

## FOOD AND DRUG ADMINISTRATION

**FIELD MANAGEMENT DIRECTIVE No. 13 A**

<b>Subject:</b> International Inspection Program	<b>Area:</b> Operations Management	<b>Date Revised:</b> October 2002
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The Division of Field Investigations (DFI)/International Operations Branch (IOB), HFC-130, is responsible for the coordination of international activities for ORA personnel. See FMD No. 13 for procedures on requesting approval for ORA international travels except matters related directly to inspectional activities.

**PURPOSE**

This Field Management Directive (FMD) describes the role and responsibility of ORA in international inspection activities. It includes the procedure for planning and scheduling international inspections, reporting results of inspectional findings, and classifying Establishment Inspection Reports (EIRs). It also outlines the requirements and procedures to be followed for appointment to the International Inspection Cadre and the selection of cadre members in ORA international inspection programs.

**BACKGROUND**

FDA has conducted international inspections since 1955. Over the years, international inspections have increased in both complexity and frequency and cover all products subject to regulation by FDA. Examples are human and veterinary drugs, biologicals, medical devices, radiological health products, low-acid canned foods, and shellfish.

**ORA HEADQUARTERS INTERNATIONAL INSPECTION RESPONSIBILITIES AND PROCEDURES****Responsibilities**

DFI is responsible for the following activities on international inspection programs:

- (a) Formulation of the annual international travel plan/budget in accordance with Staff Manual Guide 2342.1. In preparing the plan/budget, DFI will also consider ORA international activities. These may include:
  - (1) Participation in international regulatory or scientific conferences.
  - (2) Participation in counterpart government meetings and conferences.

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- (3) Provide consultancies to international organizations such as World Health Organization (WHO), Food and Agriculture Organization (FAO), and Pan American Health Organization (PAHO).

The development process starts in the last quarter of the fiscal year with a request for projected non-inspectional international travels for the following year to ORA headquarters and field units. The plan/budget also reflects a projection of:

- (1) Routine inspectional follow-ups of the current inventory of international firms.
  - (2) Center inspection assignments.
- (b) Management of the international inspection program to assure that inspections are conducted in accordance with compliance program requirements and other supplemental instructions.
  - (c) Liaison with international regulatory authorities and coordination of inspectional activities with the U.S. State Department, DHHS Office of Global Health Affairs, and other FDA components.
  - (d) Arrangement of emergency or other special international trips to conduct surveys, investigate outbreaks of food borne illness, collect evidence required in case development, and attend urgent, unplanned meetings with foreign government and industry officials for problem solving.

### Procedures

DFI conducts international inspections for one of the following reasons:

- (a) Center Requested Inspections

When inspection information on a specific firm and/or process is needed but the available information is inadequate, not current, or nonexistent, centers will request DFI to schedule an inspection(s). Other assignments include follow-up and directed inspections at the manufacturing site when it is necessary to determine if corrective actions have been implemented, investigate adverse product reports, or to determine why there are specific out-of-limits samples.

- (b) Periodic Re-inspections

Periodic re-inspections are scheduled and performed as long as the international firm remains an active exporter to the U.S. DFI considers general or specific guidance that may be offered by the centers in scheduling these re-inspections. The inspection interval and depth of coverage of inspections are consistent with the periodic inspections of FDA's domestic program insofar as practical. Foreign firms must agree to the inspection because FDA has no legal international inspection authority. However, firms may decline inspection if they decide not to distribute their products in the U.S. Firms that decline inspection may, on a case by case basis, be considered for detention without examination until such time as they permit inspection.

The primary duties of DFI when planning international inspection trips and scheduling coverage of specific firms are:

- (1) Contact the foreign firm or U.S. agent to describe FDA's reason to conduct an inspection and identify a product (s) to be covered.
- (2) Seek the firm's agreement for inspection.

- (3) Identify and mutually agree on the dates of inspection.
- (4) Arrange with district or center management for the use of appropriate inspection personnel (from the International Inspection Cadre).
- (5) Prepare trip schedules and arrange lodging and transportation for the investigator or the inspection team.
- (6) Obtain passport/visa for the inspection personnel.
- (7) Provide a Notification of Foreign Travel to FDA's Office of International Programs which will seek approval from DHHS and the State Department.
- (8) Establish contact with foreign regulatory authorities when appropriate to:
  - (i) Arrange joint inspections upon their request or at FDA's initiative, or in compliance with any existing agreement with the particular country.
  - (ii) Arrange for inspectional personnel to meet with foreign counterparts, as needed.

International inspections are usually three weeks in duration, with one inspection scheduled per week. The inspections are typically scheduled to begin on Monday with one day each week set aside for writing EIR or for extending the inspection, if needed.

The trip may begin with a briefing session in headquarters or by conference call. Briefings provide an opportunity for the investigator or the inspection team to understand and discuss the assignments and to meet with interested staff members from the center. For example, the inspection personnel may be briefed by reviewing chemists, pharmacists, pharmacologists and medical doctors regarding particular issues and products or processes to be covered during an inspection trip. The inspection personnel can also review drug master files, New Drug Applications (NDAs), Antibiotic Forms 5 and 6, previous inspection reports, and other files.

If no briefing is scheduled, the appropriate files, copies of EIRs, etc., are provided by DFI to the inspection personnel in advance of the inspection trip.

On rare occasions, upon returning from an international trip, the inspection personnel may be debriefed at headquarters with staff from the center. Debriefings are sometimes conducted if serious deficiencies/problems were encountered in a firm(s), or if information is immediately needed to enable a center to make a decision on a pending application or a decision concerning a product(s) currently in distribution in the U.S.

### **PERSONAL SAFETY AND SECURITY**

In addition, investigator safety is the agency's first consideration when scheduling foreign inspections. In doing so, DFI takes into account all available information about the country and firms visited. FDA's international travelers are encouraged to make every effort to ensure their safety while in international travel status and will provide their office with a detailed itinerary so that they can be contacted in an emergency. Travelers will also check in with their office on a routine basis.

If ORA employees encounter an emergency situation while traveling abroad and requires assistance, immediate contact should be made with DFI at 301-827-5653, or FDA's 24-hour emergency number, 301-443-1240, if it is during non-business hours in the US. International cell phones will be available for international travelers, so they can be contacted in an emergency.

The following web sites can provide useful information for international travelers:

- [Centers for Disease Control](#)

<http://www.cdc.gov>

Information on diseases in specific countries, inoculations and prevention measures.

➤ CIA Fact Book

<http://www.odci.gov>

Information on climate, population, political parties, and the economy for all countries.

There are two ways to access the Fact Book:

- 1) Click on the “World Fact book,” click on “Country Listing”
- 2) Click on “Publications and Reports”, click on “World Fact Book”, click on “Country Listing.”

➤ State Department Travel Warnings

<http://www.state.gov>

The site has information on more than 160 countries. It describes entry requirements, travel conditions, available medical facilities, areas of instability and more.

Click on search and type in Travel Warnings, click on Travel Warnings and Consular Information, click on the letter for the country. For more information, return to the search page and type in “publications.”

## **INVESTIGATOR RESPONSIBILITIES**

The inspection personnel are expected to do the following during international inspections:

- (a) Complete inspections according to program and center instructions, as assigned.
- (b) Promptly notify DFI via fax of any significant deficiencies which adversely affect the safety of products currently being shipped to the U.S., or where conditions warrant immediate center attention.
- (c) Meet with counterparts in foreign regulatory agencies to discuss inspectional findings, FDA 483s, and general inspection matters, as directed by DFI.
- (d) Complete establishment report following each inspection with submission to DFI or the applicable center within 30 working days of the end of the inspection.
- (e) Prepare a proposed endorsement with an inspection conclusion and a district decision using the definitions in FMD No. 86. For the purpose of international inspection classification, sanctions, such as those listed below, are considered Official Action Indicated (OAI). The centers have final classification on foreign inspections.
  - (1) Automatic Detention of a product.
  - (2) Issuance of a warning letter.
  - (3) Issuance of a letter stating that entries will be detained if corrections are not made promptly.
  - (4) Recommendation for withholding of a pending Application.
  - (5) Suspension of license or certification, Notice of Intent to Revoke a License, etc.

- (6) Issuance of a Notice of Hearing as prerequisite to revoking an Approved Application (i.e., NDA, PMA, etc).
- (7) Request a recall of product from U.S. distribution.
- (8) Initiation of civil action to remove offending product from U.S. distribution.
- (f) Complete FACTS profile screens for each drug, device, or biologics (except blood and plasmapheresis) facility inspected.
- (g) Prepare and submit an expense voucher within five days of return from the trip. Promptly return official passport, tape recorder, notebook computer, or any other borrowed inspectional preparation materials to DFI.
- (h) Ensure the inspections are reported into FACTS in a timely manner (within 30 working days from the end of the inspection).

A more detailed description of the responsibilities of inspection personnel is described in the current Guide to International Inspections and Travel, Issued July 1999.

### **EIRS: CLASSIFICATION AND DISPOSITION**

- (a) Information reported to DFI per tab (b) of the Investigator Responsibilities section, will be forwarded to the appropriate center by DFI. The investigator must submit the EIR in a timely manner commensurate with the District Recommendation enforcement action anticipated but not to exceed 30 working days from the end of the inspection.
- (b) All completed EIRs will be promptly forwarded to appropriate center offices based on procedures in FMD No. 86 and routing instructions provided by DFI with the inspection preparation materials.
- (c) The endorsing office will enter the appropriate inspection classification and District Decision code. Centers are expected to review the FACTS coversheets and determine the final District decision. Centers will also assure that the profile status correlates with the Final District Decision.
- (d) Inspections resulting in official action or requiring significant voluntary corrective action will be rescheduled, by DFI, for follow-up with the concurrence of the center and /or in accordance with current procedures.

### **INTERNATIONAL INSPECTION PROGRAM PERSONNEL**

DFI maintains a roster of approximately 400 Senior investigators and analysts (chemists and microbiologists) who have demonstrated sufficient experience and special expertise in one or more of the following program areas: CGMP (drugs), antibiotics, sterile products, Quality System Regulations (devices), LACF, MQSA, CGMP (biologics), and clinical and non-clinical bioresearch monitoring inspections.

National expert investigators and members of the Core Team of Team Biologics conduct international inspections and participate in international conferences and seminars as part of their duties.

Work assignments may be completed in an uncomfortable work environment or in a situation where English may not be the primary language. Investigators and analysts must show an ability to work independently of as a member of an inspection team, make sound decisions with minimum supervision; and demonstrate maturity and patience. This will enable completion of assignments in an effective and diplomatic manner.

**INTERNATIONAL INSPECTION PROGRAM PERSONNEL SELECTION PROCEDURES**

- (a) Interested individuals can submit an Application for the International Inspection Cadre to DFI, International Operations Branch, at any time. With their district management concurrence, all applications are to include a summary of investigational experience and specified skills and supervisor's recommendation.
- (b) Send Applications by mail, e-mail or fax to:  
Director, International Operations Branch (HFC-130)  
Division of Field Investigations  
Food and Drug Administration  
5600 Fishers Lane – Rm.13-71  
Rockville, MD 20857  
FAX: 301-827-6685/443-3757
- (c) Investigators are generally assigned independent international trips following attendance at the Orientation to International Inspections Course or after they have completed an orientation trip accompanied by an experienced investigator. Orientation trips will be arranged by DFI.
- (d) The Director, International Operations Branch, will temporarily excuse investigators or analysts from participation in the program (following discussion with district or center management) if they have not demonstrated the special personal attributes listed in the above section, inspection reports are not submitted in a timely manner, or for other pertinent reasons.

International inspection cadre members are expected to take at least one trip each year to maintain membership in the cadre. Investigators or analysts may request withdrawal from the program should circumstances preclude continued international travel.

The Request for Nomination and the Criteria Required for Nomination to the FDA international Inspection Cadre are shown in Attachment A and B, respectively.

**ATTACHMENT A****Request for Nomination to the FDA International Inspection Cadre**

Candidate's Name: \_\_\_\_\_

Grade Level and Title: \_\_\_\_\_

FDA Address: \_\_\_\_\_

Mail Code: \_\_\_\_\_

Phone/FAX Numbers: \_\_\_\_\_

Program Area(s) Expertise (specify the areas within the program area in which you have experience; e.g., biologics, blood banks vs. plasma centers; for devices, IVDs vs. plastics; for drugs, bulks vs. finished pharmaceuticals):

Training Courses taken to demonstrate knowledge/expertise in these program areas:

Basic Law/Evidence Development – Date:

Investigative Interviewing – Date:

Basic Drug/Device/Biologics/Food Micro./Better Processing School/BIMO (circle those that apply and give dates).

Advance Courses (course title) – Dates:

How long have you been conducting inspections? Describe the type of inspections you have conducted in your preferred Program area. (For example, sterile drug/device inspections; bulk drugs vs. finished pharmaceuticals; and capsules and aerosols vs. tablets or ointments; electronic devices vs. IVDs, etc.).

Have you ever conducted international inspections? If so, please describe the type of inspections and the dates (months/year).

Have you attended the ORA International Inspection Course. If so, when?  
For Information Purposes Only:

For Investigators in program areas with Certification Programs — Are you certified? If so, at what level? In what program area(s)?

For ALL Investigators and Analysts: What other languages do you speak, read, are proficient in?

Academic Achievements beyond a BS or BA Degree (list degrees obtained; post-graduate work; or other academic courses taken to enhance your technical abilities):

Candidate's Signature: \_\_\_\_\_

Date: \_\_\_\_\_

The following signatures and concurrences certify that the candidate meets the criteria described in FMD 13A for Investigators and Analysts conducting International Inspections.

Immediate District Management Concurrence:

Printed Name and Position: \_\_\_\_\_

Signature/Date: \_\_\_\_\_

Comments: \_\_\_\_\_

\_\_\_\_\_

District Management Concurrence:

Printed Name and Position: \_\_\_\_\_

Signature/Date: \_\_\_\_\_

Comments: \_\_\_\_\_

\_\_\_\_\_



## ATTACHMENT B

### Criteria Required for Nomination to the FDA International Inspection Cadre

#### **BASIC REQUIREMENTS:**

##### **Investigators:**

- Grade GS-12 (Journeyman Level) or above
- Completed 6-month OJT using FDA Investigational Training Manual
- Basic Law and Evidence Development Course
- Investigative Interviewing Course
- At least three years conducting independent inspections in preferred program area(s)
- Demonstrated ability to prepare concise, accurate, and timely EIRs and FDA 483s as required by IOM, FMDs, etc.
- Demonstrated ability to communicate orally.
- Excellent working knowledge of FDA's laws, policies and procedures. As a representative of the FDA and the U.S. Government, the candidate must have a demonstrated professional demeanor and ability to communicate agency requirements, policies and procedures.

##### **Analysts:**

- Grade GS-12 (Journeyman Level) or above
- Documented completion of a 6-month OJT
- Basic Law and Evidence Development Course
- At least three years conducting team inspections in preferred program area(s)
- Demonstrated ability to prepare concise, accurate, and timely EIRs and FDA 483s as required by IOM, FMDs, etc. (Only in the area of review for which they have responsibility.)
- Demonstrated ability to communicate orally.
- Excellent working knowledge of FDA's laws, policies and procedures. As a representative of the FDA and the U.S. Government, the candidate must have a demonstrated professional demeanor and ability to communicate agency requirements, policies and procedures.

#### **SPECIFIC REQUIREMENTS FOR INVESTIGATORS:**

**Drug Investigators:** Successfully completed Basic Drug Manufacturing Quality Control Course and Industrial Sterilization (or equivalent\*\*).

**Device Investigators:** Successfully completed Basic Medical Device Training Course and Process Validation or Industrial Sterilization (or equivalent\*\*).

**Biologics Investigators:** Blood Banks/Plasma Center: Completed Basic Blood Banking and Plasmapheresis Course and Advanced Blood Banking and Plasmapheresis Course (or equivalent\*\*). Biologics Products: Drug Manufacturing and Quality Control and Industrial Sterilization (or equivalent\*\*).

**Food Investigators:** Successfully completed LACF or Seafood HACCP and Basic Microbiological Training Course.

**BIMO Investigators:** Successfully completed Clinical and/or Non-Clinical Bioresearch Monitoring Training Course (or equivalent\*\*).

**SPECIFIC REQUIREMENTS FOR ANALYSTS:**

Must document training/experience to reflect adequate knowledge/skills/abilities in the program area proposed for nomination. A proven track record showing experience on team inspections, or letters of commendation, etc., for performance on team inspections.

**SPECIALIZED REQUIREMENTS FOR INVESTIGATORS AND ANALYSTS:**

(Not mandatory, except for certain program areas, as described under specific requirements, if the Investigator/Analyst can show alternate experience in lieu of FDA requirement)

Courses in:

Process Validation  
Industrial Sterilization  
Computer System Validation  
Statistical Process Control  
Orientation to International Inspections  
Epidemiology  
Pre-Approval Inspections  
Fractionation Course  
IVD Course  
Biotechnology Course  
Allergenic Products Course  
Vaccines Course

\*\*

Equivalent or alternate experience based on inspection experience (e.g., conducted three or more independent inspections in the program area showing competency and understanding of concepts along with additional OJT experience). Level II Device Certification is deemed equivalent.