Annual Report on Inspections of Establishments

CY 2022

Overview

A. 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 amended 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 the 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. On August 18, 2017, the FDA Reauthorization Act of 2017 (FDARA) (Public Law 115-52) section 901(e) further amended 510(h). The content of annual reports has been modified to reflect these amendments.[1]

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 biologics regulated as drugs, and devices to register their establishment(s) and submit a listing of every product in commercial distribution to 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. FDA uses the Official Establishment Inventory (OEI), a database maintained by the Office of Regulatory Affairs (ORA), as well as other databases to identify the 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 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 FDA.

Additionally, section 510 of the FD&C Act includes requirements to establish a risk-based schedule for the inspection of drug and device establishments. The risk-based schedule must consider the known safety risks of the establishments, including the inherent risk of the drug or device 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.

[1] Amendments to reporting requirements under section 510(h) of the FD&C Act made by the Food and Drug Omnibus Reform Act of 2022 (FDORA). title III of Division FF of the Consolidated Appropriations Act, 2023 (P.L. 117-328, December 29, 2022) will be addressed in the next annual report under section 510(h).

Table of Contents

Acronym List

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
CGMP	Current Good Manufacturing Practice
CVM	Center for Veterinary Medicine
CY	Calendar Year
FACTS	Field Accomplishments and Compliance Tracking System
FDA	Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDARA	FDA Reauthorization Act of 2017
FDASIA	Food and Drug Administration Safety and Innovation Act
FDF	Finished Dosage Form
FDP	Finished Drug Product
FY	Fiscal Year (October 1 – September 30)
ORA	Office of Regulatory Affairs
QS	Quality Systems
R&L	Registration and Listing

I. Introduction

A. Information Presented in This Report

FDASIA section 705 amended 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. A further amendment to section 510(h)(6) of the FD&C Act in section 3101(a)(2)(H) of the 21st Century Cures Act (Public Law 114-255) changed the annual reporting requirement from fiscal year (FY) to calendar year (CY), and section 901(e) of FDARA changed the annual reporting date to May 1.

Section 510(h)(6)[1] of the FD&C Act states:

> ANNUAL REPORT ON INSPECTIONS OF ESTABLISHMENTS.
>
> Beginning in 2014, not later than May 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 calendar year; and
>
> (ii) the number of such domestic establishments and the number of such foreign establishments that the Secretary inspected in the previous calendar year;
>
> (B) with respect to establishments that manufacture, prepare, propagate, compound, or process an active ingredient of a drug or a finished drug product, 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 section 510(h)(6) of the FD&C Act for CY 2022.

[1] As in effect immediately prior to enactment of FDORA.

B. Data Collection and Definitions

The FDA product Centers[2] 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)

Data for the registration information contained in this report were generated by FDA's registration databases for CY 2022. Data for the inspection information contained in this report were generated from ORA's Field Accomplishments and Compliance Tracking System (FACTS) for CY 2022.

The data consist of the numbers of inspections conducted at drug and device establishments to evaluate compliance with current good manufacturing practice (CGMP), including both routine CGMP for drugs and Quality Systems (QS) regulations for devices, as applicable. These routine drug and device inspections will hereafter be referred to collectively as "CGMP inspections." The hours of work spent preparing for, conducting, and documenting CGMP inspections, as reported by FACTS from FDA staff, were used to calculate the percentage of ORA's field medical product non-user fee funding that supported those inspections.

FDA continued throughout the Coronavirus (COVID-19) pandemic to conduct inspectional and oversight work determined on a case by-case basis to be critical to FDA's public health mission.[3] With respect to pre-approval and pre-license inspections, FDA has continued to use other tools and approaches where possible, including requesting existing inspection reports from other trusted foreign regulatory partners through mutual recognition and confidentiality agreements, requesting information from applicants, and requesting records and other information directly from facilities and other inspected entities.

In May 2021, FDA released the "Resiliency Roadmap for FDA Inspectional Oversight" report[4] detailing not only the effect of the pandemic on our inspectional activities for each regulated commodity in FDA's portfolio, but also our detailed plan for a more consistent state of operations and our priorities going forward. In the weeks following publication of the Roadmap, FDA determined that conditions were appropriate to begin a transition toward "standard operational levels" described in the Roadmap for domestic surveillance inspections, starting on

[2] More information on the FDA product Centers and ORA can be found at: www.fda.gov/aboutFDA/Centersoffices/default.htm.

[3] See guidance for industry, "Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers," published in August 2020 and updated on January 29, 2021, for a discussion of the types of inspections that would be deemed "mission-critical."

[4] See www.fda.gov/media/148197/download.

July 1, 2021. By the end of September 2021, we had exceeded the goals we set for the transition and were returning to a more normal state of operations. On February 2, 2022, FDA determined that beginning on February 7, 2022, the Agency would resume conducting domestic surveillance inspections across all commodities given the decline in COVID-19 cases across the country.[5] Throughout all these activities, the Agency remained committed to the health and safety of its investigators and providing the protection needed to safely inspect facilities and conduct investigations at the ports and in Agency laboratories.

Tables 1 and 3 show data only about drug establishments; Table 2 shows data only about device establishments; Tables 4 and 5 show data about both drug and device establishments. The numbers reported in Table 4 are only for CGMP inspections. However, registered drug and device establishments are subject to other types of inspections, such as product-specific inspections, pre-approval and pre-license inspections, and for-cause inspections. Therefore, while Tables 1 and 2 show registered drug and device establishments respectively, Table 4 shows the specific subset of the CGMP domestic and foreign inspections FDA may conduct at those establishments. Table 5 shows the percentage of the ORA field medical product non-user fee funding involved in conducting domestic and foreign drug and device establishment CGMP inspections.

The financial data are reported on a fiscal year basis; all other data provided in this report are based on the calendar year ending December 31, 2022.

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

[5] Press announcement re-shift to conducting domestic surveillance: https://www.fda.gov/news-events/press-announcements/fda-roundup-february-4-2022

II. Drug and Device Establishment Registration

A. Domestic and Foreign Drug Establishments

In CY 2021, a total of 16,930 drug establishments registered with FDA pursuant to section 510 of the FD&C Act. As of December 31, 2022, 10,074 domestic and 5,014 foreign drug establishments registered with FDA, bringing the total number of CY 2022 registered drug establishments to 15,088. The following tables provide data about domestic and foreign registered drug establishments.

Table 1: Number of Domestic and Foreign Registered Drug Establishments

Location	CY 2017	CY 2018	CY 2019	CY 2020	CY 2021	CY 2022
Domestic	9,092	9,687	9,464	10,068	10,985	10,074
Foreign	4,103	4,241	4,161	9,354	5,945	5,014
Total	13,195	13,928	13,625	19,422	16,930	15,088

B. Domestic and Foreign Device Establishments

In CY 2022, a total of 43,713 medical device establishments registered with FDA. The following table provides data about domestic and foreign registered device establishments.[6]

Table 2: Number of Domestic and Foreign Registered Device Establishments

Location	CY 2017	CY 2018	CY 2019	CY 2020	CY 2021	CY 2022
Domestic	13,596	13,707	13,857	16,190	15,546	20,289
Foreign	12,755	13,143	14,287	26,088	18,408	23,424
Total	26,351	26,850	28,144	42,278	33,954	43,713

[6] For the purposes of this report, CDRH registration counts reflect the total number of firms that registered during the year, including those that deactivated their registrations later in the year. The breakdown by establishment type included in the Medical Device User Fee Act (MDUFA) quarterly report covers only those that were still active at the end of each quarter or fiscal year.

C. 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 CY 2017 through CY 2022:

Chart 1: Number of Domestic and Foreign Registered Drug Establishments

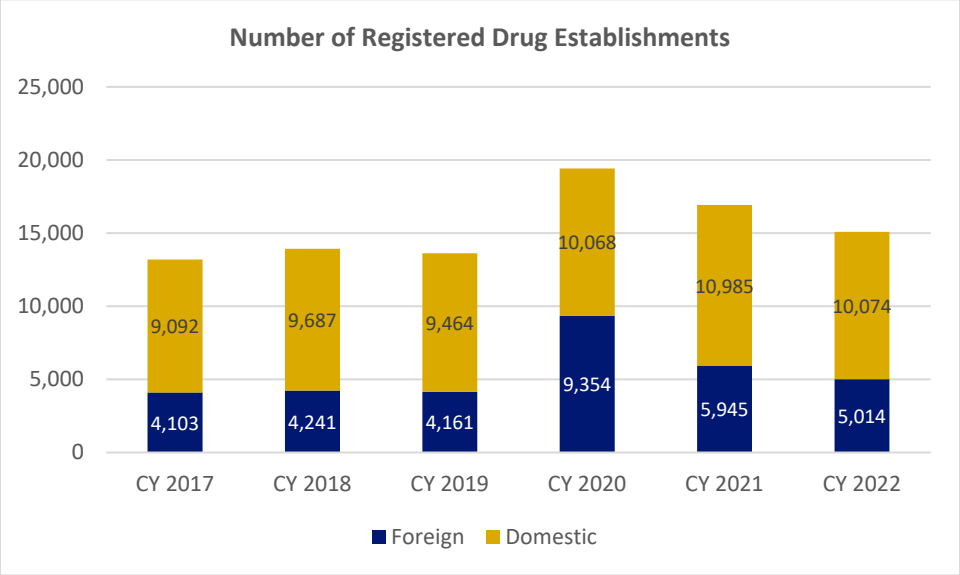
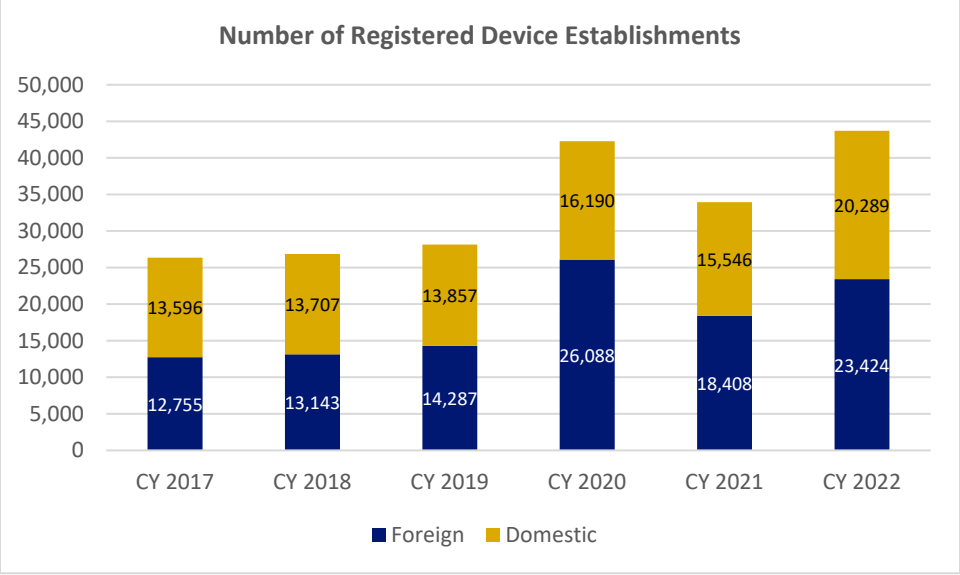


Chart 2: Number of Domestic and Foreign Registered Device Establishments



III. Registered Drug Establishments by Type

In CY 2022, a total of 4,992 establishments registered as Finished Drug Product (FDP) establishments and 1,874 establishments registered as Active Pharmaceutical Ingredient (API) establishments.

The table below provides a breakdown of the number of establishments that registered as FDP and API establishments in CYs 2017 through 2022.

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. This report excludes drug establishments registered as section 503B drug compounders (or Outsourcing Facilities).

Table 3: Types of Registered Drug Establishments

	FDP	API	Other	Total
CY 2017	4,482	1,590	7,123	13,195
CY 2018	4,183	1,701	8,044	13,928
CY 2019	3,864	1,709	8,052	13,625
CY 2020*	9,249	1,837	8,336	19,422
CY 2021*	6,891	1,822	8,217	16,930
CY 2022	4,992	1,874	8,222	15,088

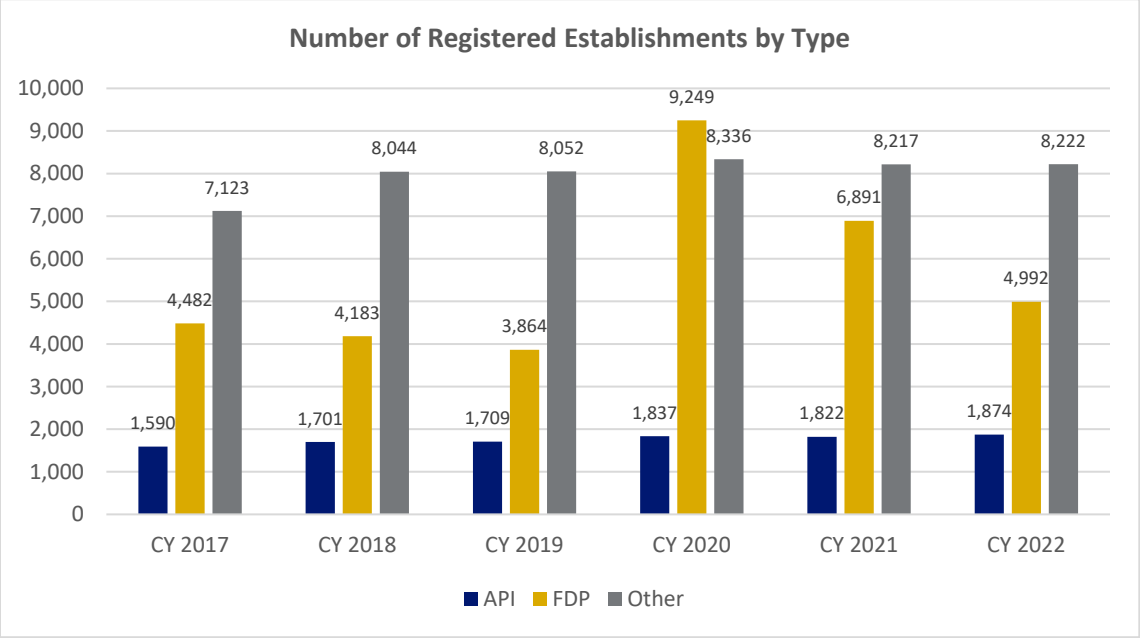
*After the declaration of the COVID-19 public health emergency in January 2020, consumers and health care personnel were experiencing difficulties accessing alcohol-based hand sanitizers. The increase in demand led to a surge of non-traditional manufacturers like alcohol distilleries and certain industrial chemical establishments beginning to produce hand sanitizer products (and thus being required to register, given that hand sanitizer is a drug). To help address the shortage situation, in early March 2020, CDER published three guidance documents outlining temporary policies for the preparation of alcohol-based hand sanitizer and alcohol for use in hand sanitizer.
On October 12, 2021, the Agency announced[7] that on December 31, 2021, it was withdrawing the temporary guidances for alcohol-based hand sanitizer products because the supply of alcohol-based hand sanitizers from traditional manufacturers had increased, and most consumers and healthcare personnel were no longer having difficulty obtaining these products (also, many non-traditional manufacturers had discontinued these products and de-registered). As of December 31, 2021, these guidances have been withdrawn and firms manufacturing alcohol-based hand sanitizer products under these temporary policies were required to stop making new hand sanitizer products on December 31, 2021, and stop distribution of any remaining hand sanitizer products produced under the guidances by March 31, 2022. FDA asked manufacturers to deregister their establishment(s) if they were no longer producing drug products.

The data sources for the reported FDP and API establishments are the registration databases maintained by CDER and CVM, 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.

[7] www.fda.gov/news-events/press-announcements/fda-brief-fda-withdrawing-temporary-guidances-alcohol-based-hand-sanitizers

The following chart shows registered drug establishments by type for CYs 2017 through 2022.

Chart 3: Number of Registered Drug Establishments by Type



IV. Drug and Device Establishment Inspections

FDA completed a total of 2,442 CGMP inspections of registered drug and device establishments in CY 2022.[8] The following tables show domestic and foreign inspection data for drugs and devices for CYs 2017 through 2022.

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

Location	CY 2017	CY 2018	CY 2019	CY 2020	CY 2021	CY 2022
Domestic	3,479	3,297	3,139	879	1,311	2,061
Foreign	1,457	1,321	1,200	204	57	381
Total	4,936	4,618	4,339	1,083	1,368	2,442

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

[8] While section 510(h)(6)(C) of the FD&C Act calls for the percentage of the budget associated with the "inspections described under subparagraph (A)," i.e., those inspections conducted in CY 2022 as reported above, FDA believes that continuing to report the budget by FY as in past years gives a more accurate picture of its drug and device inspection resource use. For example, the underlying data points that are used to calculate the total non-user fee funding reported in this report, such as the Prescription Drug User Fee Act (PDUFA) inflation rate and fully loaded full-time equivalent (FTE) cost, are based on the FY.

V. 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 CGMP inspections of domestic and foreign drug and device establishment by fiscal year.[9] In addition to CGMP inspections, ORA conducts many other types of establishment inspections, such as product-specific, pre-approval, and pre-license inspections, Good Laboratory Practice inspections, bioequivalence inspections, and inspections of clinical investigators, Institutional Review Boards, and application sponsors.

As the risks associated with the pandemic challenged our ability to conduct inspections, FDA continued to use every available tool to ensure that our regulatory responsibilities were met efficiently and in a timely manner. One of FDA's priorities is to develop an enterprise-wide policy and procedure for the use of Remote Regulatory Assessments. These assessments, which include record requests made under FD&C Act section 704(a)(4) authority and requests for voluntary submission of records and remote interactive evaluations, have been used throughout the pandemic to fortify our oversight efforts where inspections were not possible. Our fundamental goal is to maximize our resources in every way possible to achieve the optimal public health outcomes. We remain committed to our mission to promote and protect the health of the American public and ensure access to safe and quality products.

The ORA total non-user fee funding for FY 2022 was $1,164,523,000. Approximately $331,433,000 of this amount was devoted to field medical product programs (hereafter referred to as "field medical product non-user fee funding"), while the remaining $833,090,000 was devoted to field programs for other products (e.g., foods). The total field medical product non-user fee funding is calculated by adding the non-user fee appropriated funding for human drugs, human biologics regulated as drugs, animal drugs, and devices and radiological health field programs.

ORA Non User Fee Funding	FY 2022
Medical Product Programs	$331,433,000
Field Programs for Other Products	$833,090,000
Total	$1,164,523,000

[9] While section 510(h)(6)(C) of the FD&C Act calls for the percentage of the budget associated with the "inspections described under subparagraph (A)," i.e., those inspections conducted in CY 2022 as reported above, FDA believes that continuing to report the budget by FY as in past years gives a more accurate picture of its drug and device inspection resource use. For example, the underlying data points that are used to calculate the total non-user fee funding reported in this report, such as the PDUFA inflation rate and fully loaded FTE cost, are based on the FY.

The field medical product non-user fee funding includes all field activities that support FDA's human biologics regulated as drugs, 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 $331,433,000 field medical product non-user fee funding, approximately $125,102,000 was used for domestic drug and device establishment CGMP inspections, and approximately $31,691,000 was used for foreign drug and device establishment CGMP inspections during FY 2022.

Medical Product Non-user Fee Funding	FY 2022*
Domestic drug and device establishment CGMP inspections	$125,102,000
Foreign drug and device establishment CGMP inspections	$31,691,000
Total	$156,793,000

* In accordance with national guidelines due to the COVID-19 pandemic restrictions, ORA scaled back foreign and domestic inspection work and targeted its resources on the highest-risk facilities and industries. As a result, the percentage of field medical product non-user fee funding used to fund domestic and foreign drug and device establishment CGMP inspections was significantly lower in FYs 2020 and 2021. In FY 2022, ORA continues to make progress returning towards pre-COVID-19 inspection levels.

.

The numbers reported above are derived from the total FDA investigator and laboratory analyst hours reported by 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 non-user fee funding used for both domestic and foreign drug and device establishment CGMP inspections. These percentages are based solely on the estimated cost for FY 2022 of ORA's field program resources. Field program resources include operational costs, such as 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 2022 the percentage of the field medical product non-user fee funding used to fund domestic drug and device establishment CGMP inspections was approximately 37.75 percent.[10]

The percentage of the field medical product non-user fee funding used to fund foreign drug and device establishment CGMP inspections was approximately 9.56 percent.

Table 5 below shows the percentage of the ORA field medical product non-user fee funding involved in conducting domestic and foreign drug and device establishment CGMP inspections in FYs 2017 through 2022.

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

In addition to the total non-user fee funding described above, user fee funds are authorized to support ORA's field medical product program under amendments[11] made to the FD&C Act by the Prescription Drug User Fee Amendments of 2017 (PDUFA VI), the Generic Drug User Fee Amendments of 2017 (GDUFA II), the Medical Device User Fee Amendments of 2017 (MDUFA IV), the Animal Drug User Fee Amendments of 2018 (ADUFA IV), the Animal Generic Drug User Fee Amendments of 2018 (AGDUFA III), the Biosimilar User Fee Amendments of 2017 (BsUFA II), and the Compounding Quality Act. These numbers were not included in the calculations for this report.

Table 5: Percentage of ORA Field Medical Product Non-User Fee Funding Used to Fund Drug and Device Establishment CGMP Inspections

Location	FY 2017	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
Domestic	45%	44%	44%	12%	25%	38%
Foreign	31%	29%	29%	4%	1%	9%
Total	76%	73%	73%	16%	26%	47%

[11] The PDUFA, MDUFA, GDUFA, and BSUFA user fee programs were recently reauthorized for FYs 2023-2027 under amendments to the FD&C Act made by the FDA User Fee Reauthorization Act of 2022, Division F of the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023 (P.L. 117-180, September 30, 2022).

Appendix A: Definitions of Key Terms

"Active Pharmaceutical Ingredient" - means any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body. Active pharmaceutical ingredient does not include intermediates used in the synthesis of the substance. (21 CFR 207.1)

"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. The term 'device' does not include software functions excluded pursuant to section 520(o) of the FD&C Act. (Section 201(h)(1) of the FD&C Act (21 U.S.C. 321(h)(1)))

"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 U.S.C. 321(g)))

"Finished Drug Product" - means a finished dosage form (e.g., tablet, capsule, or solution) that contains at least one active pharmaceutical ingredient, generally, but not necessarily, in association with other ingredients in finished package form suitable for distribution to pharmacies, hospitals, or other sellers or dispensers of the drug product to patients or consumers. (21 CFR 207.1)

This report was prepared by FDA's Office of Planning, Evaluation, and Risk Management 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), the Center for Veterinary Medicine (CVM), and the Office of Regulatory Affairs (ORA). For information on obtaining additional copies, please contact:

Office of Planning, Evaluation, and Risk Management
Office of the Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002
Phone: (301) 796-4850
E-mail: OPERM_ADMIN_Team@fda.hhs.gov

This report is available on FDA's home page at https://www.fda.gov/.