Draft Guidance for Industry, FDA Staff, and FDA-Accredited Third-Parties

Requests for Inspection by an Accredited Person under the Inspection by Accredited Persons Program Authorized by Section 201 of the Medical Device User Fee and Modernization Act of 2002

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Preface

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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. Introduction

Manufacturers of Medical Devices May Be Eligible To Have Third-Party Inspections of Their Establishments

Section 201 of the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) (Public Law 107-250) amends section 704 of the Federal Food, Drug, and Cosmetic Act (the act) by adding subsection (g). (21 U.S.C. 374(g)). This amendment authorizes FDA to establish a voluntary third party inspection program applicable to manufacturers of Class II or Class III medical devices who meet certain eligibility criteria. Under this new Inspection by Accredited Persons

Program (AP Program), such manufacturers may elect to have third parties that have been accredited by FDA (accredited person or AP) conduct some of their inspections instead of FDA.

The AP Program applies to manufacturers who currently market their medical devices in the United States and who also market or plan to market their devices in foreign countries. Such manufacturers may need current inspections of their establishments to operate in global commerce.

One benefit of the new program is that it will allow manufacturers greater control over the timing of their inspections. In addition, because some of the APs accredited by FDA are already recognized by other countries as persons authorized to conduct inspections of device establishments, it is possible that in some cases a single AP inspection will meet the requirements of more than one regulatory authority, thereby reducing the need for multiple inspections of the same establishment.

This guidance will help device establishments determine whether they are qualified to participate in the AP Program. Any establishment that is interested in obtaining additional information about eligibility or other matters addressed in this document may contact CDRH. Because the APs who have been approved by FDA will have to complete training before they may begin conducting independent inspections under the new program, the APs will not be available to companies for several months from the date of this guidance.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Discussion

Under the act, domestic manufacturers of Class II or Class III medical devices must be inspected for compliance with Good Manufacturing Practice (GMP) requirements and other applicable requirements at least once every two years. (21 U.S.C. 360(h)). One major benefit of the AP Program is that it enables eligible manufacturers to schedule such inspections at the same time they will be inspected by other regulatory authorities or organizations, thereby reducing the number of disruptions to the establishment's normal operations.

Following the enactment of MDUFMA, FDA accredited 15 APs to perform inspections under the AP Program. FDA used stringent selection criteria in its selection of APs to help ensure that third-party inspections under this program do not present any actual or apparent conflicts of interest. Those APs who were selected are in the process of completing training so they can soon begin conducting independent inspections under the AP Program. Once independent AP inspections are

underway, FDA will review the reports prepared by the APs following inspection to determine if your firm is in compliance with GMPs and other requirements.

The list of APs prepared by FDA is available on the Internet at http://www.fda.gov/cdrh/ap-inspection/ap-inspection.html. You may select any of the APs listed, provided you meet all of the eligibility criteria for the AP Program. The next section of this guidance describes in detail the eligibility criteria applicable to manufacturers who wish to participate in the AP Program.

III. Information about how to participate in the AP Program

Who may participate in the AP Program?

The AP Program is open to domestic U.S. device establishments, as well as foreign establishments that are required to register with FDA under section 510(i) of the act, provided such establishments otherwise meet the program's eligibility criteria.

What are the eligibility requirements for participating in the AP inspection program?

Based on requirements found at Section 704(g) of the act, you must satisfy the following criteria in order to be eligible to participate in the program:

1. You "manufacture, prepare, propagate, compound, or process" class II or class III medical devices. (Sec. 704(g)(1) of the act.) The shorthand term "manufacture" will be used for convenience throughout this document instead of listing each of these activities (i.e., "manufacture, prepare, propagate, compound, or process") repeatedly. ;

2. You market at least one of the devices in the United States;

3. You market or intend to market at least one of the devices in one or more foreign countries and **one or both** of the following two conditions are met:

   (a) One of the foreign countries certifies, accredits, or otherwise recognizes the AP you have selected as a person authorized to conduct inspections of device establishments, or

   (b) Your firm submits a statement that the law of a country where you market or intend to market your devices recognizes an inspection by the FDA

or by the AP. (Sec. 704(g)(6)(A)(iii)(I), (II) of the act.);

4. Your most recent inspection performed by FDA, or by an AP under this program, was classified by FDA as either "No Action Indicated (NAI)" or "Voluntary Action Indicated (VAI)." (Sec. 704(g)(6)(A)(i) of the act.); and

5. You submit a notice to FDA requesting clearance (approval) to use an AP, identify the AP you selected, and FDA agrees to the use of the selected AP. (Sec. 704(g)(6)(A)(ii).).

A. Device Eligibility Requirements[1]

Is your medical device eligible?

- Only establishments that manufacture (which term includes preparing, propagating, compounding, or processing) devices that are either class II or class III may be **eligible** for inspection under the AP Program. (Sec. 704(g)(1)). In addition, to be eligible, at least one of these devices must be marketed in the United States and at least one must be marketed, or intended to be marketed, in one or more foreign countries. (Sec. 704(g)(6)(A)(iii) of the act.) FDA cannot waive these requirements or provide a variance.

- If you do not manufacture a class II or class III device, market at least one such device in the United States, and market or intend to market at least one such device in a foreign country, your establishment is **not eligible** for inspection under the AP Program.

How can you show that you market or intend to market a device in a foreign country?

The following are examples of ways you can show that you market or intend to market a device in a foreign country:

- A distribution agreement, purchase order, or order acknowledgement issued by a foreign customer;

- A marketing application submitted by your firm to a foreign government; or

- Appropriate clearance documents from the foreign government to your firm.

[1] Unless otherwise noted, a reference to "requirements" in the following section refers to the requirements under section 704(g) of the act.

Is it necessary that one of the devices marketed or intended to be marketed in a foreign country is a class II or class III device?

- Yes. At least one of the devices that you market in the United States must be a class II or class III device, and at least one of the devices you manufacture for commercial distribution in a foreign country must be a class II or class III device. (Sec. 704(g)(1) and (g)(6)(A)(iii) of the act.)

- You should include the specific name(s) of the device(s) and the PMA or 510(k) number(s) of these class II or III devices in your request to FDA for clearance to use an AP.

- The device you market in the United States and the device you market or intend to market in one or more foreign countries do not have to be the same device, as long as they are manufactured in the same establishment.

B. Foreign Country-Related Eligibility Requirements[2]

What do you need to know about the inspection process of the foreign country or countries where you will market your medical device?

At least one foreign country where you market or intend to market your class II or class III device must either:

- certify, accredit, or otherwise recognize the AP you have chosen as a person authorized to conduct device inspections; or

- recognize device inspections by the FDA or AP. (Sec. 704(g)(6)(A)(iii)(I) and (II) of the act.)

  For example, one foreign country where you market or intend to market the device may certify the person you selected as an AP as authorized to conduct inspections of device establishments. This would satisfy the condition of recognition by a foreign country of the AP you selected.

[2] Unless otherwise noted, a reference to "requirements" in the following section refers to the requirements under section 704(g) of the act.

How can you identify APs that are recognized by a foreign country as authorized to conduct inspections of device establishments?

- FDA's Internet site mentioned earlier (http://www.fda.gov/cdrh/ap-inspection/ap-inspection.html) lists the APs approved by FDA and provides information on APs that foreign countries recognize. We recommend that you verify that the foreign country recognizes the AP prior to hiring the AP to conduct an inspection of your manufacturing facility.

Alternatively, how can you show that a foreign government recognizes device inspections by the FDA or AP?

There are at least three ways to show that a foreign government recognizes device inspections by the FDA or AP:

- First, a country may already accept FDA's Certificates to Foreign Governments or Certificates of Exportability. These certificates specifically include FDA's acknowledgement of compliance with GMP requirements. You may be able to obtain information about whether a particular country accepts these FDA certificates by contacting the appropriate foreign liaison. A list of foreign liaisons is provided at http://www.fda.gov/cdrh/devadvice/391.html.

- A letter from an appropriate foreign government office should be adequate, provided it states that device inspections by the FDA or AP are recognized. The list of foreign liaisons mentioned above may be useful for this purpose.

- You could prepare and submit to FDA a signed statement that the law of a foreign country in which you market or intend to market your device, recognizes inspections by the FDA or AP for the purpose of evaluating manufacturing operations and compliance. Your written statement should be accompanied by a copy of the relevant foreign law (translated into English).

C. Inspection History

How does your inspection history affect your participation in the AP Program?

- Your most recent FDA-classified device inspection is one of the factors that determines your eligibility to participate in the AP Program. (Sec. 704(g)(6)(A)(i) of the act.)

- Inspections are classified according to three categories:

    - No Action Indicated (NAI); this means there were no deviations or only minor deviations from the applicable Quality System/Good Manufacturing Practice (QS/GMP) requirements. (See 21 U.S.C. 360j(f)(1)(A) of the act and regulations at 21 CFR Part 820).
    - Voluntary Action Indicated (VAI); this refers to minor to significant QS/GMP deviations.
    - Official Action Indicated (OAI); this refers to significant QS/GMP deviations and warnings.

- You may qualify for the AP Program if your most recent device inspection, performed either by FDA or by an AP under the AP Program, was classified by FDA as either NAI or VAI. (Sec. 704(g)(6)(A)(i)). In addition, in assessing your eligibility to use an AP, FDA may ask you to provide compliance data including complete reports of GMP inspectional findings from audits that occurred at your firm within the past 24 months. (Sec. 704(g)(6)(B)(iii)). FDA may also ask you or the AP you selected for information concerning the relationship between your firm and the AP. (Sec. 704(g)(6)(B)(ii)(II)).

- Under the AP Program, the AP will discuss any objectionable conditions with you at the conclusion of the inspection, and will provide a written inspection report to you and FDA. FDA will classify your inspection as either NAI, VAI, or OAI based on the information provided by the AP.

What information should I submit concerning my firm's inspectional history?

To facilitate our review of your recent inspectional history, your request to participate in the program should include the following information.

- Your request should identify the date of your firm's most recent device inspection that was classified by FDA. As stated previously, to be eligible, your most recent device inspection, performed either by FDA or by an AP under the AP Program, must have been classified as NAI or VAI. (Sec. 704(g)(6)(A)(i)). Because this is a new program and the APs are still in the process of completing the necessary training, there have not yet been any independent AP inspections performed under this program. Until such time as the APs begin performing independent inspections under this program, FDA will consider the most recent inspection of the establishment by FDA. Once independent AP inspections are underway, you may instead identify the date your firm was inspected by an AP if that is the most recent inspection of your firm that FDA classified.

- If you received a list of inspectional observations at the conclusion of the inspection, please provide a copy with your request. FDA uses Form FDA-483 to record inspectional observations.

- Please provide a copy of the inspection report provided to you after the inspection.

Does an OAI classification from FDA mean that I cannot participate in the AP Program?

- No. In the case of a device establishment for which FDA classified the results of the most recent inspection of the establishment by an AP as OAI, the establishment may petition FDA to determine its eligibility for further AP inspections. (Sec. 704(g)(6)(C)).

- The device establishment should meet all the other eligibility requirements and explain in the petition how it has corrected the violations.

- FDA will respond to the petition within 30 days of receiving it.

D. Accredited Person (AP) Selection

How do you obtain FDA agreement to use an AP?

- Submit a written request to FDA asking for clearance (approval) to use an AP. Your request should also identify the AP you intend to use. (Sec. 704(g)(6)(A)(ii)(I) and (II) of the act.)

- You may select an AP from the list on the FDA Web site previously mentioned - http://www.fda.gov/cdrh/ap-inspection/ap-inspection.html.

- FDA will then provide clearance and approve your selection, or request additional information to help inform its decision. (Sec. 704(g)(6)(A)(ii), (B) of the act.) If FDA requests compliance data or other information, FDA must make a decision about your eligibility to use an AP, and about your AP selection, within 60 days after you provide the requested information. If FDA does not notify you of its decision within 60 days, your firm is deemed to have clearance to have an inspection performed by the AP you have selected. (Sec. 704(g)(6)(B)(iv) and (v)).

- If FDA denies your firm's request for clearance to use an AP or rejects its selection of an AP, FDA will provide your firm with a statement of the reasons for its decision. (Sec. 704(g)(6)(B)(iv) and (v)).

- If FDA grants your request to use the AP you have selected, you are responsible for paying the AP for its services. The amount of compensation is to be determined by agreement between your firm and the AP. (Sec. 704(g)(8)).

E. Requests for Participation in the AP Program

Does my request have to be in a particular format?

No. However, your request needs to identify the AP you have chosen and include information that shows you meet the eligibility criteria (sec. 704(g)(6)(A) of the act).

If a foreign country recognizes the AP you selected as a person authorized to conduct inspections of device establishments, you may support your statement to that effect by referring to any relevant information from FDA's websites.[3] Alternatively, you may show that the law of the foreign country recognizes an inspection by the FDA or an AP by submitting the documentation discussed earlier in this guidance (e.g., a letter from an appropriate foreign government official).

Will FDA notify you if your application is not complete?

Yes. If FDA needs more information about your firm, its inspectional history, the AP you have chosen, or other eligibility criteria, we will contact you as soon as possible. We intend to respond to each request within 30 days. (Sec 704(g)(6)(B)(i) of the act.)

If FDA does not respond within 30 days after it receives your request, your request is deemed approved, and you may make arrangements for the AP you have selected to inspect your facility. (Sec. 704(g)(6)(B)(i) of the act.)

Where should you send your request to participate?

You should send your request to participate in the AP Program to—

Field Programs Branch (HFZ-306)

[3] This information is available at: www.fda.gov/cdrh/ap-inspection/ap-inspection.html

Office of Compliance
Center for Devices and Radiological Health
2094 Gaither Road
Rockville, MD 20850.

Does the AP Program affect other FDA agreements and obligations?

Inspections conducted under the AP Program do not affect FDA's other agreements or operations or change obligations concerning FDA regulations that affect your device. (See generally sec. 704(g)(1), (9), and (14) of the act.)

- Although the AP Program makes it possible for eligible device establishments to use, with FDA's approval, third parties to perform their inspections, nothing in this program affects FDA's broad authority to conduct its own inspections of device establishments under the act. (See sec. 704(g)(9)).

- The provisions of the AP Program do not affect agreements with foreign countries established to carry out the functions of the Office of International Relations at the Department of Health and Human Services. (See sec. 704(g)(14)).

FDA-Accredited Third-Party Inspection Checklist

This checklist may be used to help you determine if you qualify for inspection by an FDA-accredited third party (AP). A GMP inspection of your manufacturing operations may be conducted by an AP, instead of by FDA, provided you meet the following criteria and you obtain FDA approval of your request for participation in the AP Program.

The Devices

1.__ You market a class II or class III device in the United States.

2.__ You market or plan to market a class II or class III device in one or more foreign countries.

Foreign Government

3.__ A foreign government in a country where you market or plan to market a class II or class III device recognizes either:

(a) the AP you have selected as a person authorized to conduct device inspections. Check FDA's list of APs at http://www.fda.gov/cdrh/ap-inspection/ap-inspection.html, or

(b) an inspection by the FDA or an AP. Ways that you may demonstrate this include—

- Submitting information showing that the foreign government accepts FDA's Certificates to Foreign Governments or Certificates of Exportability (see the Foreign Liaison List for devices at http://www.fda.gov/cdrh/devadvice/391.html), or
- You have a letter from an appropriate government official that says it recognizes an inspection by FDA or the AP, or
- The foreign country's laws recognize device inspections by the FDA or an AP, and you submit a written a statement to that effect together with a translated version of the relevant foreign law.

History of Inspection

4.__ Your most recent inspection performed by FDA or by an AP under this program was classified by FDA as either "No Action Indicated" (NAI) or "Voluntary Action Indicated" (VAI).