

***2016 Annual Report on Inspections of
Establishments in FY 2015***



**Food and Drug Administration
Department of Health and Human Services**

Acronyms

API – Active Pharmaceutical Ingredient

CBER – Center for Biologics Evaluation and Research

CDER – Center for Drug Evaluation and Research

CDRH – Center for Devices and Radiological Health

CVM – Center for Veterinary Medicine

cGMP – Current Good Manufacturing Practices

FACTS – Field Accomplishments and Compliance Tracking System

FDA – Food and Drug Administration

FDASIA – Food and Drug Administration Safety and Innovation Act

FDF – Finished Dosage Form

FDP – Finished Drug Product

FD&C Act – Federal Food, Drug, and Cosmetic Act

FY – Fiscal Year (October 1 – September 30)

ORA – Office of Regulatory Affairs

QS – Quality Systems

R&L – Registration and Listing

Overview

Background

On July 9, 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144) was signed into law. FDASIA section 705 amends section 510(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 USC 360(h)) to require, among other things, that the Food and Drug Administration (FDA or Agency) make available on an annual basis through the Agency's website reports on inspections of establishments registered under section 510 of the FD&C Act.

Section 510 of the FD&C Act requires manufacturers, repackers, and relabelers that engage in the manufacture, preparation, propagation, compounding, or processing of human or veterinary drugs, human biological products, and devices to register their establishment(s) and submit a listing of every product in commercial distribution to the FDA. This information helps FDA maintain a catalog of all human and veterinary drugs, biological products, and devices in commercial distribution in the United States. In addition, there are many drug and device establishments that register with FDA that do so voluntarily and are not obligated to be inspected by FDA. FDA uses the Official Establishment Inventory, a database maintained by the Office of Regulatory Affairs (ORA), as well as other databases to identify the subset of registered establishments that are subject to inspection.

Section 704(a) of the FD&C Act provides FDA with authority for inspections, specifically providing authority for duly appointed employees of the FDA or designated officers to enter, at reasonable times, and inspect, at reasonable times and within reasonable limits and in a reasonable manner, facilities under the jurisdiction of the FD&C Act. An inspection is a careful, critical, official examination of a facility to determine its compliance with certain laws and regulations administered by the FDA.

Additionally, FDASIA section 705 includes requirements to establish a risk-based schedule for the inspection of drug establishments. The risk-based schedule must consider the known safety risks of the establishments, including the compliance history of the establishment, the inherent risk of the drug manufactured, prepared, propagated compounded or processed at the establishment, the record, history, and nature of recalls linked to the establishment, and the inspection frequency and history of the establishment.

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Introduction

Information Presented in This Report

FDASIA section 705 amends section 510(h) of the FD&C Act (21 USC 360(h)) to require, among other things, that FDA make reports on inspections of registered establishments available on an annual basis through the Agency's website. Section 510(h)(6) of the FD&C Act states:

ANNUAL REPORT ON INSPECTIONS OF ESTABLISHMENTS.

Beginning in 2014, not later than February 1 of each year; the Secretary shall make available on the Internet Web site of the Food and Drug Administration a report regarding--

- (A)(i) the number of domestic and foreign establishments registered pursuant to this section in the previous fiscal year; and
- (ii) the number of such domestic establishments and the number of such foreign establishments that the Secretary inspected in the previous fiscal year;
- (B) with respect to establishments that manufacture, prepare, propagate, compound, or process an active ingredient of a drug, a finished drug product, or an excipient of a drug, the number of each such type of establishment; and
- (C) the percentage of the budget of the Food and Drug Administration used to fund the inspections described under subparagraph (A).

This report satisfies the annual reporting requirement set forth by FDASIA section 705 for Fiscal Year (FY) 2015.

Data Collection and Definitions

The FDA product Centers¹ included in this Annual Report are:

- Center for Biologics Evaluation and Research (CBER)
- Center for Drug Evaluation and Research (CDER)
- Center for Veterinary Medicine (CVM)
- Center for Devices and Radiological Health (CDRH).

¹ More information on the FDA product Centers and the Office of Regulatory Affairs can be found at: www.fda.gov/aboutFDA/Centersoffices/default.htm.

- Data for the registration information contained in this report were generated by FDA’s registration databases for FY 2015. Data for the inspection information contained in this report were generated from ORA’s Field Accomplishments and Compliance Tracking System (FACTS) for FY 2015.

The data consist of the numbers of inspections conducted at drug and device establishments to evaluate compliance with Good Manufacturing Practice (GMP), including both Current Good Manufacturing Practices (cGMP) for drugs and Quality Systems (QS) regulations for devices, as applicable. These drug and device inspections will hereafter be referred to as “GMP inspection(s).” The hours of work spent preparing for, conducting, and documenting GMP inspections, as reported into FACTS by FDA staff, were used to calculate the percentage of ORA’s field medical product budget authority that supported those inspections.

Tables 1, 2, 3, and 5 show data about both drug and device establishments; Table 4 shows data only about drug establishments. As noted above, the numbers reported in Table 3 are only for GMP inspections. However, registered drug and device establishments are subject to other types of inspections, such as product-specific only, pre-approval inspections for drugs. Therefore, while Tables 1 and 2 show registered drug and device establishments, Table 3 shows a subset of the types of inspections FDA may conduct at those establishments, i.e., GMP inspections. Table 5 shows the percentage of the ORA field medical product budget authority involved in conducting domestic and foreign drug and device establishment GMP inspections.

Unless otherwise noted, all data provided in this report are as of September 30, 2015.

Definitions of key terms used throughout this report can be found in Appendix A.

Drug and Device Establishment Registration

Domestic and Foreign Drug Establishments

In FY 2014 a total of 12,949 drug establishments registered with the FDA pursuant to section 510 of the FD&C Act. As of September 30, 2015, 9,349 domestic and 3,785 foreign drug establishments registered with FDA, bringing the total number of FY 2015 registered drug establishments to 13,134. The following table provides data about registered drug establishments by domestic and foreign location.

Table 1: Number of Registered Drug Establishments by Location

Location	FY 13	FY 14	FY 15
Domestic	9,120	9,330	9,349
Foreign	3,493	3,619	3,785
Total	12,613	12,949	13,134

Domestic and Foreign Device Establishments

In FY 2015, a total of 24,625 medical device establishments registered with FDA. The following table provides data about registered device establishments by domestic and foreign location.²

Table 2: Number of Registered Device Establishments by Location

Location	FY 13	FY 14	FY 15
Domestic	12,468	12,930	12,988
Foreign	9,385	10,522	11,637
Total	21,853	23,452	24,625

² For the purposes of this report CDRH R&L counts are not reflective of the actual number of registrants but reflect the number of unique firms registered and should not be confused with MDUFA R&L numbers.

www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/default.htm.

Domestic and Foreign Drug and Device Establishment Registrations

The following two charts show the number of domestic and foreign drug and device establishments registered in FY 2013, FY 2014, and FY 2015:

Chart 1: Number of Registered Drug Establishments by Location

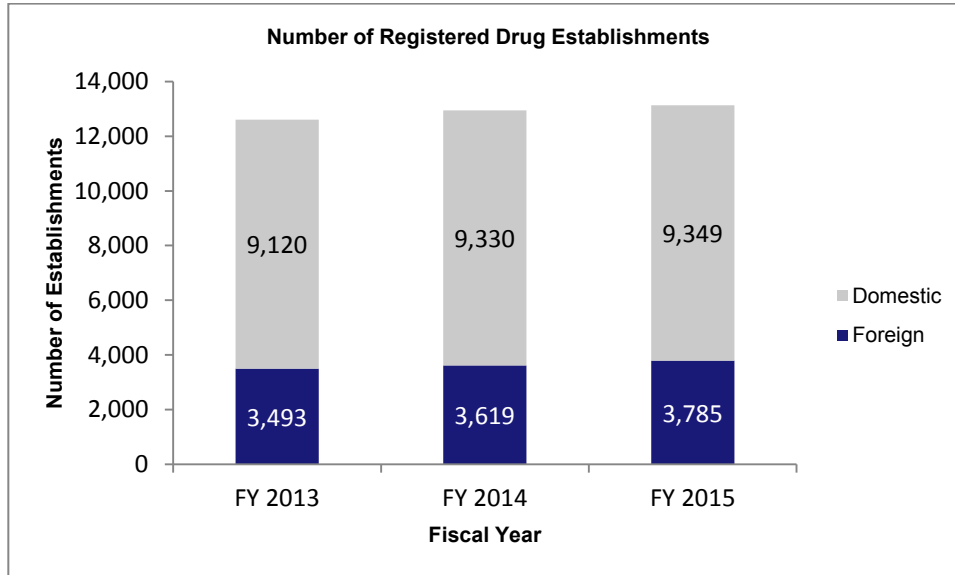
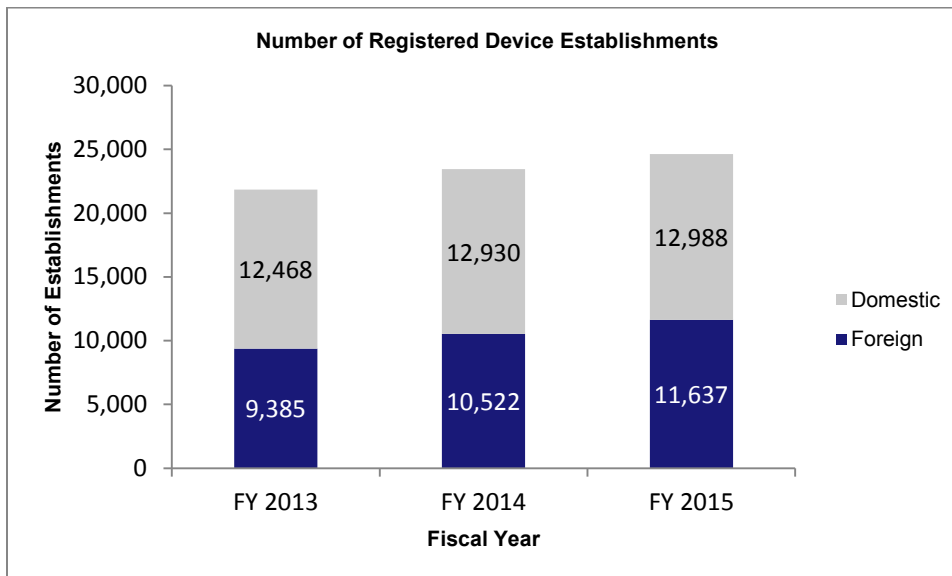


Chart 2: Number of Registered Device Establishments by Location



Registered Drug Establishments by Type

In FY 2015, 4,349 establishments registered as Finished Drug Product (FDP) establishments and 1,522 establishments registered as Active Pharmaceutical Ingredient (API) establishments.

Currently, FDA’s registration databases do not collect information regarding establishments that manufacture, prepare, propagate, compound, or process only excipients; therefore those establishments are not captured in this category. The table below provides a breakdown of the number of establishments that registered as FDP and API establishments in FY 2013, FY 2014, and FY 2015.

For the purposes of this report, if an establishment manufactures, prepares, propagates, compounds, or processes both FDP and API, it is counted as an FDP establishment. API establishments are involved solely in the production of an API. The “Other” category includes but is not limited to establishments that manufacture, prepare, propagate, compound, or process medical gases or medicated feed; and establishments that register through the registration system maintained by CBER.

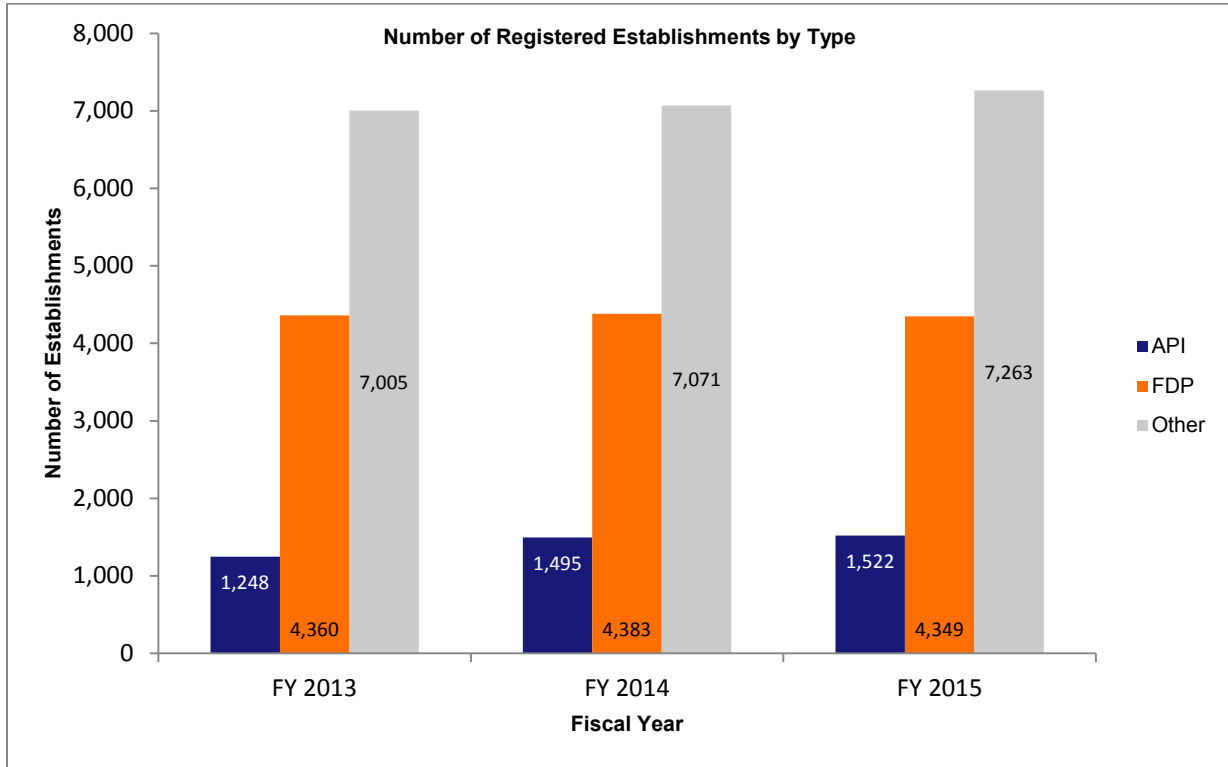
Table 3: Type of Registered Establishments

	FDP	API	Other	Total
FY 2013	4,360	1,248	7,005	12,613
FY 2014	4,383	1,495	7,071	12,949
FY 2015	4,349	1,522	7,263	13,134

The data sources for the reported FDP and API establishments are the registration databases maintained by CDER and CVM, currently the only drug registration data sources that include such information. Establishments that produce certain types of biological products register through the registration system maintained by CDER.

The following chart shows registered drug establishments by type for FY 2013, FY 2014, and FY 2015.

Chart 3: Number of Registered Establishments by Type



Drug and Device Establishment Inspections

FDA completed a total of 5,615 GMP inspections of registered drug and device establishments in FY 2015. Furthermore, the following table shows inspection data for drugs and devices for FY 2013, FY 2014, and FY 2015 by domestic and foreign location.

Table 4: GMP Inspections of Registered Domestic and Foreign Drug and Device Establishments

Location	FY 13	FY 14	FY 15
Domestic	4,858	4,175	4,055
Foreign	1,138	1,379	1,560
Total	5,996	5,554	5,615

These inspection numbers include cGMP inspections for drugs and QS inspections for Class II and Class III devices.³ However, the number of cGMP inspections does not include other types of inspections that FDA conducts (such as product-specific only, pre-approval inspections of drug establishments and inspections of Class I device establishments). The number of inspections of animal drug establishments includes GMP inspections of some non-registered facilities and inspections that are conducted by states under a contract with FDA.

³ Domestic device establishments engaged in the manufacture, propagation, compounding, or processing of a class II or class III medical device are subject to biennial inspection under 510(h)(2) of the FD&C Act.

Percentage of FDA Budget Used to Fund Establishment Inspections

FDA is able to provide the percentage of ORA's field medical product program resources involved in conducting domestic and foreign drug and device establishment GMP inspections. In addition to GMP inspections, ORA conducts many other types of establishment inspections such as product-specific only pre-approval inspections, Good Laboratory Practice inspections, bioequivalence inspections, and inspections of clinical investigators, institutional review boards, and application sponsor inspections.

The ORA total budget authority for FY 2015 was \$934,454,000. Approximately \$265,084,000 of the ORA total budget authority was devoted to field medical product programs (hereafter referred to as "field medical product budget authority"), while the remaining \$669,370,000 was devoted to field programs for other products (e.g., foods). The total field medical product budget authority is calculated by adding the non-user fee appropriated funding for human drugs, biologics, animal drugs, and devices and radiological health field programs. This calculation assumes that the field programs for animal drugs comprise 15 percent of the field's total animal drugs and feed budget authority.

The field medical product budget authority includes all field activities that support FDA's biologics, human drugs, animal drugs, and medical device programs by assessing compliance with applicable laws and regulations. These activities include inspecting establishments, conducting sample analyses, examining products offered for entry into the United States, and certain emergency preparedness and response activities for FDA-regulated medical products. Of the \$265,084,000, approximately \$113,750,000 was used for domestic drug and device establishment GMP inspections, and approximately \$69,716,000 was used for foreign drug and device establishment GMP inspections.

The numbers reported above are derived from the total FDA investigator and laboratory analyst hours reported into FACTS for the field medical product inspections. The estimated cost of these hours was then used to calculate the percentage of the field medical product budget authority used for both domestic and foreign drug and device establishment GMP inspections. These percentages are based solely on the estimated cost for FY 2015 of ORA's field program resources. Field program resources include operational costs, such as onsite inspections of establishments and support personnel. These percentages do not include other resources related to the reported inspections, such as resources utilized in resulting compliance or enforcement activities involving inspected establishments.

In FY 2015 the percentage of the field medical product budget authority used to fund domestic drug and device establishment GMP inspections was approximately 43 percent.⁴

⁴ This percentage does not include inspections of animal drug establishments conducted by the states under a contract with FDA.

The percentage of the field medical product budget authority used to fund foreign drug and device establishment GMP inspections was approximately 26 percent.

Table 5 below depicts the percentage of the ORA field medical product budget authority involved in conducting domestic and foreign drug and device establishment GMP inspections in FY 2013- FY 2015.

In addition to the total budget authority described above, user fee funds are made available to support ORA's field medical product program under the Prescription Drug User Fee Amendments of 2012 (PDUFA), the Generic Drug User Fee Amendments of 2012 (GDUFA), the Medical Device User Fee Amendments of 2012 (MDUFA), the Animal Drug and Animal Generic Drug User Fee Reauthorization Act of 2013 (ADUFA and AGDUFA), the Biosimilar User Fee Act of 2012 (BSUFA), and the Drug Quality and Security Act (DQSA). These numbers were not included in the calculations for this report.

Table 5: Percentage of ORA Field Medical Product Budget Authority Used to Fund Drug and Device Establishment GMP Inspections

Location	FY 13	FY 14	FY 15
Domestic	47%	41%	43%
Foreign	18%	23%	26%
Total	65%	64%	69%

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Appendices

Appendix A: Definitions of Key Terms

Active Ingredient - For the purposes of this report, the term "active ingredient" as it appears in section 510(h)(6)(B) means "active pharmaceutical ingredient" as defined in *Guidance for Industry: Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients*⁵: "Any substance or mixture of substances intended to be used in the manufacture of a drug product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body."

"Device" - means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. Section 201(h) of the FD&C Act (21 USC 321(h)).

Class II and III devices – medical devices are classified into Class I, II and III. Regulatory control increases from Class I to Class III. The device classification regulation defines the regulatory requirements for a general device type. Most Class I devices are exempt from Premarket Notification 510(k), most Class II devices require Premarket Notification 510(k), most Class III devices require Premarket Approval. A description of device classification and a link to the Product classification Database is available at www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/default.htm

"Drug" - means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C). Section 201(g) of the FD&C Act (21 USC 321(g)).

⁵ <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm200364.htm>.

Finished Drug Product - For the purposes of this report, we are considering the term “finished drug product” as it appears in section 510(h)(6)(B) to mean “drug product” as defined in 21 CFR 210.3(b)(4): “a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more ingredients.”



**Department of Health and Human Services
Food and Drug Administration**



This report was prepared by FDA's Office of Planning in collaboration with the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), Center for Veterinary Medicine (CVM), and the Office of Regulatory Affairs (ORA). For information on obtaining additional copies contact:

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