an NOOH using the sample document provided in Exhibit 5-23. The NOOH should be prepared **within 30 days** of a center's decision that a clinical investigator's written or oral explanation is inadequate, or after it is clear the clinical investigator has chosen not to respond to the NIDPOE. The center should consult with OCC during the preparation of the NOOH and clear the NOOH in accordance with center procedures. The center-approved NOOH and the administrative record (which includes the NIDPOE file and all follow-up information/documents) should be forwarded to OCC for review and clearance. **Within thirty (30) working days** of receipt, OCC should concur or provide comments to the BIMO Program Unit as to what is necessary to achieve concurrence with the NOOH.

Within five (5) working days of OCC concurrence, after incorporating any OCC additions/changes, the BIMO Program Unit forwards both the paper and electronic copies of the NOOH and the administrative record to the Division of Compliance Management and Operations (DCMO). DCMO has **five (5) working days** to review and clear the NOOH for

signature. If DCMO, during its review, proposes substantive changes to the NOOH, DCMO will clear their proposed changes with OCC, who will consult with the BIMO Program Unit when necessary. **Within five (5) working days** of receiving OCC feedback regarding suggested substantive changes, DCMO will forward the NOOH and the administrative record to the Associate Commissioner for Regulatory Affairs (ACRA) in the Office of Regulatory Affairs (ORA) for review and signature. The ACRA should sign the NOOH, or provide comments to DCMO as to what is necessary to achieve his/her signature, **within five (5) working days** of receipt. Upon receipt of the signed NOOH (**within one (1) working day**), DCMO date stamps and issues the NOOH to the clinical investigator and/or his/her counsel by certified mail (return receipt requested) or other documented method of transmission. If delivery of the NOOH cannot be confirmed, the Director, DCMO, will contact the local district office and request that the NOOH be delivered by FDA personnel. The Center will provide the district with addresses and alternative locations for delivery. Upon issuance of the NOOH, DCMO provides a copy of the signed NOOH to the center BIMO Program Unit, which is responsible for appropriately distributing copies of the NOOH within FDA (see NIDPOE distribution list above).

The NOOH provides that the investigator has **ten (10) working days** from receipt of the NOOH to request a hearing. If the clinical investigator does not respond within this time frame, the clinical investigator will be deemed to have waived the right to a regulatory hearing and the agency will make a decision on the matter based on the facts available to the agency.

DCMO will advise the center BIMO Program Unit of the response (or lack thereof) to the NOOH letter after ten (10) working days. Subsequent actions are discussed and determined by the center BIMO Program Unit, OCC, and DCMO as outlined in the Sample Notice of Opportunity for Hearing in Exhibit 5-23. The center BIMO Program Unit is responsible for preparing a memo for summary decision regarding the disqualification.

See SMG 7711 for details of the process to be followed after issuance of a NOOH (http://www.fda.gov/AboutFDA/ReportsManualsForms/StaffManualGuides/ucm052928.htm)..

The clinical investigator disqualification proceedings described above are summarized in the flowchart found in Exhibit 5-20.

5-10 EXHIBITS

5-1 Model Section 305 Notice
5-2 Model Charge Sheet
5-3 Model Charges
5-4 Legal Status Sheet
5-5 Information Sheet
5-6 Summary Format - Section 305 Meeting
5-7 Notification of Non-Prosecution
5-8 Timeframes for Administrative Detention of Food (AD of Food) – Appellant's Deadlines
5-9 Timeframes for AD of Food – FDA's Deadlines

Exhibit 5-1
MODEL SECTION 305 NOTICE

SECTION 305 NOTICE

In reply refer to:
Sample No.
Product

Firm Name and Individual Date
Street Address
City, State, Zip

Investigation by this Administration indicates your responsibility for violations of the Federal Food, Drug, and Cosmetic Act, and other Federal Laws, as described in the attached Charge Sheet, with respect to the following:

Shipment of an article labeled in part "Cream Style White Sweet Corn Net Weight 5 lb 10 oz" by (Firm, Location), to (Firm, Location), on or about (date).

A meeting has been scheduled for (day, date, time) at (location), to give you an opportunity to present your views on this matter. The enclosed **INFORMATION SHEET** explains the purpose and nature of the meeting, and how you may reply. If no response is received on or before the date set, our decision on whether to refer the matter to the Department of Justice for prosecution will be based on the evidence in hand.

By direction of the Secretary of the Department of Health and Human Services:

Compliance Officer

(IMPORTANT: NOTE ALL ENCLOSURES CAREFULLY)

Enclosures:
Legal Status Sheet (3)
Charge Sheet
Information Sheet
Regulations

Exhibit 5-2
MODEL CHARGE SHEET

CHARGE SHEET

(In Connection with Enclosed Section 305 Notice)

Sample Nos.	Sample Nos.
Sample #, Product	Sample #, Product
Sample #, Product	Sample #, Product
Sample #, Product	Sample #, Product
Sample #, Product	Sample #, Product
Sample #, Product	Sample #, Product
Sample #, Product	Sample #, Product

PROHIBITED ACT: Section 301(a) of the Federal Food, Drug, and Cosmetic Act. The introduction or delivery for introduction into interstate commerce of any food that is adulterated.

CHARGES: The articles are adulterated in the following respects:

Sample #)
Sample #)
Sample #)
Sample #) They contain insect fragments and rodent hair fragments.
Sample #)
Sample #)
Sample #)
Sample #)
Sample #)
Sample #) It contains insects, insect fragments, and rodent hair fragments.
Sample #) It contains insect fragments.
Sample #) It contains insect larvae, insect fragments, and rodent hair fragments.

All Samples) The factory in which the articles were prepared was infested with insects and rodents which may have contaminated the articles.

Exhibit 5-3
MODEL CHARGES

SPECIMEN CHARGE

(Do not quote the section of the Act listed below on the Charge Sheet)

Adulterated Foods

402(a)(1)

- The soybeans contain an added poisonous or deleterious substance, namely, crotalaria seeds, which may render them injurious to health.
- The frozen eggs contain added salmonella microorganisms, pathogenic bacteria, which may render them injurious to health.
- The article contains selenium, a poisonous or deleterious substance, in a quantity that would ordinarily render it injurious to health.

402(a)(2)(A)

- The articles contains an added deleterious substance, namely, metal fragments, which is unsafe since it is not required in the production of this food and can be avoided by good manufacturing practices.
- The cod fillets contain oxytetracycline that is unsafe, since oxytetracycline is not required in the production of this food and can be avoided by good manufacturing practices.

NOTE: Generally, the use of Section 402(a)(2)(A) as a basis for charges should be limited; other sections, such as 402(a)(1), are usually preferred.

402(a)(2)(B)

- The berries contain heptachlor, which is not generally recognized as safe, and for use of which a tolerance has not been prescribed by regulation.
- The cabbage contains excessive Toxaphene.

402(a)(2)(C)

- The article contains a food additive, namely lead, which is unsafe within the meaning of Section 409(a) since its use and intended use are not in conformity with a regulation or exemption in effect.

402(a)(2)(D)

- The meat intended for human food contains a new animal drug, namely MGA, which is unsafe in that there is no approved new animal drug application in effect for this use.

402(a)(3)

- The article contains insect parts and insect excreta.
- The article contains rodent excreta pellets.
- The nuts are rancid.
- Some of the cans contain decomposed salmon.
- The catsup contains decomposed tomatoes.

- The peanut butter contains grit.

402(a)(4)

- The factory (warehouse) in which it was prepared and packed (held) was infested with rodents and insects, which may have contaminated it.

402(a)(5)

- Some of the boxes contain emaciated and diseased birds.
- Some of the boxes contained birds that were not slaughtered but that died from other causes.

402(a)(7)

- The article has been subjected to radiation, not provided for by the Food Additives Regulations.

402(b)(1)

- The article is deficient in Vitamin B.
- The butter contains less than 80% milkfat.

402(b)(2)

- Mineral oil has been used to replace part of the vegetable oil.
- Chicory has been used in part instead of coffee.

402(b)(3)

- Blemished, old potatoes have been colored and waxed to resemble new potatoes and to conceal the blemishes.

402(b)(4)

- The ground pepper contains ground olive seeds.
- The poppy seeds are brown and have been artificially colored to appear to be blue poppy seeds.

402(c)

- The article contains a color additive, namely, "butter yellow," not permitted by regulation for use in food.
- The article contains a color additive, namely, FD&C Purple Number 8, for which no tolerance has been established.

402(d)

- Some pieces of the candy contain a metallic toy.
- The candy is filled with alcohol.

402(e)

- The article contains vegetable oil that is rancid.
- The milk used to manufacture the butter contained flies and manure.

Misbranded Foods

403(a)

- The label falsely represents it to contain a significant amount of honey but the amount present, if any, is inconsequential.
- The label bears statements that falsely represent, in the setting in which they are presented, that the article will supply an unusually large amount of protein in a quantity which is low in calories, and that the article is therefore of significant value for weight reducing.
- The labeling falsely represents that the product contains copper, folic acid, cobalt and calcium pantothenate.
- The label falsely represents the article to be canned peas, whereas the article is canned spinach.

403(b)

- It was offered as lemon extract by the price list sent to the consignee on or about May 2, XXXX, but it is in fact an extract of lemon grass oil.

403(c)

- The word "Imitation" on the label is in type of smaller size and less prominence than the type in which the words "Vanilla Extract" appear.
- The label fails to bear the name "Imitation Strawberry Preserves."

403(d)

- The can has a depressed top and bottom and contains a thick corrugated inner liner, which give the container the appearance of containing more nuts than it does.
- The container is slack-filled.

403(e)(1)

- The label fails to bear the name of the manufacturer, packer, or distributor.

403(e)(2)

- The label statement "net weight 4 oz." is inaccurate.
- The article is short weight.

403(f)

- The statement of ingredients on the label is inconspicuous.
- The name and address of the manufacturer is printed on the cellophane bag in white ink and lacks contrast with the white candy mints contained therein.

403(g)(1)

- The article is represented as raspberry preserves but contains less fruit than the standard of identity requires.
- The article purports to be French dressing but contains less fat than specified in that standard.
- The egg noodles are deficient in egg solids content.

403(g)(2)

- The article is bleached flour but the label does not state that it is bleached.
- The article purports to be enriched macaroni, and its label fails to bear the name of that food.
- The article purports to be Fruit Butter, but its label fails to bear the name of the optional ingredient, lime juice, present in the food.

403(h)(1)

- The article contains excessive blemished fruit but its label does not bear the statement of substandard quality prescribed for canned peaches.
- Its quality falls below the standard for canned tomatoes, since it contains excessive peel.

403(h)(2)

- The cans are underfilled but the label does not bear the statement of substandard fill prescribed for canned peas.

403(i)(1)

- The article is ground cinnamon but its label does not bear the name "ground cinnamon."

403(i)(2)

- Flour is present but is not named in the label listing of ingredients.
- The label fails to bear a statement of ingredients of the article by their common or usual names.

403(j)

- Its label fails to bear a statement of the percentage of the USRDA for the vitamins B(1), B(2), niacinamide and the mineral iron, as required by the special dietary regulations.
- The label fails to state the percent by weight of methylcellulose present; and in juxtaposition with name of such constituent, the word "non-nutritive," as required by the special dietary regulations.

403(k)

- The labeling fails to state the fact that a chemical preservative has been added.
- The article is artificially colored, but its labeling fails to state that fact.

403(l)

- The oranges contain biphenyl (diphenyl applied post harvest), but its shipping container fails to bear labeling declaring the name and function of the pesticide chemical.

403(m)

- The article is a color mixture but its label does not declare the name of the color components contained therein.

Adulterated Drugs

501(a)(1)

- The aspirin tablets contain rodent hairs.

501(a)(2)(A)

- The plant in which the aspirin tablets were manufactured was infested with rodents which may have contaminated them.

501(a)(2)(B)

- The door of the sterile filling room was left open while filling bottles of an eye solution.
- The methods used in its packing do not conform to current good manufacturing practices in that Isopropyl alcohol is labeled as Citrate of Magnesia.

501(a)(3)

- Its container is composed in part of lead, which may render the contents injurious to health.

501(a)(4)(A)

- The color used is in excess of the limits prescribed in the regulations.

501(a)(4)(B)

- FD&C Red #4 intended for use in a drug for internal administration, and such use is for coloring purposes only.

501(a)(5)

- The article is a new animal drug and there is no approved new animal drug application in effect for this drug.

501(a)(6)

- The cattle feed contains a new animal drug, namely Carbadox, which is unsafe in that there is no approved new animal drug application in effect for this use.

501(b)

- The article purports to be an official NF drug but fails to comply with the compendium's standard for strength.
- It contains cresol, a substance not permitted by the U. S. Pharmacopeial Monograph for Water for Injection, which the drug purports to be.
- Magnesium carbonate, which the NF formula requires in Solution of Magnesium Citrate, has been replaced by sodium carbonate.

501(c)

- The article contains Neomycin Sulfate which is below the potency declared on the label.
- The quality of the article namely, Rubber Prophylactics, falls below that which it is purported to possess.

501(d)(1)

- The article has been mixed or packed so as to reduce its quality or strength.

501(d)(2)

- P-aminosalicylic acid has been substituted in part for conjugated para-amino salicylic ascorbate.

Misbranded Drugs

502(a)

- Its labeling represents it as a treatment for influenza and related diseases, but it is not an effective treatment for these diseases.
- The article falsely claims that it will remove ascarids from hogs.

502(b)(1)

- Its label does not bear the name and place of business of the manufacturer.

502(b)(2)

- Its label does not bear an accurate statement of the quantity of contents.

502(c)

- The statement "24 tablets" appears on the back label and is on a pink label in red type.

502(e)(1)(A)(i)

- The label does not show that the drug is aspirin.

502(e)(1)(A)(ii)

- The quantity of bromide per tablet is not stated on the label.
- Its label fails to list all of the active ingredients.

502(f)(1)

- The directions do not state the uses of the drug.
- Its (O-T-C drug) labeling does not contain directions adequate for the treatment of diabetes, for which use the drug is recommended in advertising (as distinguished from labeling).
- The prescription drug lacks adequate full disclosure information.

502(f)(2)

- The labeling does not warn against use of the drug in case of nausea, vomiting, abdominal pain, or other symptoms of appendicitis.
- The labeling gives no warning that use of the drug in excess of what the directions call for may result in nervousness and sleeplessness.

502(g)

- It is not packaged in tight containers as required by the United States Pharmacopoeia.

502(i)(1)

- The container is slack-filled.

502(i)(2)

- It is an imitation of citrate of magnesia.

502(i)(3)

- The article, namely argel leaves, is offered for sale as senna.

502(j)

- It is dangerous to health when one tablet is taken every three hours as recommended in the labeling.
- It is dangerous to health when taken in the dosage suggested in its labeling.

502(m)

- The label fails to provide directions for use to preclude adding excessive color additive to the drug.

502(n)(1)

- The advertisement for Miltown which appeared in the May 19, 20XX edition of the Pleasant Medical Journal did not show the established name.

502(n)(2)

- The advertisement for "Triple Sulfa" tablets which appeared ____ etc. ____ did not list the active ingredients by their established names.

502(n)(3)

- The advertisement for "Triple Sulfa" tablets which appeared in the May 19, 20XX edition of _____ contained or recommended indications for use or a dosage recommendation, but not the brief summary of side effects, contraindications, and effectiveness.

502(o)

- The potassium chloride tablets were manufactured in an unregistered plant.

503(b)(4)(A)

- The label for the article, namely chloralhydrate, does not bear the symbol “Rx only”.

503(b)(4)(B)

- The aspirin tablet label bears the symbol “Rx only,” but the drug is not entitled to such designation.

505(a)

- The article, namely, Meprobamate, is a new drug and was shipped in interstate commerce without an approved new drug application.

Cosmetics

601(a)

- The article contains paraphenylenediamine, a coal tar dye which is a deleterious substance, but its label does not carry adequate warnings or directions to make a preliminary patch test before use.
- It contains formaldehyde, a deleterious substance.

601(b)

- Some of its components contain rodent excreta pellets.

601(c)

- The plant in which the article was prepared was infested with rodents.

601(d)

- Its container is composed in part of lead.

601(e)

- The color used is not authorized by the regulations (or is in excess of the limits prescribed in the regulations.)

602(a)

- The article is represented as containing a substantial amount of lanolin, but lanolin is a minor constituent of the cream.

602(b)(1)

- The label for the eye shadow does not bear the name and location of the manufacturer, namely, New York Pencil Co., Inc., New York, N.Y.

602(b)(2)

- The article does not bear a statement of the quantity of contents.

602(c)

- The statement of the quantity of contents appears on the bottom of the container (oval jar).

602(d)

- The nontransparent container is composed of an outer and inner wall with a 1/8 inch space between the walls.

602(e)

- The label fails to provide directions for use to preclude adding excessive color additive to the cosmetic.

Title 42

351(a)

- The Source Plasma (Human) was drawn and shipped from an unlicensed establishment.

- The label fails to bear the expiration date and license number of the establishment.

351(b)

- The label states the blood is Hgb negative, but the records show the unit is Hgb positive.
- The donor number on the unit label is false.
- The product is pooled serum, but the label falsely states it was drawn from one donor.

351(c)

- Inspection of the establishment by a duly authorized investigator was refused.

351(e)

- Officers of your firm interfered with the investigator in the performance of his duties by refusing to provide necessary records for his review.

Title 18, Section 1001

- The firm was aware that test animals had died, but concealed that fact.
- You advised FDA Investigators that you had no connection with the study, knowing the statement to be false.
- The study that was submitted with NDA 80-125 contains fictitious entries.
- The documents submitted in support of your application contain false statements.

Exhibit 5-4
LEGAL STATUS SHEET

SAMPLE NO: _____

A. STATUS OF FIRM AT TIME OF ALLEGED VIOLATIONS

Date _____

Full name of firm _____

Please check and fill in appropriate section below:

1. Corporation ☐ Year Incorporated _____ Under laws of what state? _____

   Names and Titles of principal officers

   _____
   (include first name and middle initial)

   _____

   _____

2. Partnership ☐

   Name of each partner

   _____
   (include first name and middle initial)

3. Sole Ownership ☐

   Name of Owner

   _____
   (include first name and middle initial)

B. STATUS OF FIRM AT PRESENT TIME

Date: _____

☐ Same as above ☐ Different

Full name of firm _____

1. Corporation ☐ Year Incorporated _____ Under laws of what state? ____

Names and titles of principal officers

_____
(include first name and middle initial)

2. Partnership

Name of each partner

_____
(include first name and middle initial)

3. Sole Ownership

Name of Owner _____
(include first name and middle initial)

Signature _____

Title _____

Exhibit 5-5
INFORMATION SHEET

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

INFORMATION SHEET IN CONNECTION WITH ENCLOSED SECTION 305 NOTICE

OBJECT OF THE MEETING

This meeting is scheduled to give the person or persons who appear to be responsible for the violations of the **Federal Food, Drug, and Cosmetic Act**, and other Federal Laws, as specified in the attached Charge Sheet an opportunity to explain voluntarily any circumstances connected with the preparation, handling, shipment, or sale of the articles involved which would indicate that criminal action should not be taken. You are not compelled, however, to answer. Any civil action which may have been taken against the goods involved, such as seizure, does not preclude prosecution of those responsible for the violation: the meeting concerns the possible criminal action only. A copy of the Federal Food, Drug, and Cosmetic Act and regulations for its enforcement may be had upon request.

NATURE OF THE MEETING

This **meeting** is informal and confined to questions of fact. For your convenience in submitting required information concerning the status of your firm both on the date of response to this notice and on the date of alleged violation, the attached Legal Status forms may be filled out and returned with your answer, whether written or by personal appearance. Your answer may consist of the disclosure of any pertinent facts, letters, files, guaranties, shipping documents, analyses, arguments, etc., which you feel may present valid reasons why you should not be prosecuted.

GUARANTIES

In the case of articles that are adulterated or misbranded when introduced in interstate commerce the Federal Food, Drug, and Cosmetic Act (the Act) places responsibility on the interstate shipper, even though he may be only the distributor and not the manufacturer. Distributors may relieve themselves of responsibility if they hold a legal guaranty under Section 303(c) of the Act. If the articles were sold to you by a person residing in the United States and guaranteed by such person to comply with the provisions of the Act, you should submit:

Evidence of that fact, and

A statement as to whether the product at the time of the apparent violation by you was in the identical condition and bore the same labels as when received by you from the guarantor, and

The full name of the person who, if called upon, can identify the pertinent records and testify to the facts as you present them.

HOW TO ANSWER

You may appear in person or by attorney or other designated representative, or you many submit your response in the form of a letter in lieu of personal appearance. If written response is made, please submit your letter and all accompanying documents in **triplicate.** Documents submitted at personal appearance should be in **triplicate. All documents should be conspicuously identified by the reference number shown on the upper right corner of the Section 305 Notice.**

RESULT OF THE MEETING

After the meeting has been held and all the facts considered, if it is the conclusion of the Secretary of the Department of Health and Human Services that prosecution should be recommended, the facts in the matter will be transmitted to the Department of Justice for appropriate action

FORM FDA 466a (7/80) PREVIOUS EDITION IS OBSOLETE.

Exhibit 5-6
SUMMARY FORMAT - SECTION 305 MEETING

SUMMARY

FIRM AND INDIVIDUAL CITED:

SAMPLE NO. AND PRODUCT:

DATE OF MEETING:

WHERE HELD:

PRESENT:
(List attendees - name, title, etc.)

WRITTEN SUMMARY:

_____
Compliance Officer
_____District

(distribution)

Exhibit 5-7
NOTIFICATION OF NON-PROSECUTION

Dear_____:

Pursuant to 21 CFR 7.85(h), this is to advise you of the decision not to proceed with criminal prosecution of (firm name and/or individual name or names) based on the charges set forth in the Section 305 Notice dated_____.

This decision is based on the evidence we have at this time and does not preclude the initiation of criminal prosecution, based in whole or in part on any or all of the charges set forth in the Notice, should new evidence or subsequent violations of the law reveal the need for such action. In such case, a new Section 305 Notice will issue except as provided in 21 CFR 7.84(a)(2) and (3).

_____
District Director

Exhibit 5-8
TIMEFRAMES FOR ADMINISTRATIVE DETENTION OF FOOD

Appellant's Deadlines

	Perishable Food	Non perishable Food
Requesting a Hearing	See "Filing an Appeal," below.	4 calendar days Notice of intent to request a hearing must be filed within 4 calendar days of receipt of detention order—or FDA will not grant the hearing. Request for hearing must be filed within 10 calendar days from receipt of detention order.
Filing an Appeal	2 calendar days Appeal must be filed within 2 calendar days of receipt of detention order (the appeal may or may not include a request for a hearing)	10 calendar days Appeal must be filed within 10 calendar days of receipt of detention order.

Exhibit 5-9
TIMEFRAMES FOR ADMINISTRATIVE DETENTION OF FOOD

FDA's Deadlines

Holding a Hearing	2 calendar days If the Appeal includes a request for a hearing, and FDA grants the request, the hearing must be held within 2 calendar days after the date the appeal is filed.
Written Report of the Hearing	Noon of the fifth calendar day The presiding officer must issue a written report that includes a proposed decision confirming or revoking the detention by noon on the fifth calendar day after the appeal is filed. The appellant then has 4 hours to submit comments. The presiding officer must issue a decision on the appeal within five calendar days after the appeal is filed. [See "Decision on an Appeal (with or without a hearing)" below]
Decision on an Appeal (with or without a hearing)	5 calendar days If a detention order is appealed, the presiding officer must issue a decision on the appeal, in the form of an order confirming or revoking the detention, within 5 calendar days after the appeal is filed. If the presiding officer fails to confirm or terminate the detention order within this time frame, the detention is deemed terminated.
Seizure of Perishable Foods	4 calendar days to send recommendation to DOJ If FDA initiates a seizure action against Perishable Food, FDA will send the seizure recommendation to the Department of Justice within 4 calendar days after the detention order is issued, unless extenuating circumstances exist. If the fourth calendar day is not a working day, OCC must advise DOJ on the last working day before the deadline of its plans to recommend a seizure and will send the seizure as soon as practicable on the first working day after the non-work day.

Exhibit 5-10
MODEL GENERAL SUMMARY OF INFORMATION –
Administrative Detention of Food*

(District Letterhead)

Date

Mr. John E. Smith
XYZ, Inc.
123 Smith Lane
Anywhere, MS

Dear Mr. Smith:

This is a General Summary of Information in Support of Detention DN 90222.

We intend to present the following information to support our action:

1. Epidemiological data developed by the Centers for Disease Control and Prevention (CDC) and public health officials in the states of California, Oregon, and Washington.
2. Analytical data based on samples of 5 ounce packages of "Snackies" food treats collected by FDA, and other government and state agencies.
3. Form FDA 483 Inspectional Observations issued to John E. Smith, owner of XYZ, Inc.
4. Establishment Inspection Report dated July 1, 2004.
5. Pages from Quality Control Log of XYZ, Inc. dated June 20, 2004.
6. Testimony of Erin Pendleton, Investigator, reporting her observations and her discussion with Mr. Jones, V.P., Quality Assurance.

Sincerely yours,

District Director

*Not to be used when the detention order is based on classified information. Consult with OCC to determine what, if any, information can be provided consistent with safeguarding the information and its source.

Exhibit 5-11
MODEL COMPREHENSIVE STATEMENT–
Administrative Detention of Food*

(District Letterhead)

Date

Mr. John E. Smith
XYZ, Inc.
123 Smith Lane
Anywhere, MS

Dear Mr. Smith:

The following is a Comprehensive Statement of the Basis for Detention Order DN 90222.

The Centers for Disease Control and Prevention (CDC) and public health officials in the states of California, Oregon, and Washington conducted epidemiological studies that revealed that 5 ounce packages of “Snackies” food treats with a sell by date of 6/12/2004 (or lot #1234) have been associated with outbreaks of food-borne illness in those states.

Samples of 5 ounce packages of "Snackies" food treats collected by FDA and other government and state agencies were analyzed by FDA and found to contain *Salmonella enteritidis. Salmonella* is an organism which can cause serious and sometimes fatal infections in young children, frail or elderly people, and others with weakened immune systems.

During a July 1, 2004 inspection of your establishment, FDA Investigator _____ (name) observed that XYZ, Inc.’s routine sampling program revealed that 5 ounce packages of "Snackies" food treats with a sell by date of 6/12/2004 (or lot #1234) contained *Salmonella enteritidis*.

This information indicates that the article of food presents a threat of serious adverse health consequences or death to humans.

Sincerely yours,

District Director

*Not to be used when the detention order is based on classified information. Consult with OCC to determine what, if any, information can be provided consistent with safeguarding the information and its source.

To be used when the detention order (Detention Notice - Form FDA 2289) may not serve as the Comprehensive Statement because the "reason for detention" is not described in sufficient detail. When the detention order may serve as the Comprehensive Statement, the letter need only include a copy of the detention order and reference the "reason for detention" as the Comprehensive Statement.

Exhibit 5-12
MODEL HEARING CONFIRMATION LETTER–
Administrative Detention of Food

(Region/OE Letterhead)

Date

Mr. John E. Smith
XYZ, Inc.
123 Smith Lane
Anywhere, USA

Dear Mr. Smith:

I am confirming the information listed below discussed during our telephone conversation of today.

The hearing you requested on the appeal of the administrative detention of your article of food will be held on (date) at the (_____) district office, (street address, city, state, Zip Code) at (time) a.m/p.m.

The hearing will be a closed hearing because the proceedings constitute an open investigatory record. This means that only you, your counsel, witnesses, and employees as well as FDA representatives will be allowed to attend.

The regulations on administrative detention (21 CFR Part 1, subpart K) state that 21 CFR Part 16 will be followed in conducting the hearing. However, the regulations on administrative detention make the following exceptions to Part 16:

1. The detention order under 21 CFR 1.393, rather than the notice under 21 CFR 16.22(a), provides notice of opportunity for the hearing and is part of the administrative record of the regulatory hearing under 21 CFR 16.80(a).
2. A request for a hearing must be addressed to the FDA District Director in whose district the article of food involved is located.
3. The provision in 21 CFR 16.22(b), providing that a person not be given less than 3 working days after receipt of notice to request a hearing, does not apply.
4. The provision in 21 CFR 16.24(e), stating that a hearing may not be required to be held at a time less than 2 working days after receipt of the request for a hearing, does not apply.
5. 21 CFR 1.406, rather than 21 CFR 16.24(f), describes the statement that will be provided to an appellant where a detention order is based on classified information.
6. 21 CFR 1.404, rather than 21 CFR 16.42(a), describes the FDA employees, e.g., Regional Food and Drug Directors or other officials senior to a District Director, who preside at hearings.
7. The presiding officer may require that the hearing be completed within 1 calendar day, as appropriate.
8. 21 CFR 16.60(e) and (f) do not apply to the hearing. The presiding officer must prepare a written report of the hearing. All written material presented at the hearing

will be attached to the report. The presiding officer must include as part of the report of the hearing a finding on the credibility of witnesses (other than expert witnesses) whenever credibility is a material issue, and must include a proposed decision, with a statement of reasons. The hearing participant may review and comment on the presiding officer's report within 4 hours of issuance of the report. The presiding officer will then issue the final agency decision.

9. 21 CFR 16.80(a)(4) does not apply to the hearing. The presiding officer's report of the hearing, and any comments on the report by the hearing participant under 21 CFR 1.403(h), are part of the administrative record.
10. No party shall have the right under 21 CFR 16.119 to petition the Commissioner of Food and Drugs for reconsideration or a stay of the presiding officer's final agency decision.
11. If FDA grants a request for an informal hearing on an appeal of a detention order, the hearing must be conducted as a regulatory hearing pursuant to regulation in accordance with 21 CFR Part 16, except that 21 CFR 16.95(b) does not apply to the hearing. With respect to the regulatory hearing on an appeal of a detention order, the administrative record of the hearing specified in 21 CFR 16.80(a)(1), (a)(2), (a)(3), and (a)(5), and 1.403(i) constitutes the exclusive record for the presiding officer's final decision on an administrative detention. For purposes of judicial review under 21 CFR 10.45, the record of the administrative proceeding consists of the record of the hearing and the presiding officer's final decision.

I am authorized by 21 CFR 10.19 and 21 CFR 16.60(h) to waive, modify, or suspend any provision under 21 CFR Part 16. I am waiving, modifying, or suspending the following provisions:

1. 21 CFR 16.60(f), which requires the presiding officer to make a recommended decision with statement of reasons to the deciding official, is not applicable because I am the Deciding Official as well as the Presiding Officer in this instance.
2. Pursuant to 21 CFR 1.403(k), 21 CFR 16.95(b) does not apply.
3. 21 CFR 16.60(b), which provides that all parties may confront and conduct reasonable cross-examination of any person (except for the presiding officer and counsel for the parties) who makes any statement on the matter at the hearing, is modified. Reasonable questioning will be allowed instead.

If feasible, at least one day before the hearing, you are to provide the District Director with written notice of, or a copy of, if the District Director could not reasonably be expected to obtain a copy, any published articles or written information you intend to present or rely upon at the hearing as required by 21 CFR 16.24(g).

Any written communication you forward or present to me must be sent by you to all other participants to the hearing as required by 21 CFR 16.44(c).

You are requested to provide at the hearing a brief summary of any lengthy documents you intend to present at the hearing.

If you have any additional questions on the procedures I will follow at the hearing, you may contact me at (phone number) prior to the hearing.

Sincerely yours,

Presiding Officer

Exhibit 5-13
MODEL ORDER –
Administrative Detention of Food – Short Form[1]

(Region/OE Letterhead)

Date

Order

Mr. John E. Smith
XYZ, Inc.
123 Smith Lane
Anywhere, MS

Dear Mr. Smith:

Based on my review of the material (make brief reference to the documents used by the presiding officer, (e.g. epidemiological data, analytical data from samples, FDA 483, EIR, etc. and testimony) presented in the appeal of Detention Notice Number DN90222, I hereby order that the Detention Order be confirmed (revoked) because FDA has (does not have) credible evidence or information indicating that the article of food presents a threat of serious adverse health consequences or death to humans or animals.

(Include the following if classified information was used, in whole or in part, to support the detention :) This decision is based (in part) on classified information.

Sincerely,

Presiding Officer

[1]This form is to be used when a hearing is not held, or when the order cannot be consolidated with the written report of the hearing because the report cannot be completed within the time frame for issuing the order.

Exhibit 5-14
MODEL GENERAL SUMMARY OF INFORMATION
Administrative Detention of Devices

District Director Letterhead

Date

Ace Plastic Company
11124 Railroad Street
Ogallala, Nebraska 69158

Dear Sir:

This is a General Summary of Information in Support of Detention DN 60011.

We intend to present the following information to support our action:

1. Form FDA 483 list of observations issued to Albert C. Edwards, owner of Ace Plastic Company.
2. Establishment Inspection Report dated February 20, 1980.
3. Collection Report for sample of syringes.
4. Pages from Quality Control Log of Ace Plastic Company dated February 18, 1980.
5. Testimony of Sidney H. Rogers, Investigator, reporting his observations and his discussion with Mr. Edwards.

Sincerely yours,

District Director

Exhibit 5-15
MODEL COMPREHENSIVE STATEMENT*
Administrative Detention of Devices

Date

Ace Plastic Co.
11124 Railroad Street
Ogallala, Nebraska 69150

Dear Sir:

The following is a Comprehensive Statement of the Basis for Detention Order DN 60011.

FDA Investigator _____ observations:

Black unidentified spots on the needles and holes in the individual protective packaging of the sterile 2cc syringe led him/her to believe that the devices are adulterated and misbranded resulting in issuing Detention Order number DN 60011.

_____made these observations during his/her (date) inspection of your establishment.

The black spots on the needles and holes in the packages lead us to believe the product is adulterated within the meaning of (1) Section 501(a)(2)(A) of the Federal Food, Drug, and Cosmetic Act (the Act) in that the device has been prepared, packed, or held under insanitary conditions whereby it may have been rendered injurious to health; and (2) within the meaning of Section 501(c) of the Act in that its quality falls below that which it purports or is represented to possess. Further, these same observations lead us to believe that the product is misbranded per Section 502(a) of the Act because the label states the product to be sterile and the holes in the protective wrapper allow the product to be exposed to contamination.

*To be used when the detention order (FDA 2289 Detention Notice) may not serve as the Comprehensive Statement because the "reason for detention" is not described in sufficient detail. When the detention order may serve as the Comprehensive Statement, the letter need only include a copy of the detention order and reference the "reason for detention" as the Comprehensive Statement.

Exhibit 5-16
EXAMPLES OF DETAILED STATEMENTS
Administrative Detention of Devices

EXAMPLES OF STATEMENTS UNDER ITEM #15, "REASON FOR DETENTION" THAT PROVIDE SUFFICIENT DETAIL FOR THE FDA 2289 ORDER TO SERVE AS A COMPREHENSIVE STATEMENT:

1. 21 USC Section 351(c) charge.

   - Detention order cites adulteration within the meaning of Section 351(c) because the quality of the device falls below that which it claims to possess.

   - Comprehensive statement expands upon the charge in the detention order by adding: "...because the labeling specifies that the device measures "x" within ± 3 percent but tests conducted by FDA show that the device only measures "x" within ± 25 percent."

2. 21 USC Section 351(h) charge.

   - Detention order cites adulteration within the meaning of Section 351(h) in that the methods used in, etc. (tracking in plain language the applicable portion of the statute) are not in conformity with GMP requirements under 21 USC Section 360j(f) as set forth in 21 CFR Part 820.

   - Comprehensive Statement expands upon the charge in the detention order by adding: "...because (citing applicable sections of the GMP regulations and deviations from them, working directly from the FDA 483 but using common, non-statutory language."

3. 21 USC Section 352(a) charge.

   - Detention order cites misbranding within the meaning of Section 352(a) in that the labeling for the device, which states that the device will cure the common cold, is false or misleading.

   - Comprehensive statements expand upon the charge in the detention order by adding: "... because..."

The same approach should be followed in comprehensive statements where the detention order cites misbranding within the meaning of 21 USC Sections 352(f), (j), etc. The comprehensive statement simply summarizes the factual basis of district's case. If this kind of format is used for a comprehensive statement, the general summary of the information which the district will present in support of the detention (21 USC Section 321(x)(3)) need not consist of anything more than a list of documents (FDA 483, EIR, CR, Analyst Worksheet), including affidavits (for example, where the charge is based on the absence of an approved PMA or an IDE - see 21 USC Section 351(f)).

Exhibit 5-17
MODEL HEARING CONFIRMATION LETTER
Administrative Detention of Devices

RFDD Letterhead

Date

Mr. Albert C. Edwards
President
Ace Plastic Company
11124 Railroad Street
Ogallala, Nebraska 69158

Dear Mr. Edwards:

I am confirming the information listed below discussed during our telephone conversation of today.

The hearing you requested on the appeal of the administrative detention of your devices will be held on ___at the Kansas City district office, 1009 Cherry Street, Kansas City, MO at 9:00 a.m.

The hearing will be a closed hearing because the proceedings constitute an open investigatory record. This means that only you, your counsel, witnesses, and employees as well as FDA representatives will be allowed to attend.

The regulations on administrative detention 21 CFR 800.55 states that 21 CFR Part 16 will be followed in conducting the hearing, however, the regulations make the following exceptions to Part 16:

1. 21 CFR 16.22(a), concerning the issuance of a separate notice of opportunity for a hearing, is not applicable since the Detention Notice also serves as that notice.

2. 21 CFR 16.22(b), concerning the appeal being sent to the Presiding Officer, is not applicable since the regulations require the appeal to be sent to the District Director of the district where the devices are located.

3. 21 CFR 16.24(e), concerning not holding the hearing within two days of the appeal, is not applicable because of the short time frames involved. We can hold the hearing within two days of your appeal.

4. 21 CFR 16.42(a), concerning those persons who may act as the Presiding Officer, is not applicable because I have been designated by regulations as the Presiding and Deciding Official.

I am authorized by 21 CFR 10.19 and 21 CFR 16.60(h) to waive, modify, or suspend any provision under 21 CFR Part 16. I am waiving or modifying the following provisions:

1. 21 CFR 16.60(f), which requires the presiding officer to make a recommended decision with statements of reasons to the deciding official, is not applicable because I am the Deciding Official as well as the Presiding Officer in this instance.

2. 21 CFR 16.95(b)(1) and (2) which state that the Administrative Record of a Regulatory Hearing (21 CFR 16.80(a)) is the exclusive record and basis respectively for the decision. The decision will not be based on any material that is not part of the administrative record. I am modifying 21 CFR 16.95(b)(1) and (2), however, because the decision will be based in most cases, on all information presented to me prior to or during the hearing. The decision will not be based on the following information or documents if they are not received or completed by me within the time period necessary for me to review or complete them prior to making a decision as required by the Act or regulation:

   a. Information and views I have permitted to be submitted after the hearing, are not part of the official record unless the post hearing submissions and information is submitted within the time specified by me.

   b. Any transcript of the hearing.

   c. My Report of the Hearing and any comments on the report.

3. That part of 21 CFR 16.60(b) is waived which provides that all parties may confront and conduct reasonable cross-examination of any person (except for the presiding officer and counsel for the parties) who makes any statement on the matter at the hearing. Reasonable questioning will be allowed instead. Reference congressional intent: House of Representatives Report no. 94-853 and 21 CFR 16.5 and 16.60(h).

If feasible, at least one day before the hearing, you are to provide the District Director with written notice of, or a copy of if the Director could not reasonably be expected to obtain a copy, any published articles or written information you intend to present or rely upon at the hearing as required by 21 CFR 16.24(g).

Any written communication you forward or present to me must be sent by you to all other participants to the hearing as required by 21 CFR 16.44(c).

You are requested to provide at the hearing a brief summary of any lengthy documents you intend to present at the hearing.

If you have any additional questions on the procedures I will follow at the hearing, you may contact me prior to the hearing.

Sincerely yours,

Albert Smith
Regional Food and Drug Director

Exhibit 5-18
MODEL ORDER 1/
Administrative Detention of Devices

RFDD Letterhead

Date

Order

Ace Plastic Company
11124 Railroad Street
Ogallala, Nebraska 69158

Dear Sir:

Based on my review of the material (make brief reference to the documents used by the presiding officer, (e.g. FDA 483, analyst worksheet, published article, CR, EIR, etc. and testimony) presented in the appeal of Detention Order number _____, I hereby order that the Detention Order be confirmed (revoked) because there is (insufficient) reason to believe that the devices are adulterated (misbranded) within the meaning of Section _____ of the Federal Food, Drug, and Cosmetic Act in that _____. 2/

Albert Smith
Regional Food and Drug Director

1/ Short Form: To be used when separate written decision/report of the hearing must be prepared later, due to short time frame for the order.

2/ Delete "of section_____", and "in that _____" if the detention is revoked.

EXHIBIT 5-19
MODEL ORDER OF RETENTION, RECALL, AND/OR DESTRUCTION

ORDER OF RETENTION, RECALL, AND/OR DESTRUCTION

Date Issued: MMM DD, YYYY
Issued To: Name of Responsible Individual
Title
Establishment Name
Address
CITY, ST, ZIP CODE

Dear [NAME],

The Food and Drug Administration (FDA) conducted an inspection of your facility at [ADDRESS if different than above] on [MM DD, YYYY], covering the manufacture of human cell, tissue, and cellular and tissue based products (HCT/Ps) subject to Title 21, Code of Federal Regulations, Part 1271 (21 CFR Part 1271). Our review of the information and records examined and collected during the inspection show that certain HCT/Ps received and distributed by your organization may be in violation of 21 CFR Part 1271, as indicated below:

[LIST VIOLATIONS]

- Between [DATE] and [DATE], [QUANTITY/TYPE] HCT/Ps from NNN donors were distributed which were repeatedly reactive for HBsAg/HIV by EIA (21 CFR 1271.85). (Example)

Pursuant to 21 CFR 1271.440, the above referenced HCT/Ps must be:
- Recalled (if distributed), within five (5) working days of receipt of this order, under the supervision of an authorized official of the FDA, and/or
- Destroyed by an acceptable method of disposition, within five (5) working days of receipt of this order, under the supervision of an authorized official of the FDA, or
Retained until it is recalled, destroyed, the safety of the HCT/P is confirmed, or an agreement is reached with the FDA for its proper disposition under the supervision of an authorized official of the FDA.

[NAME OF FIRM], its owners, employees, and agents shall not distribute or dispose of the HCT/P in any manner except to recall and destroy it consistent with the provisions of the Order. Any other arrangements for ensuring the proper disposition of the HCT/Ps must be agreed upon in writing by [NAME OF FIRM] and an authorized official of the FDA. Such arrangements may include assurance that the HCT/P has been recovered, processed, stored, and distributed in conformance with the attached regulations (21 CFR Part 1271).

All actions taken pursuant to this Order, or otherwise related to the products subject to this Order, shall be taken under the supervision of an authorized Official of the FDA.

Within five (5) working days from the receipt of this Order, the recipient of the written Order or prior possessor of such HCT/P may appeal the Order to the District Director, [NAME], District, Food and Drug Administration, [ADDRESS, CITY, STATE, ZIP CODE] and request a hearing

on the matter in accordance with 21 CFR Part 16 (copy attached). Such manner of appeal is described in 21 CFR 1271.440(e) of the attached regulations. Failure to request a hearing within the specified time period constitutes a waiver of the right to a hearing.

Please contact [NAME], Compliance Officer, at [TELEPHONE NUMBER], to arrange for supervision of the disposition of the products.

[SIGNATURE BLOCK]
District Director

Attachments (2)
21 CFR Part 1271
21 CFR Part 16

cc: Name and Address of any other HCT/P manufacturer or organization with interest in/jurisdiction over this HCT/P.
HFM-360
HFM-100
HFC-210
HFC-230
GCF-1

Exhibit 5-20: Disqualification Proceedings Flowchart

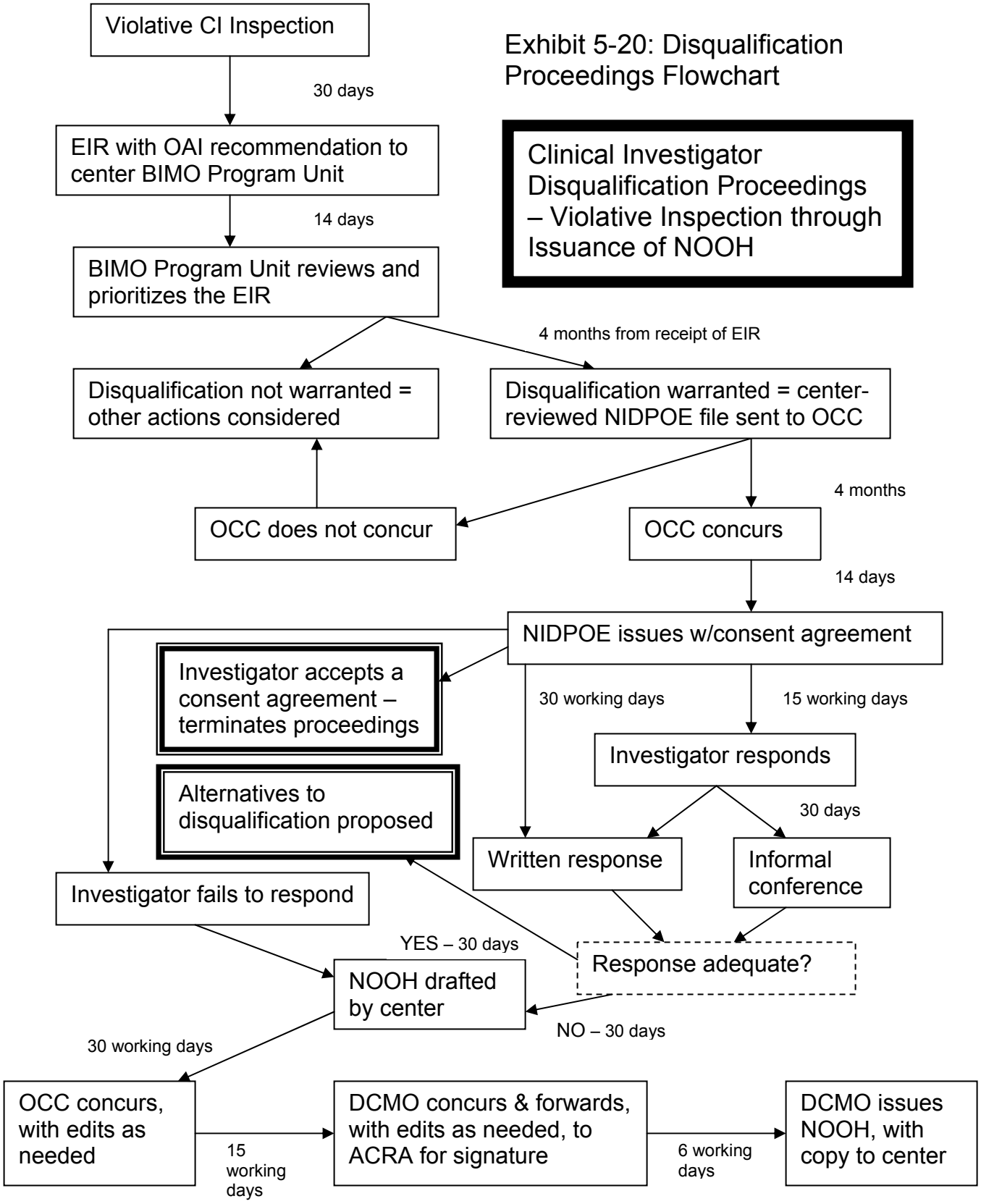

Exhibit 5-21

Sample NIDPOE

[Date]

CERTIFIED MAIL - RETURN RECEIPT REQUESTED

[*Clinical Investigator's Name* and *Address*]

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY TO EXPLAIN

Dear [*Clinical Investigator's Name*]:

Between [*inspection start date*] and [*inspection ending date*], Food and Drug Administration (FDA) (hereafter referred to as the "agency") investigators conducted an inspection of the following clinical study in which you participated: [*title of clinical study*]. This inspection was conducted as part of the FDA's Bioresearch Monitoring Program that includes inspections designed to monitor the conduct of research involving investigational products.

[For drugs, biologics, devices] Based on our evaluation of information obtained by the agency, we believe that you have [repeatedly and/or deliberately violated regulations governing the proper conduct] [and] [repeated and/or deliberately submitted false information in a required report] of clinical studies involving [an investigational new drug] [an investigational device] as published under *Title 21, Code of Federal Regulations (CFR), Part* [*312, 812*] (copy enclosed).

[*For new animal drugs]* Based on our evaluation of information obtained by the agency, we believe that you have [repeatedly and/or deliberately failed to comply with the conditions of the exempting regulations] [and] [repeated and/or deliberately submitted false information in a required report], as published under *Title 21, Code of Federal Regulations (CFR),* Part 511.1(b) (copy enclosed).

This letter provides you with written notice of the matters complained of and initiates an administrative proceeding, described below, to determine whether you should be disqualified from receiving investigational products as set forth under 21 CFR [*312.70, 812.119, 511.1(c)*].

A listing of the violations follows. The applicable provisions of the CFR are cited for each violation.

[*Insert List of Violations*]

This letter is not intended to be an all-inclusive list of deficiencies with your clinical studies of investigational [*name of investigational product*]. It is your responsibility to ensure adherence to each requirement of the law and relevant regulations.

On the basis of the above listed violations, FDA asserts that you have [repeatedly and/or deliberately failed to comply with the cited regulations] [*for new animal drugs:* failed to comply with the conditions of the exempting regulations] [and] [repeatedly and/or deliberately submitted false information] and it proposes that you be disqualified as a clinical investigator. You may reply to the above stated findings, including an explanation of why you should remain eligible to receive investigational articles and not be disqualified as a clinical investigator, in a written response or at an informal conference in my office. This procedure is provided for by regulation 21 CFR [*312.70, 812.119, 511.1(c)*].

Within fifteen (15) working days of receipt of this letter, write or call me at [*Center contact phone number*] to arrange a conference time or to indicate your intent to respond in writing. Your written response will need to be forwarded within thirty (30) working days of receipt of this letter. Your reply should be sent to [*Center contact*]. If you do not respond within fifteen (15) working days, the right to file a response will be waived.

Should you request an informal conference, we ask that you provide us with a full and complete explanation of the violations listed above. You should bring with you all pertinent documents. A representative of your choosing may accompany you. Although the conference is informal, a transcript of the conference will be prepared. If you choose to proceed in this manner, we plan to hold such a conference within 30 days of your request.

At any time during this administrative process, you may enter into a consent agreement with FDA regarding your future use of investigational articles. Such an agreement would terminate this disqualification proceeding. Enclosed you will find a proposed agreement between you and FDA.

The [*center name*] ("the Center") will carefully consider any oral or written response. If your explanation is accepted by the Center, the disqualification proceeding will be terminated. If your written or oral responses to our allegations are unsatisfactory, or we cannot come to terms on a consent agreement, or you do not respond to this notice, you will be offered a regulatory hearing before FDA, pursuant to 21 CFR Part 16 (enclosed) and 21 CFR Part [*312, 812, 511.1*]. Before such a hearing, FDA will provide you notice of the matters to be considered, including a comprehensive statement of the basis for the decision or action taken or proposed, and a general summary of the information that will be presented by FDA in support of the decision or action. A presiding officer who has not participated in this matter will conduct the hearing. The Commissioner will determine whether you will remain entitled to receive investigational articles. You should be aware that neither entry into a consent agreement nor pursuit of a hearing precludes the possibility of a corollary judicial proceeding or administrative remedy concerning these violations.

Sincerely yours,

[Designated Center Signatory + title]

Enclosures (2)

bcc:

GCF-1 (OCC)
HF-34 (GCPP)

HFC-130 (DFI)
HFC-230 (DCP/OE)
[*Center files and distribution*]
[*District Personnel, including the District Director; Director, Investigations Branch; and the district investigator(s)*]
HFD-45 (CDER/DSI)
HFM-664 (CBER/BIMO group)
HFS-205 (CFSAN BIMO group)
HFV-234 (CVM BIMO group)
HFZ-310 (CDRH/DBM)

Exhibit 5-22

Sample Consent Agreement

Agreement with Respect to Use of Investigational Products

The [*Center name*] ("the Center") of the United States Food and Drug Administration (FDA) and [*clinical investigator's name*] hereby agree as follows:

1. [*Clinical investigator's name*] conducted investigational clinical studies, including the following:

_____

_____

2. Between [*inspection start date*] and [*inspection ending date*], FDA conducted an investigation of the [*number or identify*] clinical studies performed by [*clinical investigator's name*]. As a result of the investigation, FDA determined that these studies contained sufficiently serious deficiencies to warrant the initiation of proceedings to have [*clinical investigator's name*] declared ineligible to receive investigational [*article(s)*], pursuant to 21 U.S.C. [*appropriate section*]. Specifically, FDA concluded that [*clinical investigator's name*] has:

_____

_____

_____

3. By letter dated [*date of NIDPOE letter*], the Center provided [*clinical investigator's name*] with written notice pursuant to 21 CFR [*312.70, 812.119, 511.1(c)*], of the foregoing violations and the information which led the Center to believe that [*clinical investigator's name*] [*violated FDA regulations governing the use of investigational* [*article*]] [*has submitted false information in a required report*].

4. In the written notice, the Center also invited [*clinical investigator's name*] to attend an informal conference to respond to the allegations or to provide a written response to the allegations.

5. [*Clinical investigator's name*] does not wish to contest the above allegations.

6. Beginning on the date this agreement is executed by the parties, [*clinical investigator's name*] is not eligible to receive investigational drugs, animal drugs, biologics, devices, or food additives, and is not entitled to conduct any further studies, intended or required for submission to FDA, of investigational articles regulated by FDA. [*Clinical investigator's name*] agrees to return to the sponsors of the investigational clinical studies in which [he] [she] participated, any and all remaining investigational articles in [his] [her] possession, custody, or control.

7. [*Clinical investigator's name*] waives [his] [her] opportunity to provide a written explanation and [his] [her] opportunity to attend an informal conference, and to any regulatory hearing pursuant to 21 CFR Part 16 and 21 CFR [*312.70, 812.119, 511.1(c)*].

8. This consent agreement terminates the administrative proceeding in this present matter,

which included the opportunity for an informal conference or a written explanation and a regulatory hearing pursuant to 21 CFR Part 16 and 21 CFR [*312.70, 812.119, 511.1(c)*].

9. This agreement does not preclude the United States or any other agency or private entity or person from bringing other proceedings relating to the matters underlying this agreement, and FDA's acceptance of the terms of this agreement may not serve as a defense in any proceedings that the United States or any other agency or private entity or person may initiate against [*clinical investigator's name*].

10. [*Clinical investigator's name*] acknowledges that double jeopardy would not attach should the United States bring any criminal charges against [him] [her] in connection with any matter relating to the agreement.

11. By this agreement, [*clinical investigator's name*] is disqualified as a clinical investigator. Disqualification pursuant to this agreement has the same legal effect as being disqualified pursuant to 21 CFR [*312.70, 812.119, 511.1(c)*] after a Part 16 hearing.

12. FDA is authorized to and will notify the sponsors of the investigational clinical studies in which [*clinical investigator's name*] has participated as an investigator. FDA also will notify the Institutional Review Board (IRB) with authority to oversee clinical studies performed by [*clinical investigator's name*] that [*clinical investigator's name*] has entered into this consent agreement. The notifications may contain a statement of the basis for [*clinical investigator's name*] not being eligible to receive or study investigational articles and the subsequent steps the sponsors and IRB should take.

13. FDA may make copies of this agreement available to the sponsors, IRBs and other interested parties.

14. With respect to this agreement, [*clinical investigator's name*] shall abide by the decisions of FDA; these decisions shall be considered the final decisions by FDA in this matter. FDA's decisions under this agreement shall be reviewed by any reviewing court, if necessary, under the standards set forth in 5 USC 706(2)(A).

15. [*Clinical investigator's name*] name will be added to the list of clinical investigator's entitled "Disqualified/Totally Restricted List for Clinical Investigators," which is available to the public on the web pursuant to the Freedom of Information Act (5 USC 552).

Agreed to:

_____ _____

[*Clinical investigator's name*] Date

_____ _____

[*Designated Center signatory + title*] Date

Exhibit 5-23

Sample Notice of Opportunity for Hearing (NOOH)

[Date]

CERTIFIED MAIL- RETURN RECEIPT REQUESTED

[*Clinical Investigator's and/or his/her counsel's Name & Address*]

NOTICE OF OPPORTUNITY FOR HEARING

Dear [*Clinical Investigator and/or his/her counsel*]:

The [Center name] ("the Center"), Food and Drug Administration (FDA) has information indicating that you [repeatedly and/or deliberately violated Federal regulations] [and] [repeatedly and/or deliberately submitted false information in a required report] in your capacity as an investigator in clinical trials with [an investigational new drug] [investigational new animal drug] [an investigational device]. The [violations] [and] [submission of false information] provide(s) the basis for withdrawal of your eligibility as a clinical investigator to receive [investigational new drugs] [investigational new animal drugs][investigational devices].

Pursuant to section [*312.70, 812.119, 511.1(c)*] of Title 21, Code of Federal Regulations (CFR), the Center informed you, by letter dated [*date of NIDPOE letter*], of the specific matters complained of and offered you an opportunity to respond to them in writing or at an informal conference. That same letter gave you the option of entering into a consent agreement with the agency, thereby terminating any administrative proceedings against you. [*State how the investigator responded to this offer whether by not responding, responding in writing, or attending an informal conference*]. [The Center has concluded that your [written explanation] [explanation offered at your informal conference] is unacceptable because it fails to adequately address the violations set forth below. [By failing to respond to the letter of [*date of NIDPOE letter*], you waived your opportunity to provide a written response or for an informal conference.]

Accordingly, you are being offered an opportunity for a regulatory hearing pursuant to 21 CFR Part 16 and [*312.70, 812.119, 511.1(c)*], on the question of whether you are eligible to receive [investigational new drugs] [investigational new animal drugs] [investigational devices]. You have the right to be advised and represented by counsel at all times. Any regulatory hearing on this matter will be governed by the regulations in 21 CFR Part 16 and the agency's guidelines on electronic media coverage of administrative proceedings, 21 CFR Part 10, Subpart C. Enclosed you will find copies of these regulations.

A listing of the specific violations follows. These are the matters that will be considered at the regulatory hearing. Applicable provisions of the CFR are cited for each violation.

[*Set out violations in numbered paragraphs. Cite CFR provision for each violation*.]

Your request for a hearing should be made, in writing, within ten (10) working days of receipt of this letter and should be directed to [*name of DCMO director*], Director, Division of Compliance Management and Operation, Office of Enforcement, Office of Regulatory Affairs, Telephone [*DCMO phone number*], Fax [*DCMO fax number*]. If no response to this letter is received by that time, you will be deemed to have waived any right to a regulatory hearing, and a decision in this matter will be made based on the facts available to the agency. No hearing will be held.

A request for a hearing may not rest upon mere allegations or denials but must present specific facts showing that there is a genuine and substantial issue of fact that warrants a hearing. Pursuant to 21 CFR 16.26, a request for a hearing may be denied, in whole or in part, if the Commissioner or his delegate determines that no genuine and substantial issue of fact had been raised by the material submitted. A hearing will not be granted on issues of policy or law. Written notice of a determination of summary judgment will be provided, explaining the reasons for denial of the hearing.

If you wish to respond but do not desire a hearing, you should contact [*Name of DCMO director]* within the time period specified above and send a written response containing your reply. The letter should state that you waive your right to a hearing and that you want a decision on the matter to be based on your written response and other information available to the agency.

The agency's offer to enter into a consent agreement attached to the Notice of Initiation of Disqualification Proceedings and Opportunity to Explain letter dated [*date of NIDPOE letter*] remains available. Entering into a consent agreement would terminate the administrative proceedings, but would not preclude the possibility of a corollary judicial proceeding.

No final decision by FDA has been made at this time on your eligibility to continue to use [investigational new drugs] [investigational new animal drugs] [investigational devices]. Moreover, there will be no prejudgment of this matter if you decline to enter into a consent agreement and decide instead either to request a regulatory hearing or to request that the decision be based on information currently available to the agency.

Please inform [*name of DCMO director*] within ten (10) working days of whether you wish to request a hearing or to have this matter resolved by consent agreement or information available to the agency.

Sincerely,

[*Name*]
Associate Commissioner for
Regulatory Affairs

Enclosures (3)

bcc:
GCF-1 (OCC)
HF-34 (GCPP)

HFC-130 (DFI)

HFC-210 (DCMO)
HFC-230 (DCP/OE)
[*Center files and distribution*]
[*District Personnel, including the District Director; Director, Investigations Branch; and the district investigator(s)*]
HFD-45 (CDER/DSI)
HFM-664 (CBER/BIMO group)
HFS-205 (CFSAN BIMO group)
HFV-234 (CVM BIMO group)
HFZ-310 (CDRH/DBM)