

**Department of Health and Human Services**

**OFFICE OF  
INSPECTOR GENERAL**

**FDA WARNING LETTERS  
Trends and Perspectives**



**JUNE GIBBS BROWN  
Inspector General**

**FEBRUARY 1999  
OEI-09-97-00380**

## **OFFICE OF INSPECTOR GENERAL**

The mission of the Office of Inspector General (OIG), as mandated by Public Law 95-452, is to protect the integrity of the Department of Health and Human Services programs as well as the health and welfare of beneficiaries served by them. This statutory mission is carried out through a nationwide program of audits, investigations, inspections, sanctions, and fraud alerts. The Inspector General informs the Secretary of program and management problems and recommends legislative, regulatory, and operational approaches to correct them.

### **Office of Evaluation and Inspections**

The Office of Evaluation and Inspections (OEI) is one of several components of the Office of Inspector General. It conducts short-term management and program evaluations (called inspections) that focus on issues of concern to the Department, the Congress, and the public. The inspection reports provide findings and recommendations on the efficiency, vulnerability, and effectiveness of departmental programs.

OEI's San Francisco Regional Office prepared this report under the direction of Kaye D. Kidwell, Regional Inspector General, and Paul A. Gottlober, Deputy Regional Inspector General. Principal OEI staff included:

#### **REGION**

Brad Rollin, *Project Leader*  
Robert Gibbons, *Program Analyst*  
Scott Hutchison, *Program Analyst*  
Don Loeb, *Program Analyst*  
Steven Zerebecki, *Program Analyst*

#### **HEADQUARTERS**

Elise Stein, *Program Specialist*  
Barbara Tedesco, *Mathematical Statistician*

To obtain copies of this report, please call the San Francisco Regional Office at 415-437-7900.  
Reports are also available on the World Wide Web at our home page address:

<http://www.dhhs.gov/progorg/oei>

# EXECUTIVE SUMMARY

---

## PURPOSE

To determine (1) why the number of Food and Drug Administration (FDA) warning letters has decreased in recent years, (2) what accounts for variations in district office warning letters, and (3) how firms view the warning letter process.

---

## BACKGROUND

The FDA is the Federal agency charged with enforcing the Federal Food, Drug, and Cosmetic Act and related laws. At the headquarters level, FDA primarily is comprised of five centers and the Office of Regulatory Affairs. The Office of Regulatory Affairs coordinates compliance activities and oversees FDA's 5 regional offices, 20 district offices, and 130 resident posts.

The FDA's district offices and resident posts conduct almost all inspections of the firms that FDA regulates. When investigators find objectionable conditions, they are required to provide the firm with their findings using form *FDA-483*. If violations uncovered during an inspection meet a threshold of "regulatory significance," FDA also may issue a warning letter. Both FDA centers and district offices issue warning letters, depending on the type of firm and violation. Some warning letters issued by the district office require headquarters review and approval. The warning letter generally represents FDA's first official notification that it has found one or more products, practices, processes, or other activities that are in violation of the Food, Drug, and Cosmetic Act. The warning letter affords firms the opportunity to voluntarily correct violations prior to the initiation of formal enforcement action.

In fiscal year 1997, FDA issued 1,175 warning letters. This reversed a trend during which the number of warning letters decreased 36.2 percent from 1994 (1,626) to 1996 (1,037). District offices issue approximately 80 percent of all warning letters. The number of warning letters issued varies greatly, and concerns have been raised about this variation as well as the decrease in warning letters in general.

We interviewed staff from FDA headquarters, all district offices, and 24 firms that received warning letters during fiscal year 1996. We also analyzed warning letter and district office inspection trends and data as well as FDA's Regulatory Procedures Manual.

---

## **FINDINGS**

### **Changes in FDA policies and practices and better industry compliance have contributed to decreases in warning letters**

The FDA has fostered a more cooperative approach to industry compliance, permitting districts to find alternatives to warning letters. Other factors which contribute to the decrease include the reorganization of many districts and changes in the scope and type of inspections conducted by FDA. In addition, one-third of district offices believe that firms are themselves doing a better job of being in compliance.

### **Despite the existence of clear warning letter guidance, differences in district office attitudes, experience, and the types of firms in the district affect warning letter volume**

From 1994 to 1997, some district offices issued almost five times as many warning letters as others. While the staff size of the district offices has an obvious effect on the number of inspections and warning letters, other factors also affect the number of warning letters each district issues.

### **Firms would like to better understand the warning letter process and suggested some minor changes**

The FDA's policies and procedures governing warning letters are unclear to firms. When possible, firms would appreciate advance notice that a warning letter will be issued.

### **With some exceptions, firms were satisfied with FDA's customer service during the warning letter process**

Firms generally had positive comments about FDA investigators and district offices. Few firms contacted FDA headquarters, and customer service reviews were mixed.

---

## **RECOMMENDATION**

### **The FDA should (1) continue to improve relations and communication with industry and (2) consider issuing guidance that would authorize district offices to use *FDA-483s* and meetings to achieve compliance in lieu of warning letters**

Further development of the FDA/industry relationship is important in preserving fairness. A firm should not suffer adverse consequences solely because it is located in a different district than another firm. At the same time, we recognize the need to allow district offices considerable discretion.

---

## AGENCY COMMENTS

We received comments on the draft report from FDA in which the agency concurred with our recommendation. Where appropriate, we have made revisions in the report in response to these comments. We also have responded to several of FDA's comments in the appendix.

*This report is one of two reports concerning FDA warning letters. A companion report, "FDA Warning Letters: Timeliness and Effectiveness" (OEI-09-97-00381), determined how FDA uses warning letters and the extent to which they result in timely compliance with Federal laws and regulations.*

# TABLE OF CONTENTS

	PAGE
<b>EXECUTIVE SUMMARY</b> .....	1
<b>INTRODUCTION</b> .....	5
<b>FINDINGS</b> .....	11
Reasons for decrease in warning letters .....	11
Differences among district offices .....	14
Firms' understanding of warning letters .....	15
Firms' views of FDA's customer service .....	17
<b>RECOMMENDATION</b> .....	18
<b>APPENDICES</b>	
<b>A:</b> Agency comments .....	19
<b>B:</b> OIG response to agency comments .....	24

# INTRODUCTION

---

## PURPOSE

To determine (1) why the number of Food and Drug Administration (FDA) warning letters has decreased in recent years, (2) what accounts for variations in district office warning letters, and (3) how firms view the warning letter process.

---

## BACKGROUND

### The Food and Drug Administration

The Food and Drug Administration (FDA) within the Department of Health and Human Services is the Federal agency charged with enforcing the Federal Food, Drug, and Cosmetic Act and several related laws. At the headquarters level, FDA primarily is comprised of five centers and the Office of Regulatory Affairs.<sup>1</sup> The five centers are:

- ▶ Biologics Evaluation and Research
- ▶ Drug Evaluation and Research
- ▶ Devices and Radiological Health
- ▶ Food Safety and Applied Nutrition
- ▶ Veterinary Medicine

Each center promulgates regulations, oversees the review and approval for the marketing of new products, develops policy and compliance standards for regulated industries, and undertakes other initiatives to ensure the safety and effectiveness of products under FDA's purview. The Office of Regulatory Affairs coordinates FDA's compliance activities and oversees the activities of FDA's 5 regional offices, 20 district offices, and approximately 130 resident posts.

### On-site Inspections

Staff from FDA's district offices and resident posts conduct almost all inspections of the firms that FDA regulates.<sup>2</sup> Section 702(a) of the Food, Drug, and Cosmetic Act authorizes FDA to conduct inspections to enforce the provisions of that statute as well as other applicable laws. Inspections focus on manufacturing, laboratory, production, and/or

---

<sup>1</sup> The FDA also operates the National Center for Toxicological Research in Jefferson, Arkansas and the Engineering and Analytical Center in Winchester, Massachusetts.

<sup>2</sup> The FDA contracts with State agencies to conduct some inspections, and headquarters staff sometimes participate in inspections of foreign or domestic firms.

storage processes but may include examining a firm's administrative practices and controls as well as collecting samples, labels, and promotional materials.

The FDA requires investigators to follow a standard protocol when conducting an inspection. Upon arriving at a facility, investigators issue a Notice of Inspection (Form *FDA-482*) to the top management official. The scope of the inspection generally is determined by the type of facility being inspected, the firm's history, general knowledge about the industry and its problems, and conditions found as the inspection progresses.

Investigators are authorized to collect samples or other physical evidence while conducting inspections. Examples include food, drugs, devices, or cosmetics. Samples also may include evidence of violative conditions, such as rodent droppings or any other evidence of noncompliance with Federal laws and regulations.

When investigators find objectionable conditions, they are required to provide the top management official with their findings on an Inspectional Observations form (Form *FDA-483*). The *FDA-483* should include any observed problems with the facility, equipment, processes, controls, products, employee practices, or records. Some examples of reportable observations include:

- ▶ filthy, putrid, or decomposed substances, unsanitary conditions, or evidence of contamination;
- ▶ careless handling of rodenticides or pesticides;
- ▶ results of field tests that reveal adulteration;
- ▶ observations of faulty manufacturing, processing, packaging, or holding of food, drug, or device products as related to Good Manufacturing Practice regulations;<sup>3</sup> and
- ▶ observations indicating noncompliance with medical device reporting requirements.

Some observations require that action be taken by the centers only. The FDA's Investigations Operations Manual instructs investigators to not report observations related to most labeling issues, promotional materials, the classification of a cosmetic or device as a drug, or the classification of a drug as a new drug on the *FDA-483*. These issues are referred to the centers for compliance action.

---

<sup>3</sup> The Good Manufacturing Practice regulations specify FDA's expectations as to how firms should operate in manufacturing products regulated by the FDA. The regulation includes provisions related to personnel, quality control, facility design and maintenance, equipment, internal controls, production and process controls, packaging and labeling, storage and distribution, laboratory process, and reports and record keeping.



## Warning Letters

**What is a warning letter?** The warning letter generally represents FDA's first official notification to a firm or individual that FDA has found that one or more products, practices, processes, or other activities are in violation of the Food, Drug, and Cosmetic Act. The warning letter affords firms the opportunity to voluntarily take corrective action prior to the initiation of formal enforcement action.

The FDA is not required by law to warn firms or individuals that they are in violation of the law prior to initiating a formal regulatory action.<sup>4</sup> The FDA believes, however, that:

...documentation of notice of violative conduct strengthens the agency's position in regulatory actions by establishing that responsible individuals continued violative conduct despite warnings by the agency.<sup>5</sup>

**Who issues warning letters?** The FDA centers and district offices issue warning letters. In general, district offices issue warning letters to domestic firms based on inspections. Some centers issue warning letters for advertising and promotional violations or to foreign firms marketing products in the United States. Others, such as the Center for Veterinary Medicine, issue few or no warning letters at all.

At the district office level, although some warning letters can be issued at the discretion of the district director without center or other headquarters review or concurrence, FDA's Regulatory Procedures Manual lists numerous specific program area violations that require review by the appropriate center. Centers are required to review and approve the issuance of warning letters within 15 days of receipt. Despite this layer of review, the decision to initiate the warning letter process rests solely with the office that conducted the inspection.

The following table illustrates how many warning letters the centers and district offices issued from fiscal years 1994 to 1997. The district office tally includes all warning letters sent under district directors' signatures, including those that underwent center review:

---

<sup>4</sup> One exception to this statement is a requirement that when acting under the authority of the Radiation Control for Health and Safety Act, FDA is required by law to provide a written notification to manufacturers when the agency discovers products that fail to comply with a performance standard or that contain a radiation safety defect.

<sup>5</sup> FDA Regulatory Procedures Manual, Chapter 10, Subchapter — Prior Notice.

*District offices annually issue approximately  
80 percent of all warning letters*

Year	Total	District office-issued	Center-issued
1994	1,626	1,282 (78.8%)	344 (21.2%)
1995	1,501	1,175 (78.3%)	326 (21.7%)
1996	1,037	841 (81.1%)	196 (18.9%)
1997	1,175	1,003 (85.4%)	172 (14.6%)

In fiscal year 1997, FDA issued 1,175 warning letters. This reversed a trend during which the number of warning letters decreased 36.2 percent from 1994 (1,626) to 1996 (1,037). More warning letters are issued for devices and radiological products than for any of FDA's other product areas. In fact, from 1994 to 1997, the Center for Devices and Radiological Health issued more warning letters than any district office. The district offices issuing the most letters in 1997 were San Francisco (96), Florida (88), and Dallas (74). The district offices issuing the fewest warning letters in 1997 were Boston (16), Detroit (19), and Nashville (20).

**What does a warning letter say?** The warning letter instructs the firm to correct the issues noted and to respond in writing within 15 days of receipt of the letter. District offices coordinate with the appropriate center to determine whether a firm's response to a warning letter is adequate. If the district or appropriate center deems the firm's response adequate, it will notify other appropriate agency units. This may require a reinspection of the firm.

The FDA issues warning letters for regulatory violations, not for violations of nonregulatory guidance documents. It states that "the threshold for determination of what constitutes 'regulatory significance' is that failure to adequately and promptly achieve correction to the warning letter may be expected to result in enforcement action."

## **Subsequent Compliance Actions**

The FDA has both administrative and regulatory actions available to it to ensure compliance with the Food, Drug, and Cosmetic Act. Administrative actions include detentions, civil penalties, and requesting voluntary recalls. Regulatory actions include license revocations, license suspensions, citations, prosecutions, judicial civil penalties, injunctions, and seizures.<sup>6</sup>

---

<sup>6</sup> FDA has recall authority only for infant formula, human tissue, and certain medical devices. Recalls of other products are voluntary. License suspensions and revocations are regulatory actions taken for biologicals.

## Related Work

The General Accounting Office (GAO) issued two studies in 1997 that questioned the consistency of FDA's inspection and compliance activities:

- ▶ In "Blood Supply: FDA Oversight and Remaining Issues of Safety" (GAO/PEMD-97-1, February 1997), GAO found that FDA issued warning letters to blood suppliers inconsistently. The GAO also reported that some inspections yielded multiple *FDA-483* observations but did not result in a warning letter, while other inspections with relatively few or minor observations resulted in the issuance of a warning letter.
- ▶ In "FDA Mammography Inspections: While Some Problems Need Attention, Facility Compliance Is Growing" (GAO/HEHS-97-25, January 1997), GAO questioned the consistency of inspectors who used different criteria in citing mammography facilities. The GAO stated that FDA's monitoring and enforcement process did not ensure timely correction of deficiencies in these facilities. The GAO also noted that FDA district offices needed better information systems to manage inspections.

Based on GAO's concerns and the significant decrease in the number of warning letters issued from 1994 to 1996, we determined that this inspection was warranted.

---

## METHODOLOGY

### Interviews with FDA and Regulated Industry

We conducted either in-person or telephone interviews with each district office. We asked district office staff about their organizational structure, their experiences with warning letters, the factors that contributed to their increase or decrease in warning letters, and the responsiveness of the centers to their warning letter recommendations. In addition, we analyzed district office inspection and warning letter trend data, reviewed FDA's Regulatory Procedures Manual, and interviewed staff from FDA headquarters.

We selected a simple random sample of 40 firms that received warning letters during fiscal year 1996 and completed telephone interviews with 24 of them. The remaining firms did not return phone calls or had gone out of business. We asked firms about the violations that resulted in the warning letter and their experiences with FDA.

*This report is one of two reports on the FDA warning letter process. A companion report, “FDA Warning Letters: Timeliness and Effectiveness” (OEI-09-97-00381), describes the results of our on-site fieldwork at six FDA district offices where we conducted reviews of warning letter files and FDA follow up. In that report, we found that warning letters are an effective compliance tool. However, their effectiveness depends on committed follow-up attention by FDA. We also found that their timeliness could be improved and numerous discrepancies exist between headquarters and district office data.*

# FINDINGS

## Changes in FDA policies and practices and better industry compliance have contributed to decreases in warning letters

### The FDA has fostered a more cooperative relationship with industry

In recent years, FDA has implemented measures to ensure compliance with Federal laws and regulations by offering education and communication in lieu of warning letters. Many district offices now offer meetings to firms who receive *FDA-483s*. In addition, FDA recently revised its warning letter guidance to include the following instructions:

*In sending the firm a warning letter, the warning letter should appropriately acknowledge corrections promised during the inspection, or annotated on the FDA-483, or provided to the district in a written response.*

A meeting and/or *FDA-483* response may be adequate to avoid a warning letter. In some district offices, a meeting and a firm's promised corrections can result in a warning letter not being issued. In other district offices, the warning letter is issued regardless of the outcome of the meeting.

District office and headquarters staff agree that all tools should be used to achieve compliance. Because of this viewpoint, FDA looks at its options with flexibility. Some district office staff acknowledge that, as they become more used to using the warning letter, they increasingly look at whether headquarters is prepared to take additional action based on a firm's subsequent noncompliance. Because of the resources required to implement a civil or criminal proceeding, the answer is increasingly "no." As a result, some district offices believe that working cooperatively with the firms is the most effective and timely solution.

The FDA has implemented some recent policy changes to increase firm cooperation. These changes have contributed to the decrease in warning letters. Numerous changes in the Center for Devices and Radiological Health, for instance, have brought the industry and FDA closer in addressing compliance issues. For example, FDA now notifies medical device firms prior to arriving for inspections. This allows the firm to prepare the documentation that the investigator will request during the inspection. The FDA is currently considering extending this practice to other product areas and continues to develop new policies concerning medical device warning letters through its medical device Warning Letter Pilot.

## District office reorganizations may contribute to the decrease

Although several district officials believe that declining resources have contributed to the decrease in warning letters, FDA inspection data indicate that the number of inspections completed annually remained constant from FY 1994 to FY 1997. Some staff believe that district offices that moved from a “traditional” structure, with separate compliance and inspection branches, to a combined branch structure suffered a temporary or lasting loss of productivity. Slightly fewer than half of the district offices have combined their compliance and investigations branches.

According to staff, the attrition of experienced staff, staff difficulty understanding new roles, time required to train staff for their new roles, and the failure of self-directed teams to function adequately resulted in a loss of productivity. We analyzed inspection and warning letter trends for district offices that had reorganized as well as those that had retained a traditional structure. As the following table illustrates, district offices that had reorganized in the past several years saw their inspection and warning letter numbers decrease at higher rates than those that retained a traditional structure:

*“Reorganized” district offices have seen inspection and warning letter numbers decline faster than “traditional” district offices*

Structure	Inspections, 1994-1997	Warning Letters, 1994-1997
Reorganized	-6.9 percent	-32.0 percent
Traditional	-0.6 percent	-15.8 percent

Other factors may account for these differences. Offices that have reorganized may have implemented other changes that resulted in fewer warning letters. For example, the Kansas City district office has implemented a major educational effort that changes the traditional role of the compliance officer to an educator. In addition, other district offices that have reorganized appear to be focusing a great deal of attention on industry education and cooperation.

## District offices conduct different types of inspections than in prior years

According to district office staff, changes in inspection priorities and methods have contributed to the overall decrease in warning letters. Eight district offices and staff from FDA centers noted that the role of the district office has changed in recent years. In particular, the scope and type of inspections have changed:

- ▶ *More inspections are headquarters-directed.* District offices conduct fewer routine inspections based on their workplans. Instead, the centers frequently undertake special initiatives that require that the district offices drop everything

else in order to inspect all industry-specific firms in their jurisdictions. Recent examples include blood suppliers and mammography providers.

- ▶ *The FDA now conducts more premarket approval inspections, and they do not result in warning letters.* The FDA has attempted to streamline its product approval process to speed up the introduction of new products into the marketplace. This has included conducting an inspection prior to FDA granting approval of a new product.
- ▶ *Inspections have become more technical and complicated.* Because technology has increased the sophistication of new products, the amount of time, work, and expertise required to complete an inspection has increased dramatically.
- ▶ *Inspections have changed in scope.* As the base of scientific knowledge increases, FDA has focused on different issues when conducting inspections. For example, district offices are focusing on microbiological issues rather than filth when conducting food inspections. Whereas filth inspections could result in immediate warning letter issuance, investigators now collect samples that FDA labs analyze.
- ▶ *Some district offices focus inspection resources on previously identified violative, risky firms.* Violations uncovered during inspections of these firms typically would warrant a more serious compliance action than a warning letter.

### **One-third of district offices believe that firms are doing a better job of being in compliance**

Firms dislike warning letters, which can be used by competitors to disparage their reputations. This is especially true in the pharmaceutical industry, where a warning letter may cost a firm millions of dollars in HMO contracts. As a result, district offices believe that the threat of a warning letter is strong motivation for firms to be in compliance.

Several districts suggested that the age of a firm or of a regulation affects industry compliance. Newer firms with less experience may be unaware that certain practices violate FDA regulations. As these firms become more familiar with the rules governing their business, they are less likely to unknowingly commit warning letter infractions. Similarly, when industry becomes more accustomed to a regulation, violations are less likely to occur.

---

## Despite the existence of clear warning letter guidance, differences in district office attitudes, experience, and the types of firms in the district affect warning letter volume

The FDA's warning letter data illustrate the wide variation in the number of warning letters issued by different district offices:

*From 1994 to 1997, some district offices issued almost five times as many warning letters as others*

Most warning letters, 1994-97		Fewest warning letters, 1994-97	
San Francisco	384	San Juan	82
Florida	320	Buffalo	96
New York	303	Detroit	104

While the staff size of the district offices has an obvious effect on the number of inspections and warning letters, this is not the only factor affecting the extent to which warning letters are used. District offices vary in their philosophy and use of warning letters. Some district offices have adopted a collaborative problem-solving approach with industry. These districts have been more likely to use the *FDA-483* to achieve compliance, take a firm's *FDA-483* response into consideration, or call the firm in for a meeting in lieu of issuing a warning letter. Other district offices, however, believe it is important to put a firm's noncompliance on record by promptly issuing a warning letter, regardless of a firm's *FDA-483* response or desire for a meeting.

While district offices believe that the compliance programs clearly delineate when violations meet warning letter thresholds, they also noted the extent to which the experience of investigators, supervisory investigators, and compliance officers figures into the determination. This occurs because these staff are well-acquainted with the compliance programs, have inspected similar firms multiple times, and are more comfortable making a close judgment call.

The types of firms under a district's jurisdiction play a major role in the number of warning letters issued by a district office:

- ▶ *Districts with large, highly technical industries:* Inspections take longer to complete and frequently are complicated because of the advanced technology being used by these firms. In addition, these firms frequently have regulatory affairs staff whose sole job is to ensure compliance with FDA. As a result, a long, resource-intensive inspection may uncover no significant violations.



- ▶ *Districts saturated with smaller, less FDA-savvy firms:* These firms often are not used to dealing with a regulatory agency. They may be service industry firms (e.g., tanning salons) or firms that focus more on the distribution rather than the production of goods (e.g., importers, warehousemen). These firms frequently are not well-acquainted with FDA regulations and do not have employees whose primary responsibility is to ensure compliance with FDA. As a result, a short inspection is often likely to expose violations. In addition, FDA routinely issues warning letters to importers that fail to hold a shipment for FDA examination. This tends to generate many warning letters in large import districts.
- ▶ *Center-driven industry-specific inspection efforts:* Centers sometimes mandate that district offices conduct industrywide inspections, such as recent efforts focused on mammography establishments, blood banks, and seafood firms. These can have periodic effects on warning letter trends. A district with heavy concentrations of those industries may experience a temporary increase or decrease in warning letters. For example, when FDA initiated a nationwide effort to inspect mammography establishments, those districts with a large number of these firms experienced a surge in warning letters. On the other hand, FDA's recent efforts to implement Hazard Analysis Critical Control Point regulations in the seafood industry have focused on the education of firms. The Center for Food Safety and Applied Nutrition has instructed district offices not to issue warning letters during implementation of the regulations. As a result, districts with a high concentration of seafood firms are generating few warning letters as they focus their inspection resources on these firms.

---

## **Firms would like to better understand the warning letter process and suggested some minor changes**

### **FDA policies and procedures governing warning letters are unclear to firms**

The firms that received warning letters in 1996 are uncertain about what criteria FDA uses to determine if a warning letter is necessary. These firms believe that the step from the *FDA-483* to the warning letter was subjective. One firm that operates in more than one FDA district claimed that the same violations do not always receive consistent compliance action from FDA (e.g. a warning letter versus an *FDA-483*). Some firms believe that investigators interpret the regulations differently. More than one-half of the firms believe that their violations did not warrant a warning letter, while 38 percent agreed with FDA's decision to issue a warning letter.

Firms believe that FDA does not provide consistent and accessible guidance on what warrants a warning letter. Policy guidance publications exist, but they are not accessible

to some firms, especially those that are smaller and less sophisticated. A firm official summarized the difficulties:

*The industry is in the dark about changes in [FDA's] procedures and priorities. The FDA is not communicating procedure changes but is writing up firms who violate the changes. For example, we were written up for new training requirements that were never communicated to us in the first place.*

Another firm with a similar viewpoint requested even more guidance from FDA, saying, "FDA should give suggestions on exactly how to comply with labeling regulations. A list of suggestions would be helpful."

Firms also do not understand the role of the investigator in the warning letter process. One firm believes that the investigator who conducted the inspection was not a part of the decision to issue a warning letter.

### **When possible, firms would appreciate advance notice that a warning letter will be issued**

Some district offices warn firms that the district office is considering sending a warning letter or that they have sent a warning letter recommendation to FDA headquarters. Other district offices issue warning letters without prior notice.

Firms claim that they would respond and comply more quickly if FDA consistently told them that a warning letter was imminent. Most firms (58 percent) did not expect to receive a warning letter. However, almost half of those that did not expect the warning letter received it for violations discovered through postinspection laboratory testing, making it impossible for FDA to alert the firm during the inspection.

Firms suggested a variety of methods that FDA could use to prepare them for the warning letter. These include telephone calls, postcards, electronic mail and letters advising the firm that the warning letter is forthcoming. One-half of the firms responded to the *FDA-483* in writing, including one firm that indicated an adequate response to the *FDA-483* could preclude the issuance of a warning letter. The same firm conceded that certain violations will always "trigger" a warning letter and asked that FDA make more efforts to publicize those violations.

---

## **With some exceptions, firms were satisfied with FDA’s customer service during the warning letter process**

### **Firms generally viewed investigators as helpful and thorough, although some firms questioned their objectivity**

The majority of firms who commented on the FDA investigator’s customer service had generally positive things to say. A total of sixteen firms reported on the investigators’ customer service, and 10 were generally positive, 5 had negative things to say, and 1 simply said that investigators “vary in candor and helpfulness.” Of those who reported a positive experience, investigators were most commonly described as “helpful” and “thorough.” One firm praised the investigators, saying “they made us a better organization.” Of the five firms that reported a negative experience with the investigators, three complained about what they perceived as an inordinate amount of time the investigator spent inspecting them.

### **Most firms perceived the district offices in a positive light; however, some reported instances of staff apathy**

Three-quarters of the firms that contacted a district office had positive things to say about the office’s customer service. Sixty-seven percent of firms had contact with their district office following the issuance of the warning letter. Comments ranged from, “they were flexible in allowing us to choose the date for our second inspection,” to superlatives describing staff as “wonderful” and “excellent.” Three firms mentioned their district office was particularly helpful during the warning letter process. Those firms accepted FDA’s assistance in drafting letters of recall or resolving a credentialing problem with the State.

While most firms who contacted their district office found the experience positive, the remaining 25 percent of firms had negative experiences. The three firms that complained about their district office mentioned difficulty reaching staff, delays in approval of imported foods, unhelpful and impolite staff, and either too few employees or employees who “just don’t care.”

### **Few firms contacted FDA headquarters, and customer service reviews were mixed**

Few firms had contact with FDA headquarters. Four firms (17 percent) contacted headquarters during the warning letter process. Two firms reported positive experiences, and two firms reported negative experiences. One satisfied firm mentioned that they were “able to get to the right people” and another firm said the FDA headquarters staff were “great, they followed up well.” Comments from the two firms that had negative experiences included, “We could get no clear answers,” to their questions regarding tissue

sampling and “we got no response to our request to speed up the process of approving imported foods, especially holiday-related foods.”

## RECOMMENDATION

The warning letter is an effective tool to achieve compliance with Federal laws and regulations. In our companion report, we recommend that FDA improve the timeliness of the warning letter process and follow-up activities and revamp its warning letter data collection system to ensure accuracy.

Based on the findings in this report, we believe that FDA also should implement some minor improvements to increase fairness among district offices and improve flexibility. Specifically, FDA should:

- ▶ *continue to improve relations and communication with industry and*
- ▶ *consider issuing guidance that would authorize district offices to use FDA-483s and meetings to achieve compliance in lieu of warning letters.*

District offices vary significantly in (1) experience, (2) how they view the warning letter, and (3) their relationships with industry. As a result, there is a significant difference in how district offices handle inspection violations. While FDA has accepted this variation in the past, the move that some district offices have made toward using *FDA-483s* and meetings in lieu of warning letters has focused attention on these variations.

We believe that FDA's move towards better communication and collaboration with industry is appropriate, in light of the National Performance Review and the findings presented in this report. Further development of these relationships is important in preserving fairness. A firm should not suffer adverse consequences solely because it is located in a different district than another firm.

At the same time, we recognize the need to allow district offices considerable discretion. Developing guidance on alternatives to the warning letter will allow them to pursue other means of achieving compliance.

We received comments on the draft report from FDA in which the agency concurred with our recommendation. Where appropriate, we have made revisions in the report in response to these comments. We also have responded to several of FDA's comments in the appendix.

# APPENDIX A

## AGENCY COMMENTS



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service  
Food and Drug Administration

### Memorandum

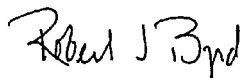
Date: NOV 30 1998

From: Deputy Commissioner for Management and Systems, FDA

Subject: OIG Draft Reports: "FDA Warning Letters: Trends and Perspectives," OEI-09-97-00380 and  
"FDA Warning Letters: Timeliness and Effectiveness," OEI-09-97-00381

To: June Gibbs Brown  
Inspector General

Thank you for the opportunity to review and comment on the two draft OIG reports, "FDA Warning Letters: Trends and Perspectives," and "FDA Warning Letters: Timeliness and Effectiveness." In general, FDA concurs with the reports and the recommendations. Our comments on both reports are attached for your consideration.

  
Robert J. Byrd

Attachment

**AGENCY COMMENTS TO THE OFFICE OF INSPECTOR GENERAL DRAFT REPORTS, "FDA WARNING LETTERS: TRENDS AND PERSPECTIVES," AND "FDA WARNING LETTERS: TIMELINESS AND EFFECTIVENESS"**

GENERAL COMMENTS

We are pleased to note, that both Warning Letter reports validate that the warning letter process works. It is highly effective in bringing firms into compliance with a moderate amount of human and resource expenditures. The process is understood by most of the regulated industry and adheres to FDA's long-standing policy of "prior warning."

It should be noted that the number of regional and district offices cited in both reports should be corrected. There are 5 Regional and 20 District Offices.

It should also be noted that the statistics provided regarding length of time between issuance of a warning letter and reinspection may be skewed somewhat, giving the appearance of untimely follow-up reinspection. For example, a significant part of NOL-DO's warning letters are addressed to the seafood industry. Much of this industry is seasonal, and that may preclude making a follow-up inspection until the firm begins processing on a regular basis the following year. Other districts may also have industry segments in the same situation.

Both reports identify the three highest and three lowest warning letter producing Districts. While the report does not directly say it, it implies that high warning letter production is good and low warning letter production is bad.

The reports do not explain:

1. The nature and complexity of the inspections conducted have increased, thus the total number of inspections conducted has dropped. One would expect to see a corresponding drop in warning letter production with fewer inspections being conducted.
2. Warning letters are issued to importers for failure to hold product for FDA examination. In a big Import District, this will drive up the number of warning letters issued. A District with a low volume import operation would correspondingly expect to issue fewer warning letters. While this can account for large differences in warning letter production between Districts, it was not mentioned in the reports.

Both reports state that FDA believes that documentation of notice (warning) strengthens later regulatory actions. The reports should also highlight that FDA also believes that most firms, when given the chance, will choose to correct violations voluntarily.

The reports note the significant decrease in the number of warning letters issued and attributes it

to changes in FDA policies and better industry compliance. The primary reason for the decrease would be the changes in FDA policy as opposed to better industry compliance. It is not clear on what basis the statement is made that industry compliance has significantly increased.

The reports state that overall the warning letter is an effective tool, but then discusses issuing new guidance for more district discretion that would reduce the number of letters issued. We should not reduce the number of letters further if the review has demonstrated that the warning letter is an effective tool.

We believe that the Trends and Perspectives report should point out that the Agency is going to undertake a medical device Warning Letter Pilot.

#### TECHNICAL COMMENTS

##### *FDA Warning Letters: Trends and Perspectives*

Page 6, third paragraph - the form FDA-483 should include all significant objectionable observations that are linked to violations of the FD&C Act or deviations from related regulations not potential problems with the firm as the sentence states and implies.

Page 7, third paragraph - Not all headquarters units' issue warning letters for advertising. For example, CFSAN does not issue such letters, and rarely issues warning letters of any sort directly from the center. The report should be specific as to the headquarters unit in question.

Page 8, second paragraph - The second sentence implies that districts are solely responsible for determining whether a firm's response is adequate. This is not correct. The district, in coordination with the appropriate center, determines whether the firm's response is adequate.

Page 10, last paragraph - It is recognized that the medical device industry initiatives are being considered by FDA for broader implementation. Currently the draft Federal Register Notice is being reviewed in the agency.

##### *FDA Warning Letters: Timeliness and Effectiveness*

Page 2, second paragraph - FDA does not verify corrections by "offering meetings."

Page 2, fifth paragraph - the warning letter is not a tool for "assuring firms achieve compliance. . .," but is a tool for providing firms an opportunity to voluntarily make appropriate corrections without enforcement actions.

Page 5, third paragraph - the form FDA-483 should include all significant objectionable observations that are linked to violations of the FD&C Act or deviations from related regulations not potential problems with the firm as the sentence states and implies.

Page 6, third paragraph - Not all headquarters units issue warning letters for advertising. For



example, CFSAN does not issue such letters, and rarely issues warning letters of any sort directly from the center. The report should be specific as to the headquarters unit in question.

Page 7, second paragraph - The second sentence implies that districts are solely responsible for determining whether a firm's response is adequate. This is not correct. The district, in coordination with the appropriate center, determines whether the firm's response is adequate.

Page 7, fourth paragraph - FDA does not verify a firm's corrective actions by initiating meetings, conference calls, or administrative or regulatory actions. A firm's statement of corrective actions or promise to make appropriate corrective action is verified during a follow-up inspection.

Page 7, fifth paragraph - This paragraph implies that FDA has recall authority. FDA recalls are primarily voluntary. Except for infant formula, certain medical devices, and human tissue, FDA has no recall authority.

Page 7, fifth paragraph - Please note that license suspensions and revocations are regulatory actions for biological products taken under the provisions of section 351 of the Public Health Service Act (PHSA).

Page 11, first paragraph - FDA does not verify compliance by "soliciting documentation" and "offering meetings." There is no requirement that FDA district offices follow-up to ensure a firm responds to the warning letter as the sentence implies.

Page 11, Table - Please change "violations" under column 2 to "observations."

Page 11, last paragraph after table - The paragraph states that for firms reinspected, investigators found repeat violations or new violations in 2/3 of the cases. It is hard to see how the conclusion is drawn that the warning letter achieved compliance in such cases.

Page 13, first paragraph - "Severity of violations," the second statement implies that the agency sends warning letters for relatively minor violations.

Page 13, third paragraph - "Type of Firm," the report should explain how the size of a firm influences the time required for it to implement corrections.

Page 13, last paragraph - A statement is made "that the centers simply have too much work to complete review within 15 days." Is this statement based on established facts or someone's opinion? The report should clarify.

Page 17, Recommendations, last paragraph - The DCMO warning letter database is not intended to be the official record for filling FOI requests and posting on the Internet.

## RECOMMENDATIONS

### OIG Recommendation - "FDA Warning Letters: Trends and Perspectives"

The FDA should (1) continue to improve relations and communication with industry and (2) consider issuing guidance that would authorize district offices to use FDA-483s and meetings to achieve compliance in lieu of warning letters.

#### FDA Response

FDA concurs with this recommendation.

FDA has fostered a more cooperative relationship with industry and will continue to improve upon those relationships through use of a variety of mechanisms of communications, such as, public workshops, web sites, guidance documents, outreach programs, teleconferences or meetings, and letters to manufacturers.

FDA further believes that guidance that would authorize district offices to use FDA-483s and meetings to achieve compliance in lieu of warning letters is already in effect. The agency has guidance which provides that FDA-483s, meetings and other types of correspondence are appropriate in certain circumstances to achieve correction.

### OIG Recommendation - "FDA Warning Letters: Timeliness and Effectiveness"

The warning letter is an effective tool for assuring that firms achieve compliance with Federal laws and regulations. To increase its effectiveness, FDA should (1) improve the timeliness of the warning letter process and follow-up activities and (2) revamp its warning letter data collection system to ensure accuracy.

#### FDA Response

FDA concurs with the recommendation.

FDA will continue to work at ensuring that inspectional findings are reviewed and appropriate corrective actions are pursued. It is our intention to improve upon our record of a decrease in time between receipt of a recommendation and response, as resources permit.

FDA has contracted with Booz-Allen and Hamilton to develop an Agency-wide system, the Field Accomplishment and Compliance Tracking Systems (FACTS) that will help to ensure accuracy.

## APPENDIX B

### OIG RESPONSE TO AGENCY COMMENTS

We offer the following additional analysis based on FDA's concerns.

At the time that this inspection began, there were six regional offices and 21 district offices as we stated in the draft report. The Mid-Atlantic and Midwest regional offices have since merged into the Central regional office, and the Buffalo district office has merged with the Brooklyn district office.

The seafood industry was the only industry in our sample that has a seasonal component. Analysis of the firms in our sample that market seafood shows that either there was no follow-up inspection conducted (most often because it was a "failure-to-hold" violation) or that reinspection was actually more timely than the average. Hence, reinspection delays resulting from the seasonal nature of the industry had either no effect or a diminishing effect on the 278-day average that we reported.

We do not intend to place any value judgments on the number of warning letters produced by a district. Our purpose in identifying these extremes is merely to indicate the wide variation in warning letter production that exists among the districts.

Analysis of FDA data indicates that while both the numbers of inspections and warning letters decreased from 1994 to 1997 (the range used for our statements in the reports), inspections decreased by 3.6 percent while warning letters fell 39 percent. In other terms, in 1994, about 9.1 inspections conducted yielded 1 warning letter. In 1997, the rate was 12.2 inspections per warning letter.

We agree that the prevalence of importers in a district could contribute to the variation in number of warning letters issued and have clarified their importance in this report.

The FDA's opinion that firms will voluntarily correct violations is highlighted in the background section of this report.

Several districts indicated that increased familiarity with FDA regulations leads to better industry compliance. We have clarified this point in this report.

Our recommendation was not intended to discourage the use of warning letters, but rather to encourage FDA to issue guidance which would allow a district office to select the tools it feels are most effective in achieving compliance in a given situation.

The medical device Warning Letter Pilot will allow FDA to use a firm's response to an FDA-483 or an untitled letter to preempt a warning letter for certain segments of the device industry. More information can be found on FDA's website or the Federal Register for August 27, 1998.

With respect to FDA's comment on "Page 11, last paragraph after table" of the companion draft report entitled *FDA Warning Letters: Timeliness and Effectiveness* (the table and paragraph now appear on page 12), we note that the paragraph below the pie chart on page 13 shows that despite the discovery of repeat or new violations on reinspection, the warning letter was still effective. As stated there, investigators believed that the violations found on reinspection were minor and that firms had made satisfactory progress towards compliance.