

FDA/Industry Partnerships: Moving toward More Equitable Enforcement

Reversing what was often an adversarial relationship, FDA has worked with representatives of the device industry to implement changes designed to improve the agency's inspection and enforcement policies.



Medical device companies see themselves as innovators in the diagnosis, cure, or treatment of disease or injury. Their success depends on providing patients early access to their technically advanced, safe, and effective devices. FDA officials see themselves as the guardians of the public health. Their mandate is to foster the introduction of new technology and to ensure that the devices designed to diagnose, cure, or treat disease or injuries do not inadvertently cause harm. One of the ways FDA accomplishes its mandate is through the inspection of device manufacturers. During the past few years, many FDA officials in the Office of Regulatory Affairs (ORA) and the Center for Devices and Radiological Health (CDRH) have begun to view industry as a partner rather than an adversary. Working with device manufacturers, FDA has implemented many changes that have improved the effectiveness of FDA inspections and made the enforcement process more equitable. These efforts need to continue, so that the industry will view the inspection process as facilitating rather than impeding timely patient access to safe and effective products.

FDA ENFORCEMENT IN THE EARLY 1990s

In November 1990, David Kessler became the Commissioner of Food and Drugs. In speeches, he repeatedly stated that FDA enforcement "needed to be taken up a notch." Under Kessler's mandate, officials in CDRH's Office of Compliance—believing that medical device manufacturers did not take FDA seriously—instituted a program under which companies who had systemic problems with their good manufacturing practices were placed on a reference list. Being on the list precluded the companies from having their 510(k) applications cleared. When the program was implemented, the medical device industry was incensed.

The Health Industry Manufacturers Association (HIMA) filed a citizen petition asserting that the agency lacked the statutory authority to link 510(k) clearance with compliance with GMP requirements. HIMA also objected to the difficulties companies had in determining whether or not they were on the list, and in getting themselves off the list. Over time, Ron Johnson, director at CDRH's Office of Compliance, and Marge Hoban, chief of the center's Field Programs Branch, remedied many of the problems. Eventually, due in large part to the reengineering efforts of Phil Phillips, deputy director for policy at CDRH's Office for Device Evaluation, FDA eliminated the reference list for Class I and Class II products.

Another Kessler initiative was to decentralize the power for enforcement actions

and delegate to officials in FDA district offices the authority to send warning letters. The district officials were instructed not to be predictable in their enforcement actions. They were to go into a firm, spot regulatory violations, and then go on to find different regulatory violations in other companies. These initiatives caused companies to be suspicious of FDA because they were fearful of unpredictable and inconsistent regulatory actions.

STIMULI TO CHANGE

In 1994, HIMA polled the industry regarding its concerns about FDA enforcement policies and developed recommendations to improve the inspection process. In meetings with officials from FDA's Office of Regulatory Affairs and CDRH, HIMA suggested items such as:

- Conducting preannounced inspections.
- Annotating the FDA 483 with completed or promised corrective actions.
- Requiring that annotations be put in context (e.g., the investigator examined 50 complaints and found that 3 had not been reported as MDRs).
- Issuing closeout letters after completion of inspections.

A group of FDA officials received similar input from the Medical Device Industry Initiatives Grassroots Task Force, an industry group consisting of representatives of national and regional medical device associations.

Cognizant of its diminishing budgetary resources and of the reasonableness of the suggestions presented, FDA in 1996 implemented a pilot program that included the items noted above. The agency subsequently surveyed the investigators and the companies being inspected, and found that most respondents in both groups believed that the pilot program improved the efficiency of inspections and the quality of communication between the investigator and the company. The program was so successful that, in March 1997, the features of the program became part of FDA's standard operating procedures for conducting medical device inspections. In addition, the program is currently being implemented on a pilot basis in other FDA centers.

To solicit additional ideas on how to further improve the inspection process, FDA throughout 1996 and 1997 met with industry officials in various cities, including Dallas, Nashville, Boston, Atlanta, Charlotte, and Orlando. Some of the suggestions coming out of these meetings included:

- Conducting joint training for industry and FDA investigators on the new quality system requirements.
- Providing the establishment inspection reports (EIRs) automatically to companies after their facilities have been inspected.
- Excluding from warning letters items that have been corrected or for which corrections have been promised.
- Increasing the time for companies to respond to FDA 483 observations, and acknowledging their responses in the warning letter.

FDA RESPONSE TO INDUSTRY SUGGESTIONS

Joint Training. In response to the industry suggestion on joint training, FDA's southwest regional office conducted joint training for FDA and industry personnel on how to comply with the MDR requirements. FDA also worked with the Food and Drug Law Institute and with national and regional device associations to present periodic teleconferences on FDA requirements for members of the industry and FDA officials. Additionally, the agency conducted joint training on how to comply with the design control portion of the new quality system regulation.

Establishment Inspection Reports. FDA has instituted a program under which it automatically provides EIRs to companies after their FDA inspections. This program has proven to be very successful, with companies better able to understand FDA's conclusions about their firm's state of compliance.

Warning Letter Pilot. Prompted by the industry's pressing concerns regarding the impact that warning letters have on corporate image and stock price, a committee of the Medical Device Industry Initiatives Grassroots Task Force, working with FDA officials, designed an 18-month pilot program. Its purpose was to preclude FDA from sending warning letters to companies who had corrected or were in the process of correcting deficiencies.

The way the program works is as follows. As of March 29, 1999, after a domestic device investigation, a company with a good record of compliance with FDA requirements will be given 15 working days to respond to deficiencies that would have previously triggered a warning letter. If the response is deemed to be satisfactory, then a warning letter will not be issued. Instead, FDA will issue a postinspectional notification letter. The letter will state that while the inspection found quality system deficiencies which, if not corrected, would warrant a warning letter, the company's written response has satisfied FDA that the company has taken or will take appropriate corrective actions. If, at a later time, FDA observes that the deviations from the quality system regulation have not been remedied, the agency may take regulatory action (seizure, injunction, and civil penalties) without notice.

The program also addresses situations that would have warranted a warning letter for failure to submit a 510(k) application or for labeling violations. Under this program, companies, in most instances, will receive an untitled letter within 30 working days of the FDA inspection. Companies will have 15 working days to respond to FDA. CDRH will then have 30 working days to consider the firm's response. If the firm's response is satisfactory, FDA will send a postinspectional letter similar to the one discussed above. Ernest Malachowski, chief operating officer of Chrisman Bynum & Johnson (Boulder, CO) and a member of the committee that designed the pilot program, says that "The changes provide the device industry with the opportunity to make corrections—and perhaps forego the receipt of a warning letter—without diminishing the agency's authority."

Inspection Evaluation Survey. For many years, industry has made various

allegations about the lack of uniformity in FDA inspections. In an attempt to get accurate data, a committee of the Medical Device Industry Initiatives Grassroots Task Force, in cooperation with University of California, Irvine (UCI) Center for Statistical Consulting, designed a medical device inspection evaluation survey to provide a mechanism by which industry can provide anonymous feedback to ORA and members of the public regarding the FDA inspection process. The survey, which began on March 1, 1999, will be conducted as a pilot program for one year.

The FDA contact for the program is Denise Dion, medical device expert investigator, who coordinated the internal distribution of the surveys to the FDA districts. Dion sees the process working in the following manner. Upon completion of an FDA inspection, the investigator will fill out the top portion of the survey that contains background information about the company and the devices it manufactures, the name of the investigator, the FDA district, whether or not a 483 was issued, and the reason for the inspection. After completing the form, the investigator will give it to an official at the firm that is being inspected, and ask him or her to complete it and return it in the stamped envelope to UCI.

Data will be entered and analyzed at UCI, with specifics about companies and investigators kept confidential. Questions asked in the evaluation include the following:

- Was there enough advance notification?
- Was it necessary to reschedule the inspection?
- Was there adequate communication during the inspection?
- Was a 483 issued?
- Were corrective actions promised, and were they annotated on the 483?
- Were the observations on the 483 appropriate?
- How did the inspection compare with past inspections?

UCI will analyze the data at the end of six months and again at the end of one year. To show trends in satisfaction and perceived problems, a comparison of the responses both nationally and by individual districts will be made. The analysis will also consider:

- The length of the inspection as a function of the type of inspection (preapproval, quality system, or other).
- Whether a 483 was issued.
- Whether there were interruptions.
- Whether any problems were perceived with the inspection.

Once the analysis is completed, the results will be widely disseminated and placed on the Web sites of FDA, HIMA, the Association of Diagnostic Manufacturers, the American Society for Quality, and the Medical Device Manufacturers Association. Lauren Andersen, president and CEO of Andersen Products (Haw River, NC) and a member of the committee that developed the survey, states that "The survey's success depends on the willingness of companies to complete it and on the candor of their responses. With good participation, this program can encourage objectivity and consistency in FDA's field operations."

QUALITY SYSTEM INSPECTION TECHNIQUE (QSIT)

For years, members of the industry complained that FDA investigators inspecting their companies focused on individual deviations from the GMP regulations rather than on whether their company had a quality system in place that was designed to manufacture safe and effective products. In 1998, a group of FDA and industry officials developed recommendations to address these concerns.

Based on the group's recommendations, a CDRH team led by Tim Wells developed a new systems approach for FDA inspections, which they called the quality system inspection technique (QSIT). QSIT is based on the premise that the quality system regulation has seven major subsystems whose requirements intersect. The subsystems are:

- Management controls.
- Design controls.
- Corrective and preventive actions.
- Production and process controls.
- Record/document/change controls.
- Material controls.
- Facility controls.

During an initial inspection, an FDA investigator will examine whether the company has the first four subsystems in place, and whether it is manufacturing products under the procedures required by those subsystems. If a company has an inspection following which no official action is indicated, subsequent inspections will be more limited.

FDA recently conducted a study of inspections using the QSIT approach in the agency's Los Angeles, Minneapolis, and Denver districts. Responses indicated that both industry officials and FDA investigators believed that QSIT inspections were efficient and focused, and provided assurance that companies had systems in place that would produce safe and effective medical devices.

Because of the QSIT study's success, FDA will implement inspections under QSIT in all districts during the first quarter of 2000. More information on QSIT is available on FDA's [Web site](#) [4].

FDA INSPECTION REQUIREMENTS

The Federal Food, Drug, and Cosmetic Act requires FDA to inspect nonexempt Class II and Class III device manufacturers every two years to ensure that they are manufacturing safe and effective products. According to the agency's plan for statutory compliance under the FDA Modernization Act, FDA is complying with its biennial inspection requirements at a level of 28%. Whether the failure of FDA to visit firms makes those companies lax is open to question. Eve Ross, counsel for W.L. Gore & Associates (Newark, DE), speaks for many companies when she says,

"We don't follow good quality practices because of FDA. Good quality is good business." Nonetheless, Los Angeles FDA compliance director Tom Sawyer states that "The FDA inspection process, in which the investigator is able to link his or her observations to the regulations, provides an important insight to firm managers intent upon complying with the law and putting high-quality products into commerce."

Today we live in a global economy, and many firms do business in Europe. According to Ken Kopesky, director of corporate compliance and audit at Medtronic Inc. (Minneapolis), "Every year, notified bodies come in and inspect our manufacturing facilities for compliance with the quality system provisions of EN ISO 9001 or 9002 and EN 46001 or 46002." Most U.S. firms believe that they would save resources if FDA would recognize the inspections by these notified bodies. Michael Gropp, chief compliance officer at Guidant Corp. (Indianapolis), states that "The situation will become more acute as authorities from other countries also develop their own quality system requirements and expectations for audits." Kim Trautman, FDA's GMP expert, says that although FDA does support the concept of eventual mutual recognition of CGMP inspections between major device markets, "full achievement of this goal is still in the future."

CONCLUSION

FDA officials partnering with industry to examine inspections and enforcement in a new light have made tremendous progress in making the process of initiating regulatory action more equitable. Wayne Barlow, CEO of Wescor Inc. (Logan, UT) and chairman of the Medical Device Industry Initiatives Grassroots Task Force, says that "the agency is operating in a more user-friendly mode than at any time during the previous decade."

When FDA Commissioner Jane Henney met with the task force in December 1998, she complimented the group on its accomplishments and challenged it to be creative in developing more initiatives that will further improve the process. One of these future challenges is for FDA to continue its involvement in ongoing initiatives to harmonize its requirements with those of the European Union and other international regulatory agencies. Such a measure would go a long way in promoting a view of the FDA regulatory process as benefiting timely patient access to safe and effective products.

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