United States Government Accountability Office

Report to the Ranking Member, Subcommittee on Environment and the Economy, Committee on Energy and Commerce, House of Representatives

May 2014

PESTICIDE SAFETY

Improvements Needed in EPA's Good Laboratory Practices Inspection Program

GAO-14-289

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GAO Highlights

Highlights of GAO-14-289, a report to the Ranking Member, Subcommittee on Environment and the Economy, Committee on Energy and Commerce, House of Representatives

Why GAO Did This Study

Pesticides used to control weeds, unwanted insects, and fungi contribute to agricultural productivity and public health by preventing crop damage and controlling pests. However, pesticides may also have adverse effects. EPA's OPP reviews applications for pesticide products and registers those that it determines do not have unreasonable adverse effects on health and the environment. EPA's OECA inspects laboratories where these pesticides are tested to ensure that the laboratories followed EPA's GLP regulations. FDA also conducts GLP laboratory inspections. GAO was asked to review EPA's GLP Compliance Monitoring Program. This report examines the extent to which EPA (1) inspects for GLP compliance laboratories that test pesticides and the challenges EPA faces in doing so, (2) uses the information obtained through GLP inspections in its pesticide decision-making process, and (3) collaborates with FDA on GLP inspections. To conduct this work, GAO reviewed relevant agency documents and data, conducted a nongeneralizeable survey of 20 laboratories, and interviewed EPA and FDA officials and laboratory and other stakeholders.

What GAO Recommends

GAO recommends, among other things, that EPA assess its authority and need for a fee-based inspection system for the GLP Program, determine why the database information to prioritize laboratories is incomplete, and that EPA and FDA develop a process to collaborate and share information on planned and completed inspections. EPA and FDA agreed with GAO's recommendations.

View GAO-14-289. For more information, contact John Neumann at (202) 512-3841 or neumannj@gao.gov

What GAO Found

The Environmental Protection Agency (EPA) inspects few laboratories that test pesticides for Good Laboratory Practices (GLP) compliance and faces challenges in selecting laboratories to inspect. For fiscal years 2009 to 2013, EPA's Office of Enforcement and Compliance Assurance (OECA) GLP Compliance Monitoring Program inspected from 51 to 80 laboratories annually from an estimated 1,400 that conducted studies used to support applications for pesticide registrations. During the same period, EPA reduced OECA's GLP Compliance Program budget and staff by about half. Laboratory and other stakeholders told GAO that not having GLP inspections can negatively affect a laboratory's business domestically and abroad. OECA prioritizes laboratories for GLP inspections using criteria that reflect, among other things, how long it has been since the last inspection and the number of studies the laboratory has conducted that have been submitted to EPA's Office of Pesticide Programs (OPP) in support of a pesticide registration application. However, GAO found that some laboratory information in the OECA database used to prioritize inspections was either inaccurate or incomplete, making it difficult to target laboratories for inspections. GAO also found that OECA is considering ways the GLP program could be run more efficiently given its recent budget cuts and concerns of stakeholders about the infrequent GLP inspections. For example, OECA officials have informally discussed the possibility of charging user fees that may be used to fund the GLP program, as the U.S. Food and Drug Administration (FDA) and many other countries do, but the agency has not conducted a formal evaluation of user fees. Without formally assessing the need for such fees, EPA cannot determine whether charging and retaining the fees would be possible and whether such fees could help make the inspection program self-sustaining.

EPA rarely uses GLP inspection results in making its initial pesticide registration decisions. An OPP official said that this is because most inspections occur after decisions have been made. OPP officials said they have not denied or revoked any pesticide registrations based on OECA GLP inspections during the past 5 years, but OPP has taken other actions, such as requiring that a study be repeated because of subsequent laboratory inspection information. According to EPA officials, OPP and OECA have communicated on an informal basis about OPP's inspection priorities before a pesticide registration has taken place.

EPA and FDA do not regularly collaborate on laboratory inspections and may be duplicating each other's work at some of these laboratories. In 1984, EPA and FDA entered into an agreement to collaborate on GLP inspections and met quarterly to discuss upcoming inspections; the agreement ended in 2004 although meetings continued until 2007. From fiscal year 2005 to 2012, EPA and FDA conducted a total of 170 GLP inspections of the same 37 laboratories. In 38 of 170 inspections, the agencies inspected the same laboratory during the same fiscal year. EPA and FDA have independent but similar sets of GLP regulations. Officials from both agencies said it would be useful to know which laboratories the other agency was planning to inspect and to have those inspection results, since each agency can only inspect a certain number of laboratories each year. Absent collaboration and information sharing with FDA on planned and completed GLP inspections, EPA will have difficulty efficiently using its limited resources to increase the number of inspections it conducts.

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Abbreviations

CFO	Chief Financial Officer
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
GLP	Good Laboratory Practices
HHS	Department of Health and Human Services
IBT	Industrial Bio-Test Laboratories
ICIS	Integrated Compliance Information System
LISA	Laboratory Information and Study Audit
MAD	Mutual Acceptance of Data
OCE	Office of Civil Enforcement
OCEFT	Office of Criminal Enforcement, Forensics and Training
OECA	Office of Enforcement and Compliance Assurance
OECD	Organisation for Economic Co-operation and Development
OIG	Office of Inspector General
OMB	Office of Management and Budget
OPP	Office of Pesticide Programs
OPPIN	Office of Pesticide Program Information Network
PRIA	Pesticide Registration Improvement Act of 2003
TSCA	Toxic Substances Control Act

U.S. GOVERNMENT ACCOUNTABILITY OFFICE
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May 15, 2014

The Honorable Paul D. Tonko
Ranking Member
Subcommittee on Environment and the Economy
Committee on Energy and Commerce
House of Representatives

Dear Mr. Tonko:

Pesticides that are used to destroy or control weeds, unwanted insects, fungi, rodents, bacteria and other pests contribute to agricultural productivity by preventing crop damage and improving public health by controlling disease carrying pests. However, the use of pesticides may also have adverse effects on human health and the environment. For example, some pesticides in large doses may contribute to the risk of cancer and other serious human health problems and may also cause environmental damage, such as contamination of water supplies or unintended impacts on species not targeted by the pesticide. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended,[1] generally requires registration of pesticides and authorizes the Environmental Protection Agency (EPA) to limit the distribution and sale of unregistered pesticides to the extent necessary to prevent unreasonable adverse effects on the environment.[2] Under FIFRA implementing regulations, EPA reviews applications for pesticide products and registers those that it determines will meet the FIFRA statutory standards for registration.[3] EPA also inspects the laboratories where these pesticides are first tested for safety. Laboratories must conduct studies in support of pesticide registration applications in accordance with regulations called Good Laboratory Practices (GLP), which are intended

[1]Act of June 25, 1947, ch. 125, 61 Stat. 163 (codified as amended at 7 U.S.C. §§ 136-136y).

[2]7 U.S.C. § 136a(a).

[3]40 C.F.R. pts. 152-180.

to ensure the quality and integrity of data.[4] GLP regulations were developed and promulgated in the United States during the late 1970s and early 1980s in response to fraudulent laboratory activities and poor laboratory practices that occurred during that time.

To monitor a laboratory's GLP compliance with these standards, EPA conducts both an audit of the studies conducted by the laboratory and submitted to EPA and an on-site inspection of the laboratory; these two types of reviews together are referred to as a GLP inspection.[5] EPA's Office of Pesticide Programs (OPP) reviews studies that support applications for registration of pesticide products submitted by study sponsors and makes registration decisions based on whether or not the pesticide products meet the FIFRA standard for registration.[6] EPA's Office of Enforcement and Compliance Assurance (OECA) has a Compliance Monitoring Program that conducts inspections to ensure that laboratories comply with the agency's GLP regulations. If OECA's inspectors find a problem with the studies they audit[7] or the laboratories they inspect, OECA submits this information to OPP for reexamination of the studies to ensure that the data they generated are valid and reliable to support pesticide decisionmaking. If OPP determines the data upon which a registration decision was based are not valid or reliable, it can ask the manufacturer of the pesticide to repeat a study, or it may initiate steps to change a registration decision.

The Food and Drug Administration (FDA), an agency of the Department of Health and Human Services (HHS), also requires that laboratories follow FDA's GLP regulations, promulgated under the Federal Food, Drug

[4]EPA implements two sets of regulations setting forth GLP standards—one under FIFRA, see 40 C.F.R. pt. 160, and one under the Toxic Substances Control Act (TSCA), Pub. L. No. 94-469, 90 Stat. 2003 (1976) (codified as amended at 15 U.S.C. §§ 2601-2697), see 40 C.F.R. pt. 792. According to EPA officials, most of its GLP inspections are conducted under FIFRA. For that reason, we have focused on GLP standards under FIFRA in this report.

[5]A "laboratory" in this report is defined as a facility where a study or part of a study is conducted. A laboratory can conduct its testing either indoors or outdoors at a field site.

[6]EPA regulations define a sponsor as (1) a person who initiates and supports, by the provision of financial or other resources, a study; (2) a person who submits a study to EPA in support of an application for a research or marketing permit; or (3) a testing facility, if it both initiates and actually conducts the study. 40 C.F.R. § 160.3.

[7]We are using the term "audit" to refer to the OECA inspectors' examination of studies.

and Cosmetic Act (FFDCA)[8] for conducting nonclinical laboratory studies of investigational drugs, medical devices, food additives, and other products to ensure the quality and integrity of the safety data.[9] In some cases, EPA and FDA receive studies from the same laboratories.

Environmental and other groups have raised concerns about OPP's pesticide registration program, as we reported in August 2013,[10] when we recommended that EPA take steps to improve the program. Pesticide manufacturers have also expressed concern about how infrequently OECA conducts GLP inspections, which they have stated affects firms' ability to register and market their products in the United States and abroad.

You asked us to review EPA's GLP Compliance Monitoring Program. This report examines the extent to which (1) EPA inspects for GLP compliance laboratories that test pesticides and the challenges, if any, EPA faces in doing so; (2) EPA uses the information obtained through GLP laboratory inspections in its pesticide decision-making process; and (3) EPA and FDA collaborate on GLP inspections.

To conduct this work, we reviewed relevant laws, regulations, EPA and FDA guidance, EPA data on pesticide studies, and GLP inspection results. We interviewed OECA and OPP officials, as well as FDA officials. We reviewed recent literature related to GLP, including information and documents found on the websites of a variety of industry, international, environmental, and academic organizations, and foreign government GLP inspection programs. To determine the extent to which EPA inspects for GLP compliance laboratories that test pesticides, we collected and analyzed documentation from EPA officials on its GLP inspection process and analyzed EPA laboratory and inspection data, the agency's use of

[8]Act of June 25, 1938, ch. 675, 52 Stat.1040 (codified as amended at 21 U.S.C. §§ 301-399f).

[9]21 C.F.R. pt. 58.

[10]EPA reviews health and environmental effects data submitted by a company and may register a pesticide or, alternatively, grant a "conditional registration" for a pesticide under certain circumstances, even though some of the required data may not have been submitted or reviewed. We recommended, in part, that EPA consider and implement options for an automated system to better track conditional registrations. See GAO, *Pesticides: EPA Should Take Steps to Improve Its Oversight of Conditional Registrations*, GAO-13-145 (Washington, D.C.: Aug. 8, 2013).

the data, and the accuracy and completeness of the data. We determined that inspection data were sufficiently reliable to present results on the number of inspections conducted during fiscal year 2009 to fiscal year 2013, based on a comparative analysis of inspection data contained in two of EPA's databases and interviews with agency officials. We determined that data on laboratories' identification numbers and addresses were not sufficiently reliable to assess the number and location of laboratories that had conducted studies submitted to EPA and, as a result, were subject to a GLP inspection. We determined the data were not sufficiently reliable, based on our analysis of the data, identification of erroneous data, and interviews with agency and laboratory representatives. However, EPA did provide estimates of the number and percentage of eligible laboratories that were inspected each year, and we used that information in this report. We obtained opinions on the GLP inspection program, including potential challenges, by interviewing individuals representing 25 entities, including laboratories; pesticide manufacturers; international organizations; environmental and health organizations; national and trade associations; and foreign government GLP programs, which we selected based on referrals from various stakeholders and EPA officials. In addition, we obtained survey responses from 20 laboratories of a nongeneralizable random sample of 53 laboratories and other entities that had sent supporting studies to OPP for a pesticide registration application for fiscal year 2010 to fiscal year 2012 to determine if they had been inspected by EPA[11] (see app. II). If they had not had a GLP inspection, we asked what impact, if any, they thought not having a GLP inspection had on their business. Although the results of this sample are not generalizable, the laboratories were randomly selected, and the results can illustrate such laboratories' experiences and challenges with GLP inspections. To assess the extent to which OPP uses the information obtained through GLP laboratory inspections in its pesticide registration decision-making process, we analyzed relevant documents and databases to determine the number of OECA's GLP inspections that produced results that were referred to OPP for reexamination, the time it took to conduct these reexaminations, and any impact the inspections had on OPP's pesticide registration decisions. To determine the extent to which EPA and FDA collaborate on

[11]While we received a total of 26 survey responses from our sample of laboratories, 6 of the 26 reported that they were not a laboratory and did not conduct GLP testing. Therefore, these 6 are considered out-of-scope for reporting our survey results. See appendix I for more detail.

inspections, we analyzed EPA and FDA GLP laboratory inspection data. We determined that the inspection data were sufficiently reliable for our purposes. We also analyzed the 20 survey responses to determine if the laboratories had conducted GLP tests or studies for submission to both EPA and FDA since 2008. We reviewed agency documents, such as a 1984 interagency agreement between EPA and FDA to cooperate on GLP inspections, and we interviewed EPA and FDA officials and laboratory representatives about the potential for the two agencies to collaborate. Appendix I contains more detailed information on our objectives, scope, and methodology.

We conducted this performance audit from November 2012 to May 2014 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

The primary federal laws that govern how EPA regulates pesticides in the United States are FIFRA and FFDCA. Under FIFRA, EPA registers pesticides distributed, used, or sold, in the United States and prescribes labeling and other regulatory requirements to prevent unreasonable adverse effects on health and the environment.[12] If use of a pesticide would result in a residue of the substance in or on food, EPA may not register a pesticide under FIFRA unless, among other things, it can determine that the residue is "safe" as defined by section 408 of the FFDCA.[13] EPA may establish a tolerance level—the maximum permissible pesticide residue in or on food or animal feed that is sold—that meets the FFDCA safety standard set forth in section 408 or may

[12]The phrase "unreasonable adverse effects on the environment" is defined in FIFRA, in part, to mean (1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard for tolerance under section 408 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 346a. This standard requires EPA to consider both the benefits and risks of using a pesticide. 7 U.S.C. § 136(bb).

[13]Under section 408 of the FFDCA, "safe" means that EPA has determined, among other things, that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide residue. 21 U.S.C. § 346a(b)(2)(A)(ii).

choose to grant an exemption for a tolerance. To obtain a pesticide registration, or petition to establish a tolerance level, a registrant (company or person) submits an application for EPA's review containing health and environmental effects data and other information on a pesticide.[14] In addition to testing conducted in a laboratory, these data can include studies based on the analysis of data collected from field applications of the pesticide and other information on the pesticide. The application is submitted with a pesticide registration fee, with the fee amount depending on certain factors, such as the type of registration action that is being requested. According to an OPP official, registrants are required to provide data relating to the pesticide's hazard and exposure levels to accompany a proposed registration. All studies submitted in support of a product registration are subjected to an initial screening and regulatory and scientific review by OPP staff to determine potential human and environmental risks. OPP reviews the applications and registers those products determined to meet FIFRA's standards for registration and other regulatory requirements so that they can be marketed domestically.

Under FIFRA, when a registrant submits an application for pesticide products to OPP, the accompanying data to support the registration are required to be prepared in accordance with the agency's GLP regulations to ensure the quality and integrity of the data in the study. Each study submitted is reviewed by OPP to see if GLP criteria have been met. OPP staff prepare science reports and/or data evaluation records to address the quality of each study. If studies submitted in support of this process contain questionable data, this can result in adverse action by OPP. For example, according to OPP officials, if OPP finds that a registrant provided false or inaccurate information about the certified limits of the active ingredients of a pesticide, or if there is a discrepancy in the number of formulas used to check concentrations, a study would be rejected, and OPP might deny such an application or request that it be withdrawn.

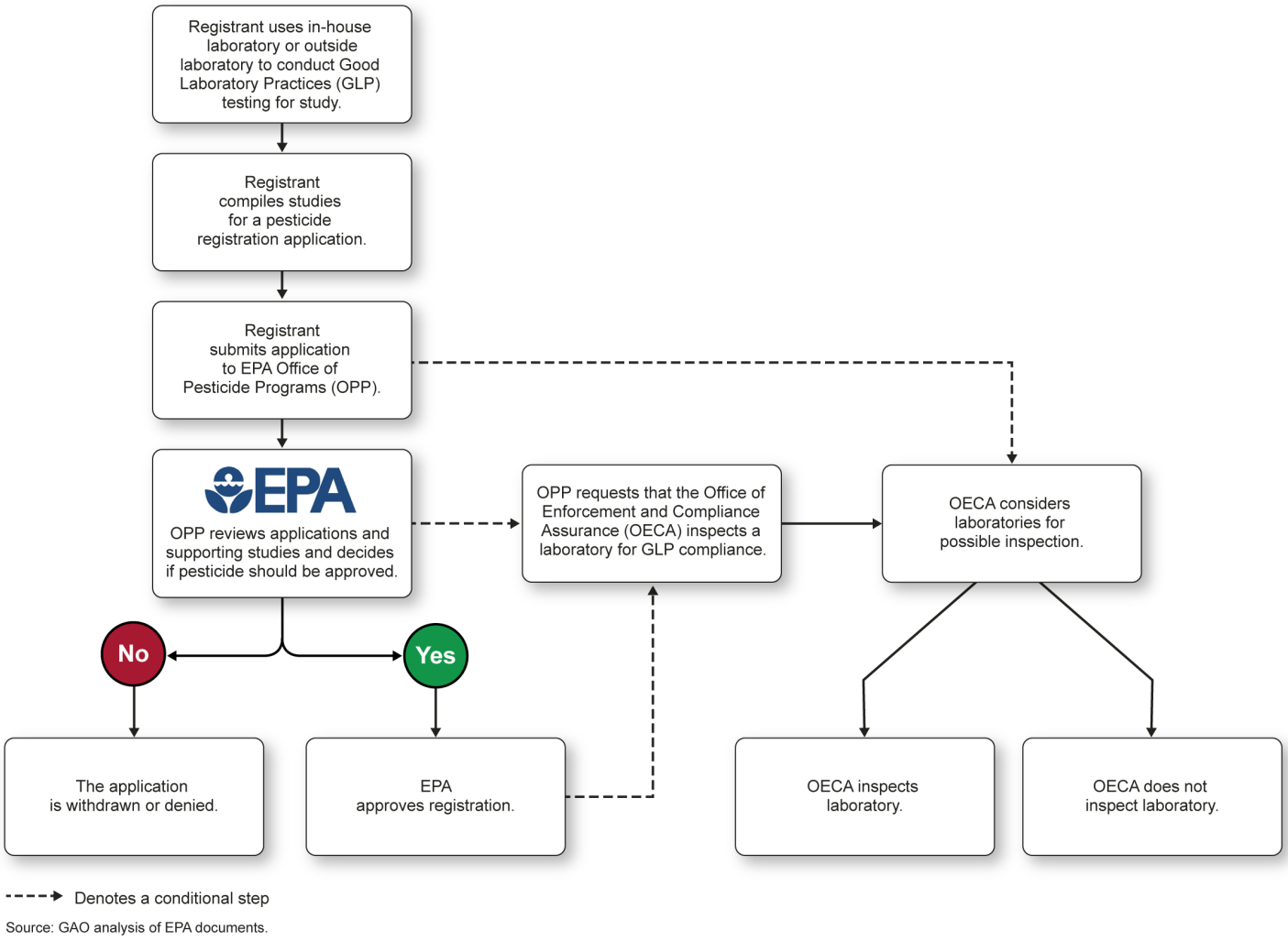
OECA's GLP Program is tasked with monitoring compliance with the GLP regulations through on-site inspections of laboratories, as well as audits of the laboratories' studies. According to EPA officials, the purpose of the

[14]According to OPP officials, applicants for pesticide registrations are usually pesticide product manufacturers. When EPA registers an applicant's pesticide product, the applicant is then called a registrant. For the purposes of this report, we refer to both applicants and registrants as registrants.

study audit is to ensure that the study was conducted in accordance with the agency's GLP regulations and that the study is supported by data generated by the laboratory. A study's sponsor or applicant must include one of the following statements in the submission: (1) that the study was conducted in accordance with GLP, (2) a detailed description of all the differences between the practices used in the study and those required by GLP, or (3) that they do not know if their study was conducted in accordance with GLP.[15] Laboratories eligible for inspection are those that have conducted studies submitted to the agency. In some instances, a single laboratory may have conducted more than one submitted study. During an inspection, OECA's GLP Program inspectors will verify the accuracy of a study's GLP compliance statement. GLP inspections can take place while OPP is still reviewing a pesticide registration application or a petition for a tolerance-setting, or it can take place after a pesticide has been registered, or the tolerance has been established. Figure 1 summarizes the pesticide registration and tolerance-setting process, as well as its relationship to OECA's inspection of GLP laboratories.

[15]40 C.F.R. § 160.12.

Figure 1: The Role of Good Laboratory Practices in the Pesticide Registration Process



Source: GAO analysis of EPA documents.

EPA and FDA have each developed their own GLP standards to address problems found with laboratory studies submitted for the agencies' review. Investigations by these agencies in the mid-1970s revealed that some studies had not been conducted in accordance with commonly accepted laboratory practices. For example, according to an industry representative, one of the first laboratories to attract regulatory and media attention was Industrial Bio-Test Laboratories (IBT), a contract toxicological research laboratory that conducted much of the U.S. toxicological testing at the time. As a result of EPA's and FDA's investigations of IBT, several hundred studies were invalidated because

of deliberate fraud, and hundreds of chemicals had to be retested. Specific findings included poor recordkeeping, testing conducted by untrained and unqualified personnel, and data fabrication. For example, data were submitted on rats that had previously been reported as deceased. As a result, in 1978, FDA formulated and published GLP regulations under FFDCA.[16] In 1983, EPA published its GLP standards for pesticide toxicology studies, and in 1989, EPA extended the standards' coverage to include nearly all research data supporting pesticide registrations under FIFRA. The Organisation for Economic Co-operation and Development (OECD), which includes more than 30 member countries including the United States, published OECD *Principles of Good Laboratory Practices and OECD Guidelines for the Testing of Chemicals* in 1981.[17]

GLP standards cover the proper handling of laboratory test substances, equipment maintenance and calibration, testing operations, study plans, quality assurance, recordkeeping and reporting requirements, and facility management, among other things. For example, when EPA conducts a GLP inspection, it determines, among other things, whether the laboratory is of suitable size and construction to facilitate the proper conduct of the studies. Specifically, an EPA inspection would determine, among other things, whether the laboratory has a sufficient number of rooms or other areas for proper separation of species and testing, as well as for the collection and disposal of contaminants and waste.

In 1981, OECD established the Mutual Acceptance of Data program designed to obtain international recognition of testing data in support of pesticide registrations. As of August 2012, there were 31 member countries, including the United States, and 5 nonmember countries, each participating on a rotating basis in evaluating each other's testing programs compared with OECD test guidelines. EPA has signed memorandums of understanding with seven countries under the Mutual

[16]43 Fed. Reg. 59,986 (Dec. 22, 1978) (codified as amended at 21 C.F.R. pt. 58).

[17]OECD is an organization of 34 industrialized countries, operating by consensus, that fosters dialogue among members to discuss, develop, and refine economic and social policies and provides an arena for establishing multilateral agreements.

Acceptance of Data Program and has a bilateral agreement with China.[18] According to EPA documents, U.S. companies seeking to sell pesticides in foreign countries and multinational companies seeking registration of pesticides to sell in the United States must meet two Mutual Acceptance of Data program criteria: (1) the country where a study was conducted has a valid and active GLP Compliance Monitoring Program and (2) the testing facility (or laboratory) was inspected by the country's GLP compliance monitoring authority. Some other countries fund their GLP inspections through fee-based systems, under which the registrant or laboratory pays a portion or all of the inspection costs. For example, according to a European Commission official, there are currently 17 European Union member countries that charge some type of fee for conducting GLP inspections. According to FDA officials, FDA charges user fees for medical and animal product application reviews; these fees, together with appropriated funds, provide resources that FDA uses for conducting GLP inspections related to such products. According to EPA officials, although the agency charges fees for review of pesticide applications by OPP, it does not charge a fee for OECA's GLP laboratory inspections.

EPA's GLP inspection process includes three stages: (1) the preinspection targeting stage, (2) the inspection stage or on-site inspection of the laboratory, and (3) the postinspection stage.

Preinspection Targeting Stage

The preinspection targeting stage includes a series of activities performed by inspectors before the actual on-site inspection is conducted. OECA's GLP Compliance Monitoring Program usually initiates its own inspections by using a targeting module—referred to as the "Neutral Scheme Targeting Module"—that automatically searches the GLP Program's Laboratory Information and Study Audit (LISA) database to target potential studies and pesticide test laboratories. The GLP Compliance Monitoring Program selects laboratories for inspection from among the population of laboratories that have conducted studies submitted to

[18]EPA has signed a memorandum of understanding with Canada, Germany, Israel, Japan, the Netherlands, Switzerland, and the United Kingdom. In addition, EPA has signed a Letter of Intent with China to mutually accept each other's GLP Program upon completion of certain criteria, and the U.S. Ambassador signed a bilateral agreement with Taiwan.

OPP.[19] Using the Neutral Scheme Targeting Module, the inspector identifies laboratories and applies numerical weights to them based on a set of criteria (e.g., the length of time since the last inspection, the severity of the last and prior inspection findings, and the number of submitted studies conducted by the laboratory) to establish a list of potential laboratories to inspect. Most laboratories are selected for inspection through the Neutral Scheme Targeting Module.[20] When laboratories are identified for inspection through use of the Neutral Scheme Targeting Module, the GLP Program Manager assesses these laboratories to determine their eligibility for inspection along with the studies selected for audit. The assessment includes performing a preliminary review of studies to determine, among other things, whether the laboratory is still in business and whether any studies conducted by the laboratory have been rejected by OPP in a review of a pesticide application. The GLP Program Manager will then prioritize and select the laboratories for inspection. Criteria for selection can include whether the eligible laboratories are in the same geographic area. The inspector determines when the laboratory will be inspected and, 10 days prior to the inspection, notifies the laboratory of the impending inspection.

Inspections can also be initiated at OPP's request or that of another EPA office. For example, as OPP reviews studies, it may have questions or problems with the supporting data. In those cases, OPP can request that OECA's GLP Program conduct an audit of particular studies and inspect the laboratories used for these studies. In addition, according to EPA officials, foreign governments can request an EPA inspection if a U.S. registrant is applying to use its pesticide in a foreign country and that country requires a GLP inspection of the U.S. laboratories whose studies are to be used in support of the registration. Finally, according to EPA officials, OECA can conduct a "for cause" GLP inspection based on a tip

[19]When pesticide registration application or tolerance level petitions are submitted to OPP, contractors enter laboratory data, such as laboratory name and address, as well as information on the studies submitted with the application, into the Office of Pesticide Program Information Network (OPPIN) database. At any given time, LISA only contains data submitted to OPP for the previous 5 years. The data are transferred to LISA from OPPIN. In contrast to EPA's process, officials from other countries told us that their GLP compliance monitoring programs select laboratories for inspection before these laboratories begin GLP testing.

[20]Some laboratories are identified for inspection through other means, such as complaints submitted.

or complaint received through anonymous phone calls, e-mails or letters about potential GLP violations at a laboratory.

Inspection Stage

The inspection stage begins with the OECA inspectors, prior to visiting a laboratory, conducting study audits and evaluating the laboratory studies submitted to OPP to determine whether they adhere to GLP standards. GLP Compliance Monitoring Program inspectors previously performed this data audit during the inspection of the laboratory. In April 2012, EPA changed its process to have inspectors audit studies before inspecting the laboratory to save time spent at the laboratory and therefore reduce travel expenses. However, OECA officials told us that its inspectors follow the old process if appropriate to the situation. The inspectors are also to verify that data generated by the laboratory support the conclusions made in the study.

Next, an inspector travels to the laboratory to perform the on-site inspection of the laboratory. As part of this inspection, the inspector performs a walk-through of the laboratory to gain an understanding of its capabilities. The inspector will ask to see and review inspection documentation associated with the laboratory, including qualifications and responsibilities of laboratory personnel, the receipt and storage of test substances, the laboratory's standard operating procedures, and animal rooms. The inspector then conducts a compliance inspection to gauge the laboratory's current practices and procedures by selecting one or two ongoing or recently completed studies from the laboratory's master schedule to see whether they adhered to GLP standards. The inspector also observes a procedure in an ongoing study to determine adherence to standard operating procedures, the study plan, and GLP, as well as whether the person performing the procedure has the appropriate education and experience.

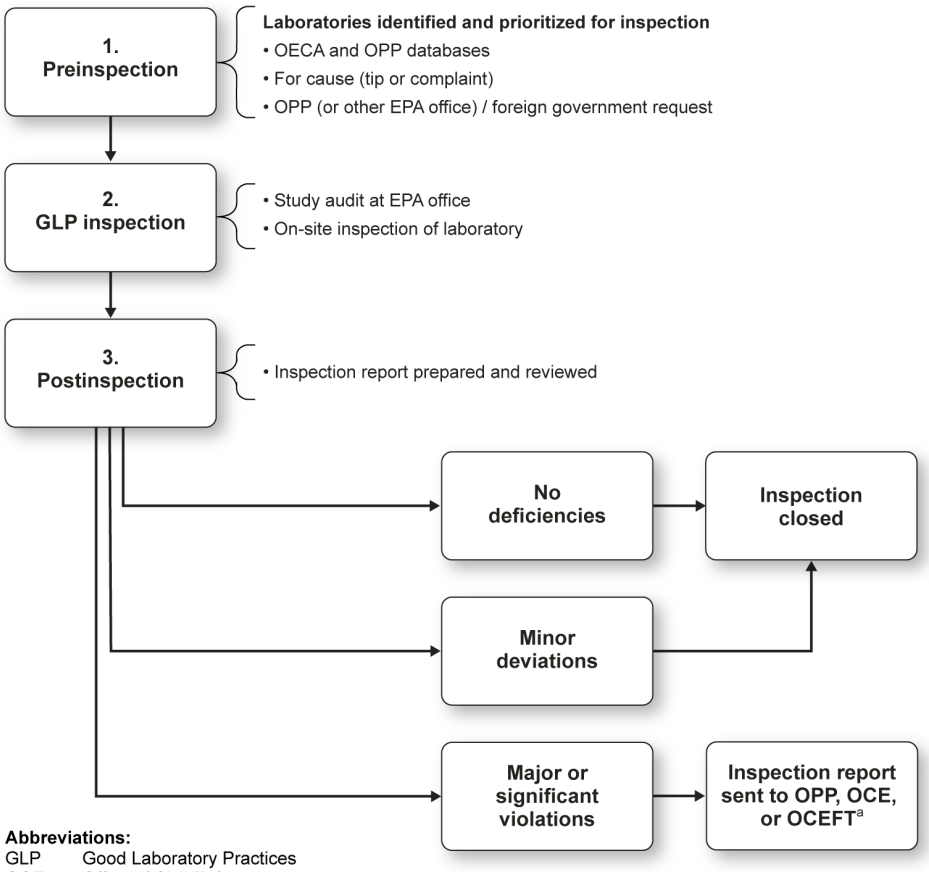
Postinspection Stage

The postinspection stage involves activities such as preparing an inspection report that contains a description of the general nature of the inspection and the laboratory being inspected. Report appendixes cover the findings from the study audits and the on-site inspection. Inspection reports are next reviewed by another GLP inspector to ensure the reports are complete and consistent. According to an EPA official, the GLP Program Manager then reviews the inspection report and assigns one of the following categories to the laboratory as specified in the Enforcement Response Policy for FIFRA GLP Regulations: (1) no GLP deficiencies noted, (2) minor GLP deviations, or (3) major/significant GLP violations. For laboratories given ratings in the first two categories, the inspector closes out the inspection and enters all the inspection information and the

review category into the LISA database. The inspector also enters some of this information, such as laboratory information, inspection dates, number of study audits, and potential deficiencies, into OECA's Integrated Compliance Information System (ICIS), which is used for OECA-wide compliance reporting results.

The GLP Program Manager sends a letter to the laboratory and the registrant notifying them of the results of the inspection and, in the case of any deficiencies, requesting assurances that appropriate action will be taken to remedy the deficiencies. In the case of a significant violation of the GLP standards that, in the opinion of the inspector, may have affected the validity and integrity of studies performed at the laboratory, the GLP Program Manager will refer this information to OPP for consideration in their decision-making process and, if appropriate, to OECA's Office of Civil Enforcement (OCE), which develops and prosecutes administrative civil and judicial cases and provides legal support for cases and investigations initiated in EPA regions. If the violation is criminal in nature, it will be referred to OECA's Office of Criminal Enforcement, Forensics and Training (OCEFT). The inspection will not be closed until OPP or OECA has made a final determination. Figure 2 summarizes the GLP inspection process.

Figure 2: EPA Office of Enforcement and Compliance Assurance (OECA) GLP Compliance Monitoring Program's Inspection Process



Abbreviations:
GLP Good Laboratory Practices
OCE Office of Civil Enforcement
OCEFT Office of Criminal Enforcement, Forensics and Training
OECA Office of Enforcement and Compliance Assurance
OPP Office of Pesticide Programs

Source: GAO analysis of EPA documents.

[a]The GLP Program Manager will refer significant violations of the GLP standards to OPP and, if appropriate, to OECA's OCE. If a violation is criminal in nature, it will be referred to OECA's OCEFT.

EPA Has Inspected Few Laboratories for GLP Compliance and Faced Challenges in Selecting Laboratories for Inspections

EPA's OECA has inspected few laboratories on an annual basis that test pesticides for GLP compliance for fiscal year 2009 through fiscal year 2013 and faced challenges in doing so. Because of resource limitations in the GLP Compliance Monitoring Program, OECA prioritizes laboratories for GLP inspections based on a set of criteria. However, our analysis showed that some laboratory information in the databases used to prioritize laboratories for inspection was either inaccurate or incomplete, and these data challenges may negatively affect prioritization. OECA officials said that budget cuts, among other things, have reduced the number of inspectors and the number of GLP inspections that can be performed. Given the concerns of some stakeholders about the infrequent GLP inspections, OECA is considering other approaches, such as charging fees or using third parties to review studies, in order to increase the number of inspections.

OECA Inspects Few Laboratories Annually, but Most Laboratories Are Not Regularly Inspected for GLP Compliance

OECA inspected from 51 to 80 laboratories each year for GLP compliance in fiscal year 2009 to fiscal year 2013, but most laboratories were not regularly inspected for GLP compliance. During this period, OECA inspected about 4 to 6 percent of 1,400 eligible laboratories each year, according to EPA data and officials.[21] In contrast, FDA's GLP compliance program guidance manual states that the program's objective is to inspect all eligible nonclinical laboratories conducting safety studies that are intended to support applications for research or marketing of regulated products approximately every 2 years.[22] Similarly, most member countries under OECD's Mutual Acceptance of Data (MAD) agreement conduct inspections of their laboratories for GLP compliance every 2 years, according to an OECD official we interviewed.

Some laboratory representatives we surveyed stated that their laboratories were not inspected for GLP compliance by EPA from 2008 to 2013. EPA officials told us they inspect as many laboratories as they can, given financial constraints. OECA officials explained that a limited number of inspectors and tight budgets have hindered their ability to perform more inspections. In fiscal year 2013, according to EPA officials, OECA had four GLP inspectors to inspect 1,400 eligible laboratories in the United

[21]According to EPA officials, approximately 1,400 laboratories conducted studies that were submitted to EPA over a 5-year time frame and are thus eligible for inspection.

[22]FDA Compliance Program Guidance Manual 7348.808.

States. OECA officials acknowledged that their four inspectors cannot inspect all 1,400 eligible laboratories for GLP compliance every 2 years. From fiscal year 2009 to fiscal year 2013, EPA reduced its GLP Compliance Monitoring Program budget and the number of full-time equivalent staff by approximately 50 percent from eight to four inspectors. EPA officials said that the reduction in the number of full-time equivalent staff was due to retirements, an inability to hire new inspectors because of budgetary constraints, and most importantly, according to these officials, the inability to find inspector candidates with the requisite skills. During this same time period, the number of studies conducted by laboratories that were submitted to OPP has remained relatively constant, except for an increase in the number of studies submitted in fiscal year 2010. Estimates of the numbers of studies submitted, inspections conducted, inspection staff and GLP budget data are shown in table 1.

Table 1: Number of Pesticide Studies Submitted, Inspections, Full-Time Equivalents, and Budget for EPA's Good Laboratory Practices (GLP) Compliance Monitoring Program from Fiscal Year 2009 to Fiscal Year 2013

	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Number of pesticide studies submitted to EPA[a]	7,791	10,093	8,715	8,326	7,123
Number of GLP inspections[b]	64[c]	71[c]	51[c]	80[c]	79[c]
Number of GLP compliance monitoring program full-time equivalents	8	8	5	4	4
GLP program budget	$1,415,000	$1,021,400	$959,500	$734,500	$702,000

Source: GAO analysis of EPA data.

[a]Multiple studies can, and do, come from the same laboratory.

[b]These numbers include inspections performed under the Federal Insecticide, Fungicide, and Rodenticide Act and exclude inspections conducted under the Toxic Substances Control Act.

[c]Inspection data were taken from EPA's Integrated Compliance Information System database because of technical problems EPA has been experiencing with the Laboratory Information and Study Audit database since July 2011.

To increase efficiency and to respond to a reduced budget and workforce, as well as to address concerns from industry and the OECD, OECA implemented changes to its GLP inspection procedures in fiscal year 2012 to try to increase the number of GLP inspections from the low of 51 conducted in fiscal year 2011. Under its revised inspection procedures, agency officials consider laboratories' geographic proximity to each other, as well as other criteria, when selecting laboratories to inspect. For example, in February 2013, the agency inspected five laboratories

located in Oregon and, in March 2013, the agency inspected two laboratories in Texas. OECA officials explained that grouping laboratory visits geographically saves travel money and staff time. In addition, they stated that a change in OECA's inspection procedures to allow inspectors to audit studies in EPA offices rather than on-site reduced the amount of time that inspectors spent at a laboratory.

Nevertheless, some stakeholders and international officials we interviewed expressed concern about the infrequent GLP inspections by EPA. Pesticide manufacturers and industry associations told us that if laboratories cannot prove GLP compliance to potential clients or to countries where their products may be used, their business can be negatively affected. According to a senior staff person at one U.S. laboratory, in 2011, the Netherlands rejected a study from a U.S.-based laboratory because the contractor laboratory that conducted the study had not been inspected by EPA. This same study had been previously submitted to EPA. Following the Netherlands' rejection of this study, the laboratory had to repeat the study and subsequently contracted with a European-based laboratory to do so. In addition, two stakeholders we interviewed said that such rejections by other countries could likely increase if U.S laboratories could not show that they had a recent GLP inspection. One laboratory representative said his laboratory may stop doing GLP testing since many registrants require proof of GLP inspections, and his laboratory had not been inspected by EPA. In addition, this laboratory representative said that if U.S. laboratories cannot show that they have had a GLP inspection, registrants may not hire them to conduct studies because of the possibility that those studies may be rejected. In our survey of laboratories, 5 of 14 respondents reported that EPA could improve its implementation of its GLP Compliance Monitoring Program by increasing the number and frequency of inspections to prevent these business consequences.[23] Twelve of 15 respondents from laboratories with study data submitted to OPP since fiscal year 2008 reported that EPA's GLP inspections had a positive effect on their business. Nine of the 12 respondents who reported positive effects of a GLP inspection indicated that the inspections enabled them to

[23]Not all respondents to our survey answered every question. We obtained survey responses from 20 laboratories from a nongeneralizable, random sample of 53 laboratories, and other entities that had sent supporting studies to OPP for a pesticide registration application for fiscal year 2010 to 2012 to ask them questions about EPA's GLP inspections. Please see appendix I for details.

prove GLP compliance to their customers, such as U.S. and international pesticide manufacturing companies, as well as to other countries' governments.

OECA Prioritizes Laboratories for GLP Inspections, but Data Challenges May Negatively Affect Its Targeting Process

OECA prioritizes laboratories for GLP inspections, but challenges with some of the data used to determine those priorities may negatively affect its targeting process. GLP Compliance Monitoring Program inspectors use the OPPIN and LISA databases to develop a list of the highest priority laboratories to inspect for GLP compliance in a given year. Once a list is generated using the Neutral Scheme Targeting Module located in the LISA database, OECA officials said they try to select laboratories that are geographically near to one another to inspect. The information used to develop this priority list is based on data transferred from OPPIN to LISA. However, our analysis showed that the laboratories' information in these databases was sometimes incomplete or inaccurate.[24]

We found that the OPPIN system currently has three categories to classify an entity's role in a study: sponsor, performing laboratory, or both. These categories do not allow EPA staff to differentiate between GLP laboratories and other entities involved in a study. As a result, we found some entities were identified in the OPPIN database as "performing laboratories," which EPA defines as facilities where a study or part of a study is conducted, when in fact they were not.[25] For example, of the respondents to our survey of performing laboratories found in the OPPIN database, six reported that they were not a laboratory and did not conduct GLP testing.[26] Of these six, three said they were consultants, two said

[24]We have previously reported issues with inaccurate data in OPPIN. In August 2013, we reported that, according to OPP officials, following an internal review of its conditional pesticide registration program that it completed in March 2011, OPP concluded that the OPPIN data on the number of conditional pesticide registrations were inaccurate. See GAO-13-145.

[25]In the *Pesticide Registration (PR) Notice 2011-3 Standard Format for Data Submitted Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and Certain Provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA)* published on November 30, 2011, EPA instructs study submitters to clearly identify on each study's title page the name of the performing laboratory. The guidance does not specify that a laboratory's identification number be included on the title page but does specify inclusion of a laboratory project identifier.

[26]We received a total of 26 survey responses from our sample of laboratories, but 6 of the 26 reported that they were not a laboratory and did not conduct GLP testing. Therefore, these 6 are considered out-of-scope for reporting our survey results.

they contract with an outside source for laboratory testing, and one was a pesticide manufacturer. We were not able to determine how or why these entities were identified as performing laboratories in OPPIN. EPA officials told us that if the entity that submits the study puts inaccurate information on a study's title page concerning who performed the study and where the study was performed, the information entered by EPA's contractors into OPPIN will also be inaccurate. EPA's documentation describing the Neutral Scheme Targeting of laboratories states that the entity's role in a pesticide study determines whether it is a candidate for inspection. If entities are inaccurately identified in OPPIN as performing laboratories, the Neutral Scheme Targeting Module will not consider the correct universe of laboratories to inspect and, as a result, inspectors need to do additional manual research to verify that the laboratory selected for an inspection is indeed an entity eligible for a GLP inspection.

We also found that address information for some laboratories was missing or inaccurate in OPPIN. For example, we found missing address information for 23 percent of laboratories listed in OPPIN.[27] In 2008, EPA updated its 1991 guidance to the contractors responsible for entering data into OPPIN.[28] The updated guidance states that the agency wants to capture the physical address for each laboratory because OECA uses this information to select laboratories for inspection. The guidance acknowledges that determining the performing laboratory in published studies is challenging, but the goal is to identify where the actual location of the research was done. Without accurate address information, there could be problems determining where the testing was actually conducted.

In addition, we found that some laboratory identification numbers were not reliable. In its November 1991 guidance, OPP states that laboratories should be assigned a unique laboratory identification number.[29] For example, we found that one laboratory that was given a ranking in fiscal year 2013 as second highest priority for a GLP inspection had an identification number that was the same as four other laboratories in four

[27]Missing address information could include missing data for any of the following: street address, city, state, or zip code.

[28]EPA, *Technical Guidance for Citation Building: Extra Hints for Coding Laboratories and Sponsors.* Apr. 1, 2008.

[29]EPA, *Revised Technical Direction for PDMS Laboratory Indexing*. Nov. 1991.

different states, making it unclear which of those five laboratories was actually the one selected for inspection.

The agency maintains two different databases to track GLP inspections, ICIS and LISA. The LISA database is used by the GLP Compliance Monitoring Program, while the ICIS database is used EPA-wide, according to officials. Because of technical problems EPA has been experiencing with the LISA database, inspection data have been entered only into ICIS since July 2011, according to officials. We reviewed inspection data contained in both databases for fiscal year 2008 to fiscal year 2013 in an effort to determine the total number of GLP inspections OECA conducted, but we were not able to match the inspection information contained in the two databases. While LISA uses laboratory identification numbers, ICIS does not. As a result, OECA may not be able to track if, or when, a specific laboratory had been inspected because the systems do not both use identification numbers. In addition, the laboratory names are not always the same in the two databases. We were also unable to match up the inspections in the two databases. Without accurate data on which laboratories have been inspected, OECA's Neutral Scheme Targeting Module scoring of laboratories most in need of inspection may be inaccurate and, therefore, manual research is required to ensure that OECA is targeting the laboratories most in need of inspection.

Based on the incomplete or inaccurate data in ICIS, LISA, and OPPIN, it is not always possible for GLP Compliance Monitoring inspectors to identify where the testing was conducted without making telephone calls to individual laboratories. The data issues also impede the agency's ability to efficiently track which laboratories need inspecting. The officials said GLP inspectors must spend time manually verifying laboratory data before deciding which laboratories to inspect. In the absence of reliable data, EPA may not have the data it needs to prioritize laboratories to inspect efficiently or effectively.

OECA Is Considering Other Implementation Approaches to Increase Inspections

OECA is considering other approaches to address laboratory representatives' and others' concerns about infrequent GLP inspections, such as using third parties or charging fees to increase the number of inspections. In August 2012, OECA developed a Budget Adjustment Plan, which provided general information on potential future approaches to the GLP Compliance Monitoring Program, including ways the program could be run more efficiently given its recent budget cuts and inability to hire GLP inspectors. In its Budget Adjustment Plan, EPA states that OECA will evaluate other implementation approaches, such as the use of a third

party to conduct GLP inspections. EPA officials told us that they have also conducted internal and informal discussions regarding the possibility of using user fees for the GLP program, but the agency has not conducted a formal evaluation of user fees. Without formally assessing the need for such fees, EPA cannot determine whether charging and retaining the fees would be possible and whether such fees could help make the inspection program self-sustaining.

In 2012, we concluded that federal user fees and charges are generally related to some voluntary transaction or request for government goods or services beyond what is normally available to the public, such as fees for patent applications and customs inspections.[30] In 2012, the federal government collected nearly $300 billion in user fees from the public.[31] In 2008, we found that well-designed user fees can reduce the burden on taxpayers to finance those portions of activities that provide benefits to identifiable users.[32] As we mentioned earlier, FDA charges user fees for medical and animal product application reviews, and these fees, together with appropriated funds, provide resources that FDA uses for conducting GLP inspections related to such products. In addition, some other countries, such as some that are members of the OECD, fund their GLP inspections through fee-based systems, whereby the registrant or laboratory pays a portion or all of the inspection costs.

According to Office of Management and Budget (OMB) Circular A-25, every 2 years, agencies should review programs that are not currently funded by user fees (such as the GLP program) to determine whether fees should in fact be assessed for government services.[33] Once user fees are implemented, revenue from the fees will be credited to the

[30]GAO, *2012 Annual Report: Opportunities to Reduce Duplication, Overlap and Fragmentation, Achieve Savings, and Enhance Revenue*, GAO-12-342SP (Washington, D.C.: February 2012).

[31]GAO, *Federal User Fees: Fee Design Options and Implications for Managing Revenue Instability*, GAO-13-820 (Washington, D.C.: Sept. 30, 2013).

[32]In May 2008, we issued a User Fee Design Guide, which examined how the four key design and implementation characteristics—how fees are set, collected, used, and reviewed—may affect the economic efficiency, equity, revenue adequacy, and administrative burden of the fees. GAO, *Federal User Fees: A Design Guide*, GAO-08-386SP (Washington, D.C.: May 2008).

[33]Office of Mgmt. & Budget, Circular No. A-25 Revised, Memorandum for Heads of Executive Departments and Establishments (July 8, 1993).

general fund of the U.S. Treasury as miscellaneous receipts unless otherwise specified by law.[34] Circular A-25 also states that it may be appropriate for an agency to request authority to retain the fee revenue if the user fees offset the expenses of a service that is intended to be self-sustaining. The OMB guidance states that agencies are to discuss the results of the biennial fee reviews and any resulting proposals in their Chief Financial Officers (CFO) Annual Report required by the Chief Financial Officers Act of 1990.[35] In its most recent CFO Annual Report (EPA Agency Financial Report) EPA discussed its biennial review of its existing user fee programs. However, it did not discuss reviewing the GLP program—or any of its other programs that are not currently funded by fees—to determine whether fees should be assessed.[36] Moreover, in March 2014, the EPA Office of Inspector General (OIG) reported that EPA did not conduct thorough biennial user fee reviews for fiscal year 2008 to fiscal year 2009 and for fiscal years 2010 to 2011, and it did not review all agency programs to determine whether they should assess fees for government services they provided.[37] Among the OIG's recommendations were that the EPA CFO discuss biennial user fee results in the EPA Agency Financial Report, coordinate with programs that claimed an exception to charging fees and costs and help determine whether fees should be assessed. Without assessing the need for user fees, EPA cannot determine whether fees could help make the laboratory inspection program self-sustaining.[38]

When asked about user fees, representatives of 8 of 12 laboratories and pesticide manufacturers told us they would support EPA user fees for

[34]The rule governing the accounting and disposition of receipts, including user fees, states that they must be deposited in the general fund of the Treasury as miscellaneous receipts unless the agency has statutory authority to do otherwise. 31 U.S.C. § 3302.

[35]Pub. L. No. 101-576, 104 Stat. 2838 (1990).

[36]EPA, *Fiscal Year 2013 Agency Financial Report*.

[37]EPA Office of Inspector General, *EPA Did Not Conduct Thorough Biennial User Fee Reviews*, 14-P-0129 (Washington, D.C.: Mar. 4, 2014).

[38]EPA acknowledges that improvements were needed to ensure that all agency programs were reviewed, in accordance with OMB Circular A-25, "User Charges, Revised," and the Chief Financial Officers Act of 1990. According to EPA officials, the agency took actions in Fiscal Year 2013 to improve its user fee review efforts by issuing a biennial user fee review guide, conducting training for its user fee programs, and established fee review procedures.

GLP inspections, and they cited more frequent GLP inspections as a possible benefit of such user fees. Representatives from the remaining 4 laboratories did not support user fees, and some of these expressed concern that a user fee system might be burdensome to smaller laboratories. However, as we previously reported, the amount of a user fee reflects the cost of providing the service, which may differ among users.[39]

EPA Rarely Used GLP Inspection Results in Initial Pesticide Registration Decisions but Sometimes Used Them for Later Reexamination

EPA rarely used GLP inspection results in making its initial pesticide registration decisions. An OPP official told us that this is because most inspections occur after those decisions have been made. According to an OPP official, pesticide registration decisions are required by statute to be made within 3 to 24 months of receipt of the pesticide application. For example, new pesticide products that are identical in their uses and formulation to one or more products already registered usually require a registration decision within 3 months.[40] However, the official stated that the GLP Monitoring Program staff cannot set up and conduct inspections of many of the laboratories involved within those time frames.

OPP and OECA officials told us that they have historically communicated on an informal basis about OPP's inspection priorities before a pesticide registration has taken place. These priorities are usually based on OPP's review of studies and the concerns that may arise from these reviews or about the sponsor or study performer. This informal communication generally involves OPP contacting OECA by telephone or e-mail to request that certain laboratories be inspected. An OPP official told us that the two offices have recently tried to make better use of the GLP inspection program in OPP's decision making. For example, according to EPA officials, in September 2012, a senior OPP official hand-delivered a document to her OECA counterpart requesting that (1) several laboratories be considered as priorities for GLP inspections in fiscal year 2013; (2) OECA focus its audit of studies on those submitted within the

[39]GAO-08-386SP.

[40]The Pesticide Registration Improvement Act of 2003 (PRIA) provides a schedule of covered applications and registration service fees, including the category or type of application, the amount of the pesticide registration service fee, and the corresponding decision review timeframe in which the agency is to make a decision. There are 189 fee categories or types of applications, each with a fee and decision review time frame. Pub. L. No. 108-199, div. G, tit. V, § 501(f)(2), 118 Stat. 419, 422 (2004) (codified as amended at 7 U.S.C. § 136w-8).

last 6 to 12 months when performing inspections under the Neutral Scheme Targeting Module in fiscal year 2013; and (3) OECA audit specific categories of studies that OPP officials considered critical to their pesticide approval decisions. An OECA official told us that as of March 2014, OECA inspectors had completed all of the eight OPP-requested inspections. An OPP official told us that OPP would like to continue to provide input to OECA prior to the beginning of each fiscal year to increase the opportunity for OPP to react to findings before a product is registered. The two offices appear to be communicating and prioritizing laboratories for GLP inspections informally, but according to an EPA official, there are no documented procedures that define the responsibilities of each office in coordinating and prioritizing GLP inspections. EPA has stated that formal procedures are not needed and that the current method of communication and coordination is satisfactory. However, by relying on informal coordination mechanisms, OECA and OPP are depending on relationships with individual officials to ensure effective coordination, and these informal relationships could end once personnel turnover occurs. Without documented procedures for effective coordination between the two offices, there is no assurance that the two offices will consistently coordinate on GLP inspections in the future. Under federal standards for internal control, agencies are to clearly document internal controls, and the documentation is to appear in management directives, administrative policies, or operating manuals.[41]

When OECA's GLP inspectors find deficiencies at a laboratory, they share the inspection reports with major or significant violations with OPP. According to OPP officials, once OPP receives the OECA inspection report, it sends it to the OPP registration division responsible for the registration (or pending registration) of products being supported by the studies audited. The OPP registration division then reviews the report and conducts a scientific reexamination of the studies that the laboratory in question conducted and that were submitted in support of the pesticide registration. Once OPP finishes its reexamination, if it finds that deficiencies affect a study's findings, OPP is to reject the study and may request that the registrant repeat the study, submit other materials that support that aspect of the registration, or perform other corrective action deemed satisfactory to OPP. After the reexamination is complete, OPP

[41]GAO, *Standards for Internal Control in the Federal Government*, GAO/AIMD-00-21.3.1 (Washington, D.C.: November 1999).

informs both OECA's GLP Compliance Monitoring Program and the registrant of the outcome.

We found that, from fiscal year 2008 to fiscal year 2012, OECA GLP inspectors referred for reexamination the inspection results from 26 laboratories and 73 studies to OPP. Table 2 lists the action taken by OPP as a result of its reexamination of studies, as of March 2014.

Table 2: Actions by EPA's Office of Pesticide Programs Based on Good Laboratory Practices (GLP) Inspection Results, Fiscal Year 2008 to Fiscal Year 2012

Action	Number of Studies
Requested study be repeated	26
Rejected study and sponsor voluntarily cancelled or voluntarily suspended registration	4
No action needed	20
Review of study still pending	23
Total	**73**

Source: GAO analysis of EPA data.

Our analysis of EPA data shows that this review process, from the initial OECA GLP inspection to completion of OPP's reexamination, takes on average about 2 years (see table 3).

Table 3: Average Time from EPA's Office of Compliance and Assurance's (OECA) Good Laboratory Practices (GLP) Inspection of Laboratory to EPA's Office of Pesticide Program's (OPP) Review of Inspection's Impact on Laboratory's Study, Fiscal Year 2008 to Fiscal Year 2012

		Average days	Average months[a]
Completed reviews (of 50 studies)	Average time from start date of OECA's GLP inspection of a laboratory to referral of inspection results to OPP	352	11
	Average time from date OECA referred inspection results to OPP to when OPP completed its review of inspection results' impact on laboratory's study	446	14
	Average time from start date of OECA's inspection to date OPP completed review of study	798	26
Reviews still pending (of 23 studies)	For those reviews that are still pending, average time from date of OECA GLP inspection to March 24, 2014	1066	34

Source: GAO analysis of EPA data.

Note: Totals may not sum due to rounding.

[a]Average months were determined by dividing the average days by 31.

According to OPP officials, OPP has not denied a pesticide registration or revoked any registrations based on OECA laboratory inspection

information during the past 5 years, but OPP has taken other actions because of that information, such as requiring a registrant to repeat a study or requesting that a registrant voluntarily cancel its registration. For example, according to data provided by an OPP official, in fiscal year 2012, 15 studies associated with an already registered pesticide product were found to be "unacceptable" based on OECA inspection information. For 10 of these studies, EPA informed the registrants that they needed to repeat the study. For the 5 others, the registrant voluntarily canceled or suspended its registration associated with the study, or the study was not a deciding factor in the products registration and therefore EPA took no further action. In addition, OPP has required that an efficacy claim be removed from the label of a registered product based on a study submitted by a laboratory not meeting GLP standards.

OPP officials explained that a single study is not likely to affect the denial or approval of a pesticide registration because OPP usually bases its registration decisions on more than one study (although OPP officials noted their decision depends on, among other things, the type of study). For example, according to OPP officials, some pesticides are the subject of more than 30 different studies before a decision is made on registration. However, these same officials stated that OPP believes that the GLP inspections are valuable not only to alert OPP to issues with study data and laboratories but to act as a deterrent to guard against the improper conduct of studies and submission of fraudulent or incorrect study data. According to OECA officials, GLP inspections often lead to positive action being taken by laboratories and pesticide registrants. They said that registrants have voluntarily withdrawn studies from OPP as a direct result of inspection notifications and inspection findings.

EPA and FDA Do Not Regularly Collaborate on Laboratory Inspections and May Be Duplicating Each Other's Work

EPA and FDA do not regularly collaborate on GLP inspections and may be duplicating each other's work by inspecting the same laboratories.[42] In 1984, EPA and FDA entered into an interagency agreement to collaborate on GLP inspections that was last renewed in 2004. Under the agreement, the two agencies agreed to collaborate in monitoring testing laboratories' adherence to GLP regulations, as well as in auditing of health-related toxicological test reports and related laboratory records. The agencies also agreed to exchange information and coordinate actions concerning active investigations, regulation correspondence, and legal or administrative action being considered against any laboratory covered under the agreement. Among FDA's responsibilities under the agreement was to conduct a certain number of on-site inspections of laboratories identified by EPA. From 2000 to 2007, FDA conducted a total of nine inspections identified by EPA (three in 2000; three in 2001; and one each in 2002, 2005, and 2007).[43] EPA officials said they also formally met with FDA officials on a quarterly and annual basis to discuss upcoming inspections, but that communication ended by 2007 when, according to EPA officials, FDA began selecting laboratories for inspection on an annual basis instead of on a quarterly basis as EPA does. FDA also shifted from having its Office of Regulatory Affairs select laboratories for inspection to a more decentralized system, whereby its centers select laboratories for inspection, which made it more difficult for EPA to learn which laboratories FDA plans to inspect because it has to coordinate with multiple centers instead of the Office of Regulatory Affairs, according to EPA officials.[44] EPA officials also said the last year FDA sent EPA a list of laboratories it planned to inspect was in 2007. They explained that, in the past, when EPA knew which laboratories FDA was going to inspect, it would ask FDA to audit a study for them and would avoid going to the same laboratory in the same year as FDA. However, since these meetings ended, EPA officials said that they do not always know if a laboratory was already inspected by FDA until they

[42]We have defined duplication as occurring when two or more agencies or programs engaged in the same activities or provided the same services to the same beneficiaries.

[43]FDA continued to perform inspections for EPA until 2007, although the agreement was not renewed after 2004.

[44]FDA consists of nine centers and offices. According to FDA officials, five of these centers conduct GLP inspections: the Center for Biologics Evaluation and Research, the Center for Devices and Radiological Health, the Center for Drug Evaluation and Research, the Center for Food Safety and Applied Nutrition, and the Center for Veterinary Medicine.

arrive on-site. If EPA knew in advance that a laboratory was inspected by FDA recently, EPA inspectors could use FDA's inspection results to inform their decision regarding whether conducting their own inspection was necessary. If FDA's inspection results were sufficient for EPA's purposes, EPA inspectors could potentially select a different laboratory to inspect in place of the one recently inspected by FDA, thereby extending limited resources. It is important to note, however, that, in some circumstances, it may be necessary for both agencies to inspect the same laboratory.

EPA officials stated that they occasionally coordinate with one of FDA's centers on GLP inspections and stated that the two agencies performed a joint GLP inspection in 2013. In addition, EPA and FDA officials also said that both agencies participate in an FDA-led work group focusing on the modernization of laboratories. Officials from both agencies said that it would be useful to know which laboratories the other agency was planning to inspect and to have the results from those inspections. Since each agency only inspects a certain number of laboratories each year, sharing such information could help both agencies leverage resources. This coordination also could increase the number of laboratories that are inspected for GLP compliance, which in turn would help ensure that the study data submitted for pesticide registrations were generated in accordance with GLP regulations. However, the agencies do not regularly collaborate on or communicate about future inspections or share results from completed inspections.

FDA conducts two types of laboratory inspections, surveillance inspections, which are periodic, routine determinations of a laboratory's compliance with GLP regulations and include a facility inspection and study audit, and directed inspections, which are inspections assigned to achieve a specific purpose, such as verifying the reliability, integrity, and compliance of critical safety studies. Because the two agencies do not regularly share GLP inspection-related information, we found that EPA and FDA may be duplicating each other's work in some of their GLP inspections. For fiscal year 2005 to fiscal year 2012, EPA and FDA

conducted a total of 170 GLP inspections of the same 37 laboratories.[45] In 38 of the 170 inspections, the agencies inspected the same laboratory during the same fiscal year (see app. III.). For example, EPA inspected a Colorado laboratory in November 2011, and FDA conducted a surveillance inspection of this same laboratory 7 months later in June 2012. Similarly, although EPA inspected a Utah laboratory in January 2012, FDA conducted a surveillance inspection of this same laboratory 5 months later, in June 2012. According to EPA and FDA officials, the GLP standards of the two agencies upon which these inspections are based are largely similar. Moreover, a senior official in OECA's GLP Compliance Monitoring Program and representatives from three laboratories that were inspected by both EPA and FDA told us that the inspections were comparable.

We also found that there is some degree of overlap in the laboratories that are eligible for inspection by the two agencies.[46] Some laboratories covered by GLP regulations conduct tests yielding data that will be submitted to only EPA, but we found that other laboratories conduct tests for review by both EPA and FDA and are, therefore, eligible for inspection by both agencies. FDA officials told us that they did not have data to identify the total number of laboratories that submit data to both agencies and would, therefore, be subject to GLP inspections by both agencies. EPA officials and stakeholders we interviewed, however, told us that laboratories that conduct toxicology testing are the most likely to perform tests that are submitted to both EPA and FDA. For example, one representative from a laboratory in Maryland that had been inspected by both EPA and FDA eight times from fiscal year 2005 to fiscal year 2012 told us that some of the information in the laboratory's toxicology studies FDA officials examined during a 2011 GLP inspection could have been shared with EPA officials. In addition, in our survey, 5 of 19 respondents indicated that their facility conducted tests or studies intended for review by both EPA and FDA. FDA officials told us that there has been no recent

[45]EPA officials provided us with an analysis that identified GLP inspections conducted by EPA and FDA at 31 laboratories. We compared these 31 laboratories with our analysis that identified 37 laboratories. We found that EPA's analysis included some additional laboratories that we could not find in our analysis. Conversely, EPA's analysis excluded some laboratories that were included in our analysis, which was based on a review of inspection data provided to us by EPA and FDA.

[46]We have defined overlap as two or more agencies or programs engaging in similar activities or providing similar services to similar beneficiaries.

communication between the two agencies on which laboratories they plan to inspect and what they may have found at inspections that were conducted, although they have communicated this information in the past. FDA officials said they would welcome a list of inspections planned and conducted by EPA.

EPA and FDA officials said that, at present, they do not share the results of completed inspections at facilities that do both EPA and FDA-related studies, and they do not have a process in place to collaborate on future GLP inspections. As a result, EPA is not learning about laboratories that FDA has inspected and at which it may have found deficiencies. Similarly, FDA is not learning about the results of EPA laboratory inspections. In addition to potentially duplicating each others' work, by not collaborating, the two agencies are missing opportunities to leverage each other's resources and expand their inspection coverage. FDA officials told us it would be helpful to know if EPA had inspected a laboratory and that it would be particularly useful if EPA shared information if the agency had found problems during its inspection. EPA officials also said collaborating and communicating on inspections would be helpful.

In April 2013, we concluded that when executive branch agencies carry out activities in a fragmented and uncoordinated way, the resulting patchwork of programs can waste scarce funds, confuse and frustrate program customers, and limit the overall effectiveness of the federal effort.[47] The federal government uses a range of mechanisms to implement interagency collaboration, such as interagency groups, and interagency agreements and memorandums of understanding.[48] Key practices state that agencies that articulate their agreements in formal documents can strengthen their commitment to working collaboratively.[49] Written agreements are most effective when they are regularly updated and monitored. As we concluded in April 2013, where federal programs or activities are fragmented, overlapping, or duplicative, there are

[47]GAO, *2013 Annual Report: Actions Needed to Reduce Fragmentation, Overlap, and Duplication and Achieve Financial Benefits*, GAO-13-279SP (Washington, D.C.: April 2013).

[48]GAO, *Managing for Results: Key Considerations for Implementing Interagency Collaborative Mechanisms,* GAO-12-1022 (Washington, D.C.: Sept. 27, 2012).

[49]GAO, *Results-Oriented Government: Practices That Can Help Enhance and Sustain Collaboration among Federal Agencies*, GAO-06-15 (Washington, D.C.: Oct. 21, 2005).

opportunities for agencies to improve the efficiency and effectiveness of government programs and activities.[50] Moreover, without leveraging its inspection resources with FDA, EPA may continue to have difficulty increasing annual GLP inspections of laboratories.

Conclusions

OECA has taken some steps to increase the number of GLP compliance inspections of laboratories conducting studies submitted to EPA for pesticide registration. However, OECA officials acknowledge that their four inspectors cannot inspect all 1,400 eligible laboratories for GLP compliance every 2 years, a time frame used by many of the countries that are members of OECD's MAD agreement. Because some laboratories have never had a GLP inspection, laboratory and industry representatives expressed concern that if OECA continues to inspect so few laboratories for GLP compliance, U.S. laboratories and manufacturers will be less competitive with foreign laboratories and manufacturers. In addition, with so many laboratories going uninspected, EPA may not have full assurance of the quality and integrity of data used to make pesticide registration decisions.

OECA officials told us that they have informally discussed the possibility of instituting user fees for the GLP program, but EPA has not conducted a formal evaluation of GLP user fees as directed by OMB guidance for programs not currently funded by such fees and, as recommended by EPA's OIG. OECA might be able to increase the number of inspections it conducts if it were to charge a fee, which may be used to fund GLP inspections, as FDA does, and as do 17 European countries. Without assessing its authority and need for user fees, EPA cannot determine whether fees could make the laboratory inspection program self-sustaining. In addition, we found that the information in EPA databases used by OECA to set priorities for laboratory inspection is sometimes incomplete or inaccurate. In the absence of reliable data, EPA may not have the data it needs to prioritize laboratories to inspect efficiently or effectively.

We commend OECA and OPP staff for communicating with each other on GLP inspection matters, including OECA consideration of OPP's recent steps to identify laboratories that OPP considers to be priorities for GLP

[50] GAO-13-279SP.

inspections. Considering OPP's request is important because most OECA inspections currently take place after OPP has made its registration decisions. However, EPA does not have documented procedures that define the responsibilities of each office in coordinating and prioritizing laboratories for GLP inspections consistent with federal standards of internal control. Without such procedures, there is no assurance that the two offices will consistently coordinate on GLP inspections in the future.

Furthermore, because EPA and FDA do not regularly share inspection-related information, as they did when they had an agreement to collaborate on GLP inspections, the agencies have inspected some of the same laboratories since 2007, while other laboratories may have gone without needed inspections. Without collaboration and information-sharing on planned and completed GLP inspections, EPA and FDA may duplicate GLP inspections, and EPA will have difficulty efficiently using its limited resources to increase the number of inspections it conducts. Officials from both agencies said that collaborating and communicating on inspections would be helpful. However, absent a formal written agreement, it is not clear that the agencies would regularly collaborate on future planned inspections and share results from completed inspections.

Recommendations for Executive Action

We are making four recommendations in this report.

To improve the OECA GLP inspection process, we recommend that the EPA Administrator take the following three steps:

1. Assess the authority and need for a fee-based inspection system, and if such a system is warranted, establish a user fee system, seeking additional legislative authority, if necessary, to make the laboratory inspection program self-sustaining.
2. Direct OECA and OPP to ascertain the exact causes of inaccurate and incomplete data in its databases and take action to ensure that the data, such as identification of performing laboratories and inspection history, are accurately recorded.
3. Direct OECA and OPP to develop documented procedures to coordinate and prioritize laboratories for inspections.

In addition, we recommend that the EPA Administrator and the FDA Commissioner develop a formal written agreement, such as a memorandum of understanding, that outlines how the two agencies plan to regularly collaborate and share information on GLP inspections and

avoid duplication of inspections so that EPA can more efficiently use its limited resources.

Agency Comments and Our Evaluation

We provided EPA and HHS with a draft of this report for their review and comment; EPA provided written comments, which are reproduced in appendix IV, and HHS provided written comments, which are reproduced in appendix V.

In its written comments, EPA stated that it agreed with our findings, conclusions, and all four of our recommendations. In response to our first three recommendations, EPA agreed

- to assess the authority and need for a fee-based GLP inspection system;
- to ascertain the exact causes of inaccurate and incomplete data and ensure that the data are accurately recorded; and,
- that OECA and OPP should develop written procedures to coordinate and prioritize GLP inspections.

In response to our fourth recommendation, EPA agreed to develop written procedures that outline how EPA and FDA will collaborate and share information on GLP inspections. EPA stated that it did not agree that a formal memorandum of understanding between the two agencies was necessary. Our recommendation did not prescribe the type of agreement the agencies should undertake and offered a memorandum of understanding as one example. We agree that written procedures developed and agreed to by both EPA and FDA will address the recommendation.

In its technical comments, EPA noted that, while EPA and FDA have similar GLP regulations, and in a small number of cases both agencies may inspect the same laboratory, EPA does not believe the work is duplicative. However, we define duplication in this report as occurring when two or more agencies or programs engaged in the same activities or provided the same services to the same beneficiaries. We continue to believe that there is a possibility of duplication when both EPA and FDA are inspecting the same laboratories within a short period of time because both agencies provide a similar service to the same beneficiaries (ensuring laboratory compliance with GLP through facility inspections and study audits). Also in its technical comments, EPA acknowledged the problems we found with the databases used for targeting GLP inspections but stated that it does not believe these problems negatively affect

targeting for inspection because OECA is able to gather the necessary information manually. While we agree that, ultimately, EPA may target the appropriate laboratories for inspection through its manual research when the databases are inaccurate or incomplete, we believe that the agency's reliance on manual research is not as efficient or effective as using databases containing accurate information.

In its written comments, HHS also agreed with our fourth recommendation. HHS also reiterated the point that there are legitimate reasons why GLP inspections may be conducted by both EPA and FDA at a single laboratory within a relatively short period of time. For example, when FDA observes significant violations during for cause or surveillance inspections, follow-up inspections may be required to verify corrective actions. HHS also provided technical comments on our report, which we incorporated as appropriate.

As agreed with your office, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time we will send copies to the EPA Administrator and the FDA Commissioner, the appropriate congressional committees, and other interested parties. In addition, the report will be available at no charge on the GAO website at http://www.gao.gov.

If you or your staff members have any questions about this report, please contact me at (202) 512-3841 or neumannj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made key contributions to this report are listed in appendix VI.

Sincerely yours,

John Neumann
Acting Director, Natural Resources and Environment

Appendix I: Objectives, Scope and Methodology

Our objectives were to examine the extent to which (1) the Environmental Protection Agency (EPA) inspects for GLP compliance laboratories that test pesticides and the challenges, if any, EPA faces in doing so, (2) EPA uses the information obtained through Good Laboratory Practices (GLP) laboratory inspections in its pesticide decision-making process, and (3) EPA and the U.S Food and Drug Administration (FDA) collaborate on GLP inspections. To address these objectives, we reviewed relevant federal statutes and regulations,[1] EPA program and guidance documents,[2] federal internal control standards,[3] Office of Management and Budget circulars[4], and previous GAO and EPA Inspector General reports.[5] We also reviewed EPA's fiscal year 2011-2015 strategic plan; EPA's fiscal year 2011, 2012, and 2013 annual agency financial reports; and EPA Office of Enforcement and Compliance Assurance (OECA) fiscal year 2012 Budget Adjustment Plan. In addition, we interviewed EPA's Office of Pesticide Programs (OPP) and OECA officials and reviewed documentation they provided to obtain further information and clarification on EPA's pesticide registration process and how it relates to the GLP process, and we interviewed FDA officials and reviewed documentation they provided on FDA's GLP process. Furthermore, we reviewed recent literature related to GLP, including information and documents found on the websites of a variety of industry, international, environment, and academia organizations, and foreign government GLP inspection programs. We interviewed about 25 representatives from these organizations. We selected these individuals based on referrals from EPA, and industry and environmental stakeholders.

[1]These statutes and regulations include Federal Insecticide, Fungicide, and Rodenticide Act, Act of June 25, 1947, ch. 125, 61 Stat. 163 (codified as amended at 7 U.S.C. §§ 136-136y); Federal, Food, Drug, and Cosmetic Act, Act of June 25, 1938, ch. 675, 52 Stat. 1040 (codified as amended at 21 U.S.C. §§ 301-399f); 21 C.F.R. pt. 58; 40 C.F.R. pts. 152-180.

[2]These program and guidance documents included *EPA, Good Laboratory Practice Standards, Inspection Manual*, (Washington, D.C.: Sept. 1993); *Enforcement Response Policy for the Federal Insecticide, Fungicide, and Rodenticide Act, Good Laboratory Practices (GLP) Regulations, Sept. 1991*.

[3]GAO/AIMD-00-21.3.1.

[4]Office of Mgmt. & Budget, Circular No. A-25 Revised, Memorandum for Heads of Executive Departments and Establishments (July 8, 1993).

[5] GAO-06-15; EPA Office of Inspector General, *EPA Did Not Conduct Thorough Biennial User Fee Reviews*, 14-P-0129 (Washington, D.C.: Mar. 4, 2014).

To examine to what extent EPA inspects for GLP compliance laboratories that test pesticides; and the challenges, if any, EPA faces in doing so, we collected and analyzed documentation from OECA officials on its GLP inspection process and analyzed EPA laboratory and inspection data, the agency's use of this data , and the accuracy and completeness of the data. Specifically, we obtained information on how OECA determines which laboratories to inspect and how EPA's Office of Pesticide Programs Information Network (OPPIN), Laboratory Information and Study Audit (LISA), and Integrated Compliance Information System (ICIS) databases are used to assist inspectors in making these decisions, as well as the type of inspection data that are entered into these databases. Regarding inspection data, we requested OECA to provide us with several data elements contained in its LISA database for the years 2000 to 2013, including name and location of laboratory inspected, reason for inspection, number and type of inspections conducted, and number and name of studies associated with the laboratory inspected. We determined that inspection data were sufficiently reliable to present results on the number of inspections from fiscal year 2009 to fiscal year 2013 as a range. Since data, such as laboratories names and addresses, as well as information on studies contained in OECA's LISA database are transferred from OPP's OPPIN, we also requested OPP provide information from OPPIN on the number of studies associated with performing GLP laboratories from fiscal year 2008 to fiscal year 2012. We analyzed this study data for accuracy and completeness. However, we determined that data for "performing laboratories," identification numbers, and addresses were not sufficiently reliable to assess the number and location of laboratories that had submitted studies to EPA. As a result, we were not able to define the universe of laboratories subject to a GLP inspection. However, EPA did provide estimates of the number and percentage of eligible laboratories that were inspected each year, and we used that information in this report.

To determine the views on EPA's GLP Compliance Monitoring Program, we interviewed individuals representing 25 entities, including laboratories, pesticide manufacturers, international organizations, environmental and health organizations, national and trade associations and foreign government GLP programs, which we selected based on referrals from various stakeholders and EPA officials. Specifically, we spoke with representatives of nine laboratories and conducted site visits to four of these laboratories located in Maryland and Illinois. We also conducted a Web-based survey of performing laboratories. For our survey, we drew a randomly selected sample of 80 performing laboratories included in the OPPIN database that sent study data to OPP from fiscal year 2010 to

fiscal year 2012. Because OPPIN does not contain e-mail addresses, we searched for laboratories' e-mail addresses and found them for 53 of the 80 laboratories that we sampled. We sent the Web-based survey to these 53 laboratories. We obtained responses from 26 laboratories and other entities. However, 6 of these 26 respondents stated that they were not a laboratory and did not conduct GLP testing. Therefore, we received usable survey responses from 20 laboratories. Not all respondents to our survey, however, answered every question. Our survey asked if the laboratory had conducted GLP testing for EPA or FDA, experienced a GLP inspection by EPA, what was the effect of having an inspection, and what improvements they thought could be made to EPA's GLP Inspection Monitoring Program. The survey results are not generalizeable to all laboratories that are covered by the GLP program, but they were randomly selected, and the results can provide examples of such laboratories' experiences and challenges with GLP inspections. We were not able to select a representative sample because some data in the OPPIN database was not sufficiently reliable.

To assess the extent to which OPP uses the information obtained through GLP laboratory inspections in its pesticide decision-making process, we analyzed relevant documents and databases to determine the number of OECA's GLP inspections that produced results that were referred to OPP for reexamination, the time it took to conduct these reexaminations, and any impact the inspections had on OPP's pesticide registration decisions.

To determine the extent to which EPA and FDA collaborate on inspections, we analyzed EPA and FDA GLP laboratory inspection data and determined that the inspection data were sufficiently reliable for our purposes. We also analyzed the 20 laboratory survey responses to determine if they had conducted GLP tests or studies for submission to both EPA and FDA since 2008. We reviewed agency documents, such as a 1984 agreement entered into by EPA and FDA to cooperate on GLP inspections and FDA's Compliance Program Guidance Manual. We interviewed EPA and FDA officials, laboratory representatives and other stakeholders about the potential for the two agencies to collaborate.

We conducted this performance audit from November 2012 to May 2014 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Appendix II: Web-Based Survey to Laboratories

GAO Survey on EPA's Good Laboratory Practices Monitoring Program

United States Government Accountability Office

Background

As you may know, EPA relies on data submitted by pesticide registrants as the basis for the agency's regulatory decisions involving pesticide product registrations and tolerances. EPA and the Food and Drug Administration (FDA) have promulgated Good Laboratory Practices (GLP) regulations to assure the quality of data. EPA relies on data submitted by registrants as the basis for the agency's regulatory decisions involving pesticide product registrations and tolerances.

By "your facility," we are referring to the following lab: (Name of lab was pre-entered here)

Lab number: (Lab number was pre-entered here)

which we understand to be located at:
(Lab address was pre-entered here)

1. **Since January 2008, has your facility conducted testing or studies in accordance with GLP?**

- ○ Yes
- ○ No
- ○ Don't Know

If you selected "Don't know," please explain.

2. **Since January 2008, has EPA performed a GLP inspection of your facility?**

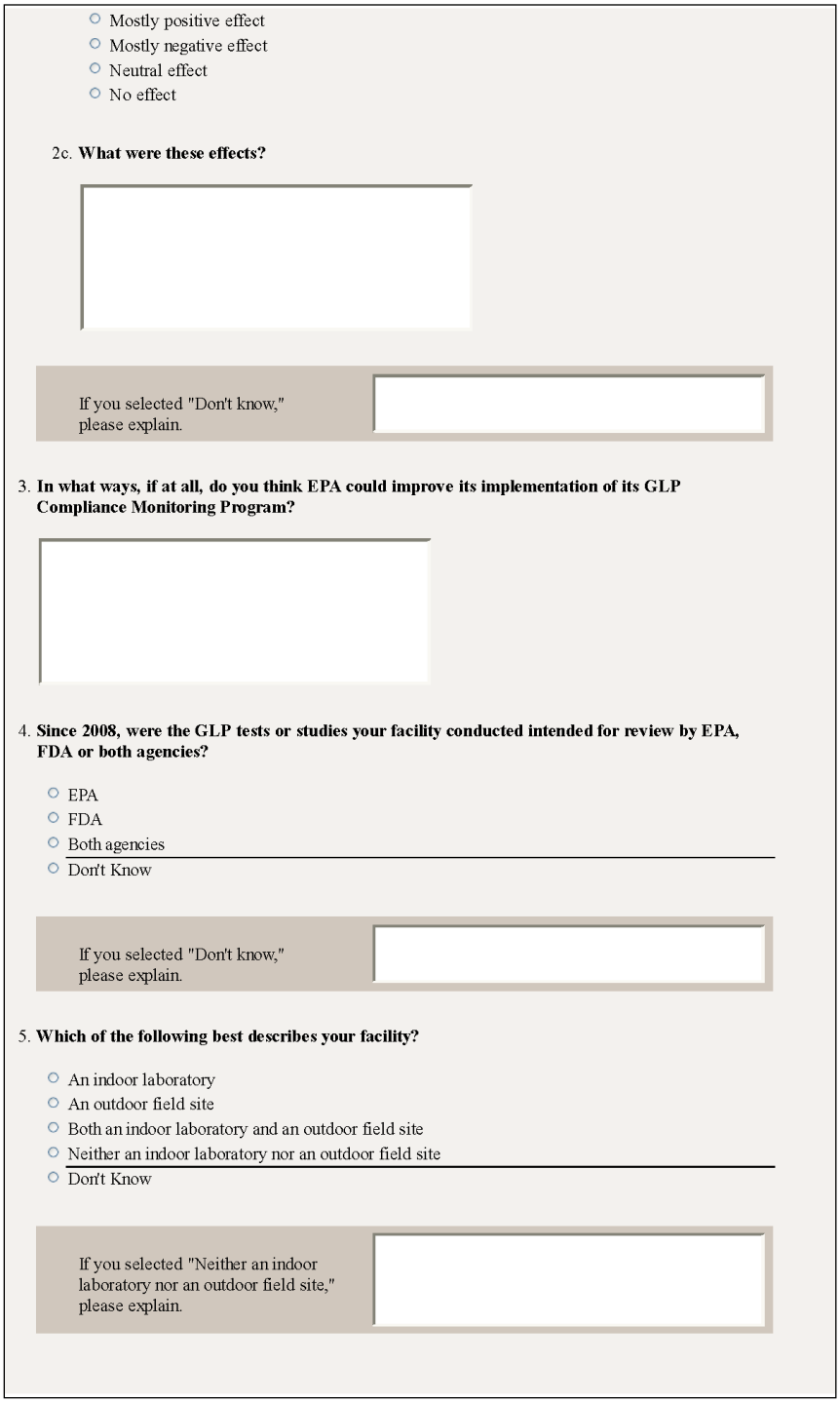
- ○ Yes
- ○ No
- ○ Don't Know

2a. **If YES, what effect, if any, did the GLP inspection have on your business?**

- ○ Mostly positive effect
- ○ Mostly negative effect
- ○ Neutral effect
- ○ No effect

What were these effects?

2b. **If NO, what effect, if any, did <u>not</u> having a GLP inspection have on your business?**



- Mostly positive effect
- Mostly negative effect
- Neutral effect
- No effect

2c. **What were these effects?**

If you selected "Don't know," please explain.

3. **In what ways, if at all, do you think EPA could improve its implementation of its GLP Compliance Monitoring Program?**

4. **Since 2008, were the GLP tests or studies your facility conducted intended for review by EPA, FDA or both agencies?**

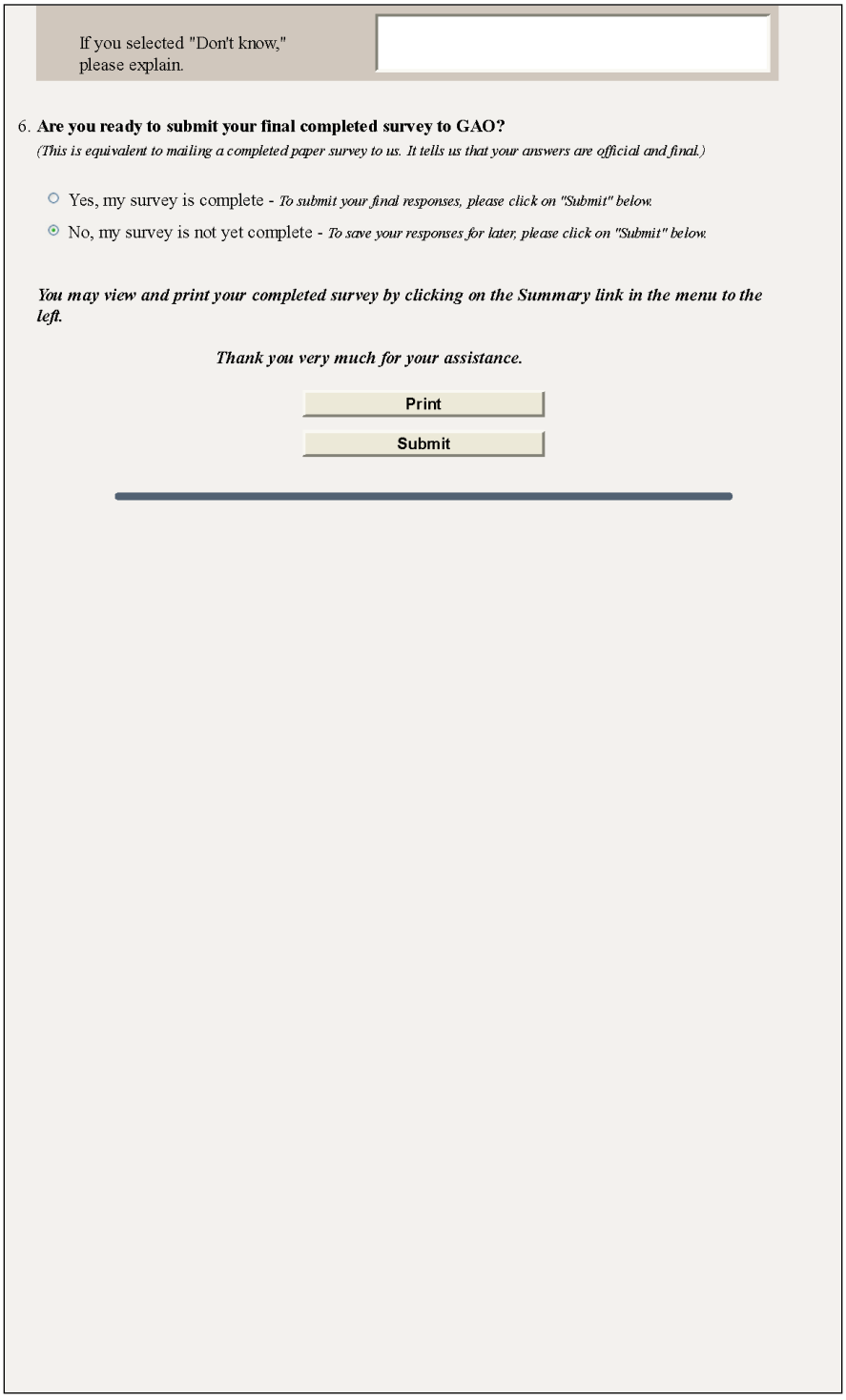
- EPA
- FDA
- Both agencies
- Don't Know

If you selected "Don't know," please explain.

5. **Which of the following best describes your facility?**

- An indoor laboratory
- An outdoor field site
- Both an indoor laboratory and an outdoor field site
- Neither an indoor laboratory nor an outdoor field site
- Don't Know

If you selected "Neither an indoor laboratory nor an outdoor field site," please explain.


If you selected "Don't know," please explain.
6. Are you ready to submit your final completed survey to GAO?
(This is equivalent to mailing a completed paper survey to us. It tells us that your answers are official and final.)
Yes, my survey is complete - To submit your final responses, please click on "Submit" below.
No, my survey is not yet complete - To save your responses for later, please click on "Submit" below.
You may view and print your completed survey by clicking on the Summary link in the menu to the left.
Thank you very much for your assistance.
Print
Submit

Appendix III: Laboratories Inspected for GLP Compliance by EPA and FDA, FY 2005-2012

Our analysis of Environmental Protection Agency (EPA) and U.S. Food and Drug Administration (FDA) Good Laboratory Practices (GLP) inspections data identified the following instances where laboratories were inspected by both agencies (see figure 3). We do not know the reason for every inspection. In some instances, EPA and FDA may have needed to conduct their own inspection.

Figure 3: Laboratories Inspected for GLP Compliance by EPA and FDA, FY 2005-2012

Laboratory location	Fiscal year 2005	Fiscal year 2006	Fiscal year 2007	Fiscal year 2008	Fiscal year 2009	Fiscal year 2010	Fiscal year 2011	Fiscal year 2012
1. Laboratory in Alabama		EPA Jan. 2006						
	FDA Sept. 2005		FDA Feb. 2007		FDA Aug. 2009			FDA Sept. 2012
2. Laboratory in Arkansas						EPA May 2010		
		FDA Aug. 2006			FDA Mar. 2009			
3. Laboratory in California			EPA Aug. 2007			EPA Feb. 2010		
	FDA June 2005		FDA Mar. 2007		FDA June 2009			
4. Laboratory in Colorado	EPA Apr. 2005							
			FDA Mar. 2007					
5. Laboratory in Colorado		EPA Feb. 2006			EPA Dec. 2008			
	FDA July 2005	FDA July 2006			FDA Sept. 2009			
6. Laboratory in Colorado								EPA Nov. 2011
								FDA June 2012
7. Laboratory in Georgia							EPA Sept. 2011	
								FDA June 2012

EPA performed inspection

FDA performed inspection

Figure continued on next page

Sources: GAO analysis of EPA and FDA data.

(Continued)

Laboratory location	Fiscal year 2005	Fiscal year 2006	Fiscal year 2007	Fiscal year 2008	Fiscal year 2009	Fiscal year 2010	Fiscal year 2011	Fiscal year 2012
8. Laboratory in Illinois	EPA Oct. 2004							EPA June 2012
		FDA Nov. 2005		FDA Mar. 2008, Sept. 2008			FDA Feb. 2011	
9. Laboratory in Illinois		EPA Nov. 2005		EPA Aug. 2008			EPA May 2011	
	FDA Jan. 2005		FDA Feb. 2007			FDA Sept. 2010		
10. Laboratory in Kansas	EPA Apr. 2005	EPA Sept. 2006		EPA Mar. 2008, Apr. 2008				
	FDA Apr. 2005	FDA Sept. 2006						
11. Laboratory in Kansas						EPA Sept. 2010		
							FDA June 2011	
12. Laboratory in Maryland	EPA July 2005			EPA June 2008				
								FDA Sept. 2012
13. Laboratory in Maryland			EPA Feb. 2007			EPA July 2010		EPA Sept. 2012
	FDA Sept. 2005		FDA inspected this lab in Sept. 2007 on behalf of EPA.	FDA Sept. 2008		FDA Aug. 2010	FDA Jan. 2011	
14. Laboratory in Massachusetts		EPA June 2006						
	FDA Mar. 2005			FDA Dec. 2007	FDA Apr. 2009		FDA Sept. 2011	

EPA performed inspection FDA performed inspection

Figure continued on next page

Sources: GAO analysis of EPA and FDA data.

(Continued)

Laboratory location	Fiscal year 2005	Fiscal year 2006	Fiscal year 2007	Fiscal year 2008	Fiscal year 2009	Fiscal year 2010	Fiscal year 2011	Fiscal year 2012
15. Laboratory in Massachusetts				EPA Aug. 2008				
	FDA Sept. 2005							
16. Laboratory in Michigan				EPA May 2008			EPA Dec. 2010	
	FDA Aug. 2005	FDA May 2006	FDA Apr. 2007	FDA Sept. 2008	FDA Nov. 2008	FDA June 2010		FDA Aug. 2012
17. Laboratory in Missouri		EPA June 2006			EPA May 2009			
		FDA June 2006						FDA July 2012
18. Laboratory in Missouri							EPA Aug. 2011	
		FDA Nov. 2005		FDA June 2008 Aug. 2008				
19. Laboratory in Montana					EPA Sept. 2009			
		FDA Jan. 2006						
20. Laboratory in New Jersey	EPA Nov. 2004		EPA Feb. 2007		EPA Jan. 2009			
		FDA Apr. 2006			FDA Sept. 2009		FDA July 2011	
21. Laboratory in New Jersey						EPA Dec. 2009		
	FDA Jan. 2005	FDA Aug. 2006			FDA Dec. 2008			

EPA performed inspection FDA performed inspection

Figure continued on next page

Sources: GAO analysis of EPA and FDA data.

(Continued)

Laboratory location	Fiscal year 2005	Fiscal year 2006	Fiscal year 2007	Fiscal year 2008	Fiscal year 2009	Fiscal year 2010	Fiscal year 2011	Fiscal year 2012
22. Laboratory in New Mexico			EPA Aug. 2007			EPA Mar. 2010		
	FDA Feb. 2005				FDA Aug. 2009			
23. Laboratory in New Mexico	EPA May 2005							
			FDA Dec. 2006		FDA Aug. 2009			
24. Laboratory in North Carolina		EPA Mar. 2006						
	FDA Nov. 2004		FDA Sept. 2007					FDA Aug. 2012
25. Laboratory in North Carolina				EPA Aug. 2008		EPA Sept. 2010		
	FDA Jan. 2005		FDA June 2007					
26. Laboratory in Ohio					EPA Apr. 2009			
	FDA Mar. 2005		FDA Aug. 2007			FDA Oct. 2009	FDA Jan. 2011	
27. Laboratory in Ohio		EPA Sept. 2006			EPA Apr. 2009			
		FDA Feb. 2006		FDA Sept. 2008	FDA Aug. 2009 Aug. 2009	FDA Jan. 2010		FDA Apr. 2012
28. Laboratory in Ohio			EPA Aug. 2007					
			FDA Mar. 2007		FDA Sept. 2009			

EPA performed inspection

FDA performed inspection

Figure continued on next page

Sources: GAO analysis of EPA and FDA data.

(Continued)

Laboratory location	Fiscal year 2005	Fiscal year 2006	Fiscal year 2007	Fiscal year 2008	Fiscal year 2009	Fiscal year 2010	Fiscal year 2011	Fiscal year 2012
29. Laboratory in Ohio					EPA May 2009			EPA Dec. 2011
			FDA Oct. 2006		FDA July 2009			
30. Laboratory in Pennsylvania			EPA June 2007		EPA Feb. 2009			EPA June 2012
	FDA Dec. 2004			FDA Oct. 2007		FDA May 2010		
31. Laboratory in Pennsylvania	EPA Aug. 2005			EPA Apr. 2008				
			FDA Oct. 2006		FDA May 2009	FDA June 2010		
32. Laboratory in Pennsylvania			EPA Nov. 2006					
		FDA Feb. 2006			FDA June 2009	FDA Aug. 2010		FDA July 2012
33. Laboratory in Texas		EPA Dec. 2005				EPA Apr. 2010		EPA Sept. 2012
	FDA Sept. 2005		FDA Jan. 2007			FDA Apr. 2010		
34. Laboratory in Utah								EPA Jan. 2012
	FDA Aug. 2005							FDA June 2012
35. Laboratory in Virginia		EPA Aug. 2006			EPA Oct. 2008			
	FDA May 2005		FDA July 2007	FDA May 2008	FDA July 2009 FDA July 2009		FDA Aug. 2011	

EPA performed inspection

FDA performed inspection

Figure continued on next page

Sources: GAO analysis of EPA and FDA data.

(Continued)

Laboratory location	Fiscal year 2005	Fiscal year 2006	Fiscal year 2007	Fiscal year 2008	Fiscal year 2009	Fiscal year 2010	Fiscal year 2011	Fiscal year 2012
36. Laboratory in Wisconsin	EPA Aug. 2005							EPA Sept. 2012
	FDA Jan. 2005		FDA May 2007	FDA June 2008		FDA Aug. 2010		
37. Laboratory in Wisconsin			EPA June 2007				EPA Aug. 2011	
		FDA July 2006		FDA Sept. 2008			FDA May 2011	

EPA performed inspection FDA performed inspection

Sources: GAO analysis of EPA and FDA data.

Appendix IV: Comments from the Environmental Protection Agency

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAY 05 2014

OFFICE OF
ENFORCEMENT AND
COMPLIANCE ASSURANCE

Anne Johnson, Assistant Director
Natural Resources and Environment
U.S. Government Accountability Office
Washington, D.C. 20548

Re: Comments on draft GAO Report "Pesticide Safety – Improvements Needed in EPA's Good Laboratory Practice Inspection Program," GAO 14-289

Dear Ms. Johnson,

Thank you for the opportunity to review and comment on GAO's draft Report *Pesticide Safety: Improvements Needed in EPA's Good Laboratory Practices Inspection Program* (GAO-014-289). The purpose of this letter is to provide EPA's response to your recommendations. This response reflects consolidated comments received from the Office of the Chief Financial Officer, the Office of Pesticide Programs, the Office of General Counsel as well as the Office of Enforcement and Compliance Assurance.

The EPA appreciates GAO's feedback on opportunities to improve the Good Laboratory Practice (GLP) inspection program. We generally agree with the GAO's findings, conclusions, and recommendations and are committed to acting on those recommendations as described below. A number of detailed technical and editorial comments on various aspects of the draft report are also noted in the enclosure.

GAO Recommendation #1
Assess the need for a fee-based inspection system, and if such a system is warranted, establish a user fee system. Seeking additional legislative authority, if necessary, to make the laboratory inspection program self-sustaining.

EPA Response #1
EPA agrees to assess the authority and the need for a fee-based GLP inspection system. The Office of Enforcement and Compliance Assurance (OECA), the Office of Pesticide Programs (OPP), Office of General Counsel (OGC) and the Office of the Chief Financial Officer (OCFO) will assess the authority and the need and feasibility of a fee-based inspection system, and, if warranted, begin taking the steps necessary to establish such a user fee system.

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GAO Recommendation #2

Direct OECA and OPP to ascertain the exact causes of inaccurate and incomplete data in the data bases and take action to ensure that the data, such as identification of performing laboratories and inspection history, are accurately recorded.

EPA Response #2

EPA agrees to ascertain the exact causes of inaccurate and incomplete data and to take action to ensure that the data are accurately recorded.

GAO Recommendation #3

Direct OECA and OPP to develop documented procedures to coordinate and prioritize laboratories for inspections.

EPA Response #3

EPA agrees that OECA and OPP should develop written procedures in the coordination and prioritization of GLP inspections.

GAO Recommendation #4

The EPA Administrator and the FDA Commissioner should develop a formal written agreement, such as a memorandum of understanding that outlines how the two agencies plan to regularly collaborate and share information on GLP inspections and avoid duplication of inspections so that EPA can more efficiently use the limited resources.

EPA Response #4

EPA agrees that we should develop written procedures that outline how EPA and FDA will collaborate and share information on GLP inspections. EPA does not agree that a formal Memorandum of Understanding at the Administrator/FDA Commissioner level is necessary. EPA will work with FDA to develop written standard operating procedures for collaboration on the GLP program.

Again, we appreciate the opportunity to review the draft report. Please direct any questions regarding our response to Gwendolyn Spriggs, at (202) 564-2439.

Sincerely,

Cynthia Giles
Assistant Administrator

Enclosure

2

Appendix V: Comments from the Department of Health and Human Services

DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

APR 30 2014

John Neumann, Acting Director
Natural Resources Environment
U.S. Government Accountability Office
441 G Street NW
Washington, DC 20548

Dear Mr. Neumann:

Attached are comments on the U.S. Government Accountability Office's (GAO) report entitled, "Pesticide Safety: Improvements Needed in EPA's Good Laboratory Practices Inspection Program" (GAO-14-289).

The Department appreciates the opportunity to review this report prior to publication.

Sincerely,

Jim R. Esquea
Assistant Secretary for Legislation

Attachment

THE DEPARTMENT OF HEALTH AND HUMAN SERVICES' (HHS) GENERAL COMMENTS TO GAO'S DRAFT REPORT "PESTICIDE SAFETY: IMPROVEMENTS NEEDED IN EPA'S GOOD LABORATORY PRACTICES INSPECTION" (GAO-14-289)

The Department appreciates the opportunity to review and comment on this draft report.

GAO Recommendation:

We recommend that the EPA Administrator and the FDA Commissioner develop a formal written agreement, such as a memorandum of understanding, that outlines how the two agencies plan to regularly collaborate and share information on GLP inspections and avoid duplication of inspections so that EPA can more efficiently use its limited resources.

HHS Response:

HHS agrees with GAO's recommendation that EPA and FDA develop an agreement that could help the two agencies better collaborate and share information on GLP inspections and minimize unnecessary GLP inspection duplication. HHS recognizes the value of this information-sharing, is examining how the two agencies can better communicate on GLP inspections, and looks forward to collaborating with EPA in the future.

While HHS concurs with GAO's recommendation and recognizes that GAO found that EPA and FDA may be duplicating work in some good laboratory practices (GLP) inspections, it is important to note that there are also legitimate reasons why GLP inspections may be conducted by both agencies at a single laboratory within a relatively short period of time. FDA and EPA are at times engaged in very different activities for unrelated beneficiaries. Although the work to support these services may be performed at the same facility, there may be little or no overlap of resources. FDA inspections of GLP laboratories may also be either surveillance-based or for cause. For-cause inspections focus on specific product applications or complaints received by the agency and may be limited to a single study or to other limiting factors. When a for-cause GLP inspection has been conducted for a specific product application and new applications are subsequently received, it may be necessary to conduct another inspection within a relatively short timeframe. In addition, when significant violations are observed during surveillance-based or for-cause inspections, follow-up inspections may be required to verify corrective actions. Finally, GLP inspections are not solely systems type inspections. A major aspect of GLP inspections is data validation, which may necessitate multiple inspections of laboratories within a relatively short period of time.

Appendix VI: GAO Contact and Staff Acknowledgments

GAO Contact

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Staff Acknowledgments

In addition to the individual named above, Anne K. Johnson, Assistant Director; Cheryl Arvidson; Mark Braza; Greg Carroll; Cynthia Grant; Angela Miles; and Patricia Moye made key contributions to this report. Richard Johnson, Stuart Kaufmann, Anna Maria Ortiz, and Dan Royer also made important contributions.