BY THE COMPTROLLER GENERAL

Report To The Congress

OF THE UNITED STATES

Legislative And Administrative Changes Needed To Improve Regulation Of Drug Industry

A considerable amount of misbranded and adulterated drug products get on the market because the Food and Drug Administration (FDA) does not have legislative authority to detain the products administratively prior to formal seizure action. The Congress should amend the Food, Drug, and Cosmetic Act to give FDA this authority.

FDA has increased emphasis on voluntary compliance with regulations. However, FDA does not know the extent to which voluntary compliance is working. FDA needs to develop a mechanism to measure the extent to which allowing voluntary corrective actions promised by firms violating FDA-administered laws and regulations result in compliance.

This report also recommends actions FDA should take to reduce the number of proposed regulatory actions which are subsequently disapproved and to improve followup on unresolved deficiencies found in prior inspections.

HHS agreed with the recommendations and pointed out a number of corrective actions that are being taken.

GAO/HRD-83-24
APRIL 5, 1983

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COMPTROLLER GENERAL OF THE UNITED STATES
WASHINGTON D.C. 20548

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To the President of the Senate and the
Speaker of the House of Representatives

This report discusses the Food and Drug Administration's efforts to regulate the drug industry. The report describes the agency's regulatory activities, the number of regulatory actions taken over the past 3 years, the reasons for the declining number of regulatory actions, and a suggested legislative change to assist the agency in seizing misbranded or adulterated drug products. Our review was made because of recent congressional and public concern expressed about the reduction in the number of enforcement actions taken by the agency.

We are sending copies of this report to the Director, Office of Management and Budget; and the Secretary of Health and Human Services.

Charles A. Bowsher

Comptroller General
of the United States

COMPTROLLER GENERAL'S
REPORT TO THE CONGRESS

LEGISLATIVE AND ADMINISTRATIVE CHANGES NEEDED TO IMPROVE REGULATION OF DRUG INDUSTRY

D I G E S T

In recent months, concern has been raised by Members of Congress and public interest groups about the significant decrease in the number of regulatory actions taken by the Food and Drug Administration (FDA) against the drug industry. GAO reviewed FDA's compliance activities to determine whether FDA is taking appropriate and timely regulatory actions against firms violating the law and FDA regulations.

EMPHASIS ON VOLUNTARY COMPLIANCE PRIMARY REASON FOR DECLINE IN REGULATORY ACTIONS

The number of regulatory actions taken by FDA decreased considerably in fiscal year 1981, but increased in one category--regulatory letters--in fiscal year 1982 because of what may be a one-time intensive effort against manufacturers of "look-alike" drugs. The primary factor influencing the decline in the number of regulatory actions in fiscal year 1981 was FDA's increased emphasis on voluntary compliance. Except for flagrant violations and violative products that present a potentially serious health hazard, the agency takes formal regulatory action only after the firms have been given an opportunity to correct detected deficiencies on a voluntary basis. Other significant factors included:

--A 24-percent reduction in the number of inspectors which, according to FDA, went from 1,183 in fiscal year 1978 to 903 in fiscal year 1982.

--An emphasis on abbreviated inspections.

--Merit pay contracts which may discourage submission of proposed regulatory actions because disapproved actions adversely affect performance ratings. (See p. 4.)

While FDA has been encouraging voluntary compliance for years, it stepped up its efforts in fiscal year 1981. In fiscal year 1982, FDA began implementation of its voluntary correction reporting system.

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Tear Sheet

(See p. 7.) Because FDA does not know the extent to which voluntary compliance is working, GAO believes FDA should develop a mechanism for measuring the extent to which the voluntary approach is resulting in compliance. FDA should give particular attention to the (1) total number of violations detected, (2) type and severity of these violations, (3) type of firms (e.g., large, small, generic, proprietary) causing the most compliance problems, (4) type of corrective actions being taken, (5) number of repeat violations, and (6) cost of the voluntary approach and its impact on the agency's inspection resources. (See p. 8.)

FDA NEEDS ADMINISTRATIVE DETENTION AUTHORITY TO KEEP MISBRANDED AND ADULTERATED DRUG PRODUCTS OFF THE MARKET

FDA records show that at least 33 percent of the 495 seizure actions approved by FDA's Office of Drugs during fiscal years 1979-81 resulted in no products being seized and in many other cases very small amounts of products were seized.

This occurred primarily because the products were moved by the firms before approval was obtained to seize the products.

FDA could have prevented a considerably greater portion of the violative products from getting on the market if it had legislative authority to administratively detain products while the proposed seizure action is processed through FDA, the U.S. Attorney's Office, and the courts. FDA has administrative detention authority for a number of products, but not drugs produced in the United States. (See p. 10.)

THE NUMBER OF DISTRICT-PROPOSED REGULATORY ACTIONS DISAPPROVED BY HEADQUARTERS COULD BE REDUCED

More timely and appropriate regulatory actions could be taken if the number of disapproved recommended actions could be reduced. About 30 percent of the 1,146 regulatory actions proposed by FDA's district offices were disapproved by FDA headquarters during the period covered by the GAO review. While many of these disapprovals

were valid, the time spent on preparing some of these could have been saved if

--FDA's Office of Drugs developed definitive policies on actions to be taken on violations involving medically insignificant drugs and technical violations of good manufacturing practice regulations,

--coordination and communication among investigators, compliance officials, and headquarters officials were improved,

--the districts submitted recommendations for regulatory action in accordance with established policy and procedures, and

--the Executive Director of Regional Operations provided additional guidance to the districts regarding what constitutes sufficient evidence to support violations. (See p. 16.)

NO EVIDENCE IN MANY CASES THAT INVESTIGATORS ARE FOLLOWING UP ON PRIOR VIOLATIONS

In three of the four FDA districts where GAO reviewed followup actions, no evidence was found in over half the cases to indicate that investigators had followed up on previously identified violations of the law and FDA regulations. Investigators are required to review the results of prior inspections before beginning an inspection, but there are no clear requirements that they should determine whether prior violations have been corrected or comment on the current status of these prior violations in the inspection report.

Taking a sample of about 10 percent of the registered drug firms in the Boston, Chicago, and Newark District Offices, GAO found that:

--In Boston, 25 inspection reports discussed 247 deficiencies. Follow-on inspections did not show the current status of 153 of the deficiencies.

--In Chicago, 14 of 28 inspection reports with identified deficiencies did not show that the deficiencies were followed up in the subsequent inspection.

--In Newark, 21 inspection reports discussed 196 deficiencies. Follow-on inspections did not show the current status of 106 of the deficiencies.

GAO did not note a similar problem in the Baltimore District Office where the regional Food and Drug Director had issued instructions to districts under his jurisdiction that all inspections and reports must discuss the status of prior violations and state reasons why any corrections had not been made. (See p. 25.)

RECOMMENDATIONS TO THE SECRETARY OF HEALTH AND HUMAN SERVICES

The Secretary should require the Commissioner of FDA to:

--Develop a mechanism to measure the extent to which voluntary corrective actions result in compliance.

--Develop and distribute to all districts definitive policies on actions to be taken on violations involving insignificant drug products and technical violations of the regulations.

--Provide additional guidance to the district offices on evidence required to support all types of proposed regulatory actions.

--Encourage greater coordination and communications among district investigators, district compliance officials, and headquarters officials to better assure that (1) district and headquarters officials agree on actions to be taken and (2) documentation to support recommended actions is appropriate.

--Revise the Inspection Operations Manual to require inspectors to (1) determine the current status of all prior unresolved deficiencies and (2) discuss the status of these deficiencies in the subsequent inspection report.
(See pp. 9, 23, and 28.)

RECOMMENDATION TO THE CONGRESS

The Congress should amend section 304(g) of the Federal Food, Drug, and Cosmetic Act by adding drug products to the language which gives FDA the authority to detain administratively medical devices. (See p. 15.)

AGENCY COMMENTS AND GAO EVALUATION

The Department of Health and Human Services stated that the report was fair and constructive in its presentation of FDA's regulation of the drug industry. The Department agreed with the recommendations in the report and pointed out a number of corrective actions that had been or were being taken. For example, the Department will develop a mechanism to measure the extent to which voluntary corrective actions result in compliance. (See app. I.)

Contents

ABBREVIATIONS

ACRA	Associate Commissioner for Regulatory Affairs
EDRO	Executive Director of Regional Operations
FDA	Food and Drug Administration
FD&C	Federal Food, Drug, and Cosmetic Act
GAO	General Accounting Office
GMP	good manufacturing practice
HHS	Department of Health and Human Services

CHAPTER 1

INTRODUCTION

An estimated 20,000 prescription and 200,000 to 300,000 over-the-counter drugs are marketed in the United States for human consumption. About 4,900 separate establishments are involved in formulating, testing, manufacturing, and repacking these products. The Food and Drug Administration (FDA), within the Department of Health and Human Services (HHS), is responsible for ensuring that the manufacturing, processing, packing, and holding of drugs, and the facilities and controls used in these processes, are such that the highest quality product feasible will be marketed. FDA is also responsible for maintaining a registration of drug establishments and a listing of drug products.

FDA's basic legislative authority for carrying out these responsibilities is the Federal Food, Drug, and Cosmetic (FD&C) Act of 1938, as amended (21 U.S.C. 301). Two provisions of the act specifically prohibit the distribution in interstate commerce or importation of articles that are adulterated or misbranded. An adulterated product is defined as one that is defective, unsafe, filthy, or not produced in conformity with current good manufacturing practices (GMPs). A misbranded product is one with labeling that is false or misleading or with labeling that fails to provide important and/or required information.

FDA consists of a headquarters staff, 10 regional offices, and 22 district offices located throughout the United States and in Puerto Rico. The Office of Drugs within the National Center for Drugs and Biologics, in conjunction with the Office of the Associate Commissioner for Regulatory Affairs (ACRA), establishes the basic policies used by FDA in implementing its drug compliance activities. In addition, ACRA's responsibilities include evaluating and coordinating all proposed legal actions to ascertain compliance with regulatory policy and enforcement objectives. The Executive Director of Regional Operations (EDRO), based on policies established by ACRA and the Office of Drugs, is responsible for coordinating the inspection and enforcement activities of FDA's field operations.

The basic mechanism used by FDA in implementing its drug enforcement strategies is the compliance program. The compliance program defines the work to be done and establishes the necessary conditions, ground rules, and reporting requirements to accomplish FDA's objectives within a specific program area, such as drug process inspections. In fiscal year 1982, the Office of Drugs had 25 compliance programs and 11 compliance circulars which called for a commitment of more than 400 staff years of field resources.

PRIOR GAO REPORTS

In our report "Problems In Obtaining And Enforcing Compliance With Good Manufacturing Practices For Drugs" (B-164031(2), Mar. 29, 1973), we recommended that FDA (1) establish more definitive guidelines specifying when products should be seized, the amount and type of documentation needed to support a seizure action, and when firms should be cited for prosecution; (2) consider establishing a time limit for receipt of a written response to warning letters; (3) correct the inventory of drug producers subject to the 2-year inspection requirement contained in the FD&C Act; (4) establish an inspection scheduling system; (5) establish guidelines to assure timely initial inspections of new drug producers; and (6) enforce the annual drug producers registration requirements.

During this review we found that FDA had corrected some but not all of the deficiencies mentioned in the prior report. We found that FDA (1) had issued more definitive guidelines, (2) had incorporated a 10-day time limit for firms' written responses to regulatory letters, (3) had established an inspection scheduling system, and (4) is inspecting newly registered firms in a more timely manner.

Although we found that FDA has taken some action to enforce annual drug registration, we encountered difficulty in determining whether all registered firms were included in each district's official establishment inventory and whether all firms that were required to register had done so. This issue will be considered for evaluation in a subsequent GAO review.

OBJECTIVES, SCOPE, AND METHODOLOGY

Our objectives in this review were to determine (1) whether FDA was taking appropriate and timely regulatory actions against firms found violating the law and FDA regulations, (2) why the number of regulatory actions have decreased, (3) the impact of downgraded or disapproved recommendations for regulatory actions on district compliance personnel, (4) the extent to which disapproved recommendations can be reduced, and (5) whether FDA headquarters has provided appropriate criteria and direction to district compliance personnel. We performed this review because of the congressional and public concern expressed about the reductions in the number of regulatory actions by FDA beginning in fiscal year 1981.

The review was performed at FDA headquarters in Rockville, Md., and at the Philadelphia, Pa.; Baltimore, Md.; Boston, Mass.; Chicago, Ill.; and Newark, N.J., district offices. We selected these districts because they represented one-third of

FDA's drug enforcement activity. We concentrated our efforts on 3 of the 25 FDA drug compliance programs: drug process inspections, drug listing and registration, and drug problem defect reporting. These three compliance programs are estimated to account for about 60 percent of the field staff time devoted to drug enforcement.

We reviewed the proposed regulatory actions submitted by the five districts included in our review during fiscal years 1979, 1980, and 1981 which were subsequently disapproved to determine the reasons for the disapprovals and whether they could have been prevented. We also reviewed a sample of approved actions to determine the timeliness of these actions.

We reviewed 35 seizures where little, if any, products were seized to determine whether all reasonable actions had been taken to remove violative products from the marketplace.

We also reviewed selected reports and other supporting documentation on inspections made by FDA during fiscal years 1979-81 to determine whether identified deficiencies had been followed up in the following inspection. To do this, we took a sample of firms from the districts' lists of registered firms after first eliminating those firms which we could identify that should not have been on the registration lists. Using this method, we selected 92 firms in 4 districts which is about 10 percent of the drug firms in those districts. We reviewed all inspection reports during this period for these firms. We identified 95 reports where deficiencies had been noted and where comprehensive follow-on inspections had been conducted. We did not perform this analysis in Philadelphia because we had not identified followup as a problem when our work in that office was performed.

We also reviewed agency policies and procedures concerning regulatory actions, appropriate laws, regulations, and manuals, and we interviewed responsible FDA officials.

Our review was conducted during the period October 1981 through February 1983. It was performed in accordance with generally accepted governmental auditing standards.

CHAPTER 2

FDA SHOULD DEVELOP A METHOD TO MEASURE THE EXTENT TO WHICH VOLUNTARY ACTION IS RESULTING IN COMPLIANCE

In recent months, considerable concern has been expressed by Members of Congress and by public interest groups about the substantial decline in the number of regulatory actions taken by FDA against drug manufacturers, processors, and repackers and FDA's increased emphasis on obtaining voluntary correction of GMP violations. Critics charge that volunteerism does not work and encourages drug firms to become lax in adhering to GMPs. Proponents argue that it is a more cost-effective approach to regulation than the more formal and time-consuming regulatory process.

Our review did not lead us to conclusions as to which of the two approaches is better, but did indicate that FDA has not developed a mechanism to determine the extent to which the voluntary approach is resulting in compliance with GMPs. Since this approach can have a significant impact on the (1) manner in which FDA uses its resources, (2) amount of resources required, and (3) manner in which FDA deals with the drug industry, we believe it is important that FDA develop a system to provide feedback on its effectiveness. This feedback would be useful in determining whether this approach is better than the more formal regulatory one in responding to those who are critical of its use.

REGULATORY ACTIONS AVAILABLE TO FDA

One of FDA's primary functions under the law is to inspect all registered drug firms biennially. FDA requires that problems uncovered during these inspections be promptly and effectively corrected by the firm. If a firm does not correct problems that have been identified, FDA procedures provide for it to take regulatory action.[1]

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[1]For the purpose of this report, a regulatory action is defined as any adverse action whether administrative or legal under consideration by FDA affecting a firm or its product.

The FD&C Act provides FDA a wide array of enforcement remedies with which it is to assure compliance, such as notice of adverse finding letters, regulatory letters, seizures, injunctions, citations, and prosecutions. Product recall is another possible method of removing or correcting consumer products that are in violation of the laws and regulations administered by FDA. Recalls are voluntary actions either initiated by a firm or requested by FDA. With these regulatory tools, used in combination or separately, FDA is able to provide some degree of assurance that a firm is in compliance with the laws and regulations regarding the manufacture and distribution of safe and effective drugs.

THE NUMBER OF REGULATORY ACTIONS HAS BEEN DECLINING, BUT INCREASED IN FISCAL YEAR 1982

The number of regulatory actions taken by FDA against firms violating the FD&C Act and FDA regulations declined considerably in fiscal year 1981. However, primarily because of an increase from 22 to 348 in "direct reference"[2] regulatory letters in fiscal year 1982 caused primarily by a concentrated FDA strategy against "look-alike" drugs, the number of regulatory actions in fiscal year 1982 increased. The following table shows the number of drug-related actions taken during fiscal years 1979-82.

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[2]"Direct reference" refers to regulatory letters which the districts are authorized to issue without prior Office of Drugs' approval.

Regulatory Actions Taken by FDA Against Drug Firms

	Fiscal year			
	1979	1980	1981	1982 (note a)
Regulatory letters	146	121	92	407
Seizures	170	228	97	82
Injunctions	11	4	1	2
Prosecutions	3	5	2	-
Others (note b)	13	7	3	1
Subtotal	343	365	195	492
Recalls	200	214	188	131
Total actions	543	579	383	623

a/Regulatory actions submitted by the districts during fiscal year 1982 and approved as of October 26, 1982.

b/These include citations (notices of hearings to be held before prosecution), disqualifications of clinical investigators, and revocations of licenses.

As shown in the table, the most significant reduction was in seizure actions taken between fiscal years 1980 and 1981, a reduction of 131 (or about 58 percent). It should be pointed out, however, that about half of the seizures in fiscal year 1980 were against only two firms. In 1981, one of the firms ceased operations and the second firm was purchased by another drug manufacturer.

While there are a number of reasons for the decline in the number of regulatory actions in fiscal year 1981, we concluded, based on our review, that the principal reason was the increased emphasis on voluntary corrective action. Other factors causing the decrease included:

--A 24-percent reduction in the number of inspectors which, according to FDA, went from 1,183 in fiscal year 1978 to 903 in fiscal year 1982.

--An emphasis on abbreviated inspections and inspection reports. According to ACRA, despite the reduction in the number of inspectors, the number of inspections increased by 11 percent in fiscal year 1981.

--Merit pay contracts which may discourage submission of proposed regulatory actions because disapproved actions adversely affect performance ratings. These contracts also require an increase in the number of inspections.

FDA officials also attributed the declining actions to FDA's correction of problems and to its clarification of unclear policies which in the past had resulted in violations because drug firms did not know what was expected of them. According to these officials, FDA has issued a variety of regulations and standards that make it clear to manufacturers what is expected, which makes compliance more likely without requiring enforcement action.

VOLUNTARY COMPLIANCE

FDA has been encouraging voluntary compliance with GMP requirements for years. For example, the Food and Drug Director of Region III, in a November 1978 directive implementing the FDA policy of voluntary compliance, stated that voluntary compliance measures should be given a chance to work and, if they failed, appropriate legal actions would be taken. All of FDA's legal action recommendations submitted to its headquarters are required to contain at least a paragraph about the opportunities for voluntary corrections and any efforts made to achieve voluntary corrections. FDA intensified the emphasis on voluntary compliance in fiscal year 1981. In an August 1981 memorandum, EDRO expressed concern that the number of voluntary corrections was not being highlighted enough to show that a good mix existed between the use of both regulatory and voluntary compliance systems. In October 1981, FDA implemented the voluntary correction reporting system.

Voluntary correction reporting system

FDA's voluntary correction reporting system is intended to record the voluntary correction of violations discovered during inspections. It was not intended to capture all voluntary corrections. The system does not include

--recalls because they are recorded elsewhere,

--corrections not directly attributable to the efforts of FDA district offices or States under contract to EDRO,

--corrections made as a result of actions other than an inspection investigation or sample analyses, and

--corrections related to a recommended regulatory action.

To report a voluntary corrective action, the district has to show that a problem was detected, that it was corrected, and that the correction was verified. A detected problem is one which was observed by FDA or referred to FDA by a State, local, or other Federal official, and it must be the result of an inspection, investigation, or sample analysis. Voluntary corrective actions taken as a result of the efforts by other FDA components, such as the Office of Drugs, would not be recorded in the system. Verification of corrective action involves a Federal, State, or local official observing such an action and reporting it in writing to FDA. The verification must be based on an inspection, an investigation, or a letter from a firm to FDA (in response to a notice of adverse finding letter) certifying the problem has been corrected. Firm responses to an inspection observation, regulatory letter, and the like are not acceptable verification of a corrective action in this system.

Although FDA's voluntary correction reporting system is making some progress in recording voluntary corrections, the evidence is not conclusive that voluntary compliance is equal to or exceeds corrections made as a result of more formal enforcement actions. For the first 6 months of fiscal year 1982, data collected by FDA showed that about 2,500 voluntary corrections had been verified by it. About 8 percent of these corrections were made by drug manufacturers. The remaining 92 percent involved corrections made by food, cosmetic, veterinary, and medical device firms. In 502 of the above cases, the voluntary corrective action involved destroying the product, which negated the need in some cases for FDA to seize the product or enjoin the manufacturer from producing the product.

CONCLUSIONS

Beginning in fiscal year 1981, FDA increased the emphasis it has given to voluntary compliance with the law and GMPs by drug firms. Like any other approach, volunteerism has advantages and disadvantages. Volunteerism appears to be a less costly approach to regulation because of the decrease in paperwork and legal action involved. Volunteerism also appears to be a more tolerable approach to the firms involved because it is likely to produce fewer confrontations and less adverse publicity. However, FDA has not documented the extent to which voluntary correction achieves compliance. Thus, we believe FDA should develop a mechanism for measuring the extent to which the voluntary compliance approach is working.

In developing this mechanism, particular attention should be given to the (1) total number of violations detected, (2) type and severity of violations detected, (3) type of firms (e.g., small, large, generic, proprietary) causing the most compliance problems, (4) type of corrective actions being taken, (5) number of repeat violations, and (6) cost of the voluntary approach and its impact on FDA's inspection resources.

RECOMMENDATION TO THE SECRETARY OF HHS

We recommend that the Secretary direct the Commissioner of FDA to develop a mechanism to measure the extent to which voluntary corrective actions result in compliance.

AGENCY COMMENTS AND OUR EVALUATION

In a draft of this report, we proposed that the Secretary of HHS direct the Commissioner to develop a system to measure the effectiveness of the voluntary compliance process. HHS concurred in principle with the proposal, but expressed some concerns about how to accomplish the objectives of the proposal. HHS stated that in the past FDA had attempted to do focused evaluations of its effectiveness in obtaining compliance, but found it difficult to measure because all factors having a bearing on the compliance policy would need to be identified and controlled. Accordingly, this would be particularly difficult today because of the (1) changes in industry technology which make compliance with the law and regulations more attainable, (2) publication of FDA regulations and guidelines which let industry management know what is expected, and (3) change in FDA policies regarding actionable inspection findings. Furthermore, one FDA official stated that he believes the agency would have to hire a consultant and spend a considerable sum to perform the type of evaluation suggested by the proposal.

Since it was not our intention for FDA to spend a large sum of money to measure the effectiveness of voluntary compliance, we have clarified this recommendation. Since FDA already follows up on promised voluntary corrections, we believe that it would not be difficult to take one step further to determine not only what corrective actions have been taken, but also the extent to which promised voluntary corrective actions have not been taken and the reasons therefor. HHS advised us that it agrees with the revised recommendation and will take the action necessary to develop the recommended mechanism.

CHAPTER 3

VIOLATIVE DRUG PRODUCTS ENTERING MARKETPLACE COULD BE REDUCED IF FDA HAD ADMINISTRATIVE DETENTION AUTHORITY

The amount of violative drug products entering the marketplace could be reduced if FDA had the authority to administratively detain these products at a firm's facility until the product is seized or other appropriate action is taken to prevent distribution. Information supplied by FDA shows that at least 33 percent of the 495 seizures approved during fiscal years 1979-81 resulted in no products being seized. In other cases, very small amounts of the violative products were seized. FDA could not take action primarily because the products were moved by the firms before action could be completed.

Although most States have authority to embargo drug products, cooperation between the States and FDA varies considerably. In most cases the States are reluctant to use their authority until they have assurance from FDA that a seizure will be approved and carried out. FDA is generally unable to provide such assurance.

FDA has authority under the FD&C Act to detain medical devices and imported products. It also has authority under various statutes administered in cooperation with other agencies to detain a number of other products. However, attempts in recent years to obtain authority to detain drug products produced in the United States have been unsuccessful.

FDA HAS FAR-REACHING DETENTION AUTHORITY--BUT NOT FOR DRUGS PRODUCED IN THE UNITED STATES

FDA has the authority to administratively detain and refuse admission into the United States a wide variety of products both under the FD&C Act and statutes administered in cooperation with other agencies, but it does not have such authority for drug products produced in the United States.

Section 304(g) of the FD&C Act (21 U.S.C. 334) provides that during an inspection of a facility, FDA may detain a medical device that is believed to be adulterated or misbranded. The detention period cannot exceed 20 days. (During that period the device may not be used, moved, altered, or transferred unless authorized by FDA or the device is released by FDA.)

This section also provides that if a longer period of detention is required to institute seizure or injunction action, the device may be detained for no more than 30 days. Presently, FDA's implementing regulations apply only to devices intended for human use.

Section 801 of the FD&C Act (21 U.S.C. 381) gives FDA authority to refuse admission of any food, drug (including biological products), devices, and cosmetics which are being imported into the United States, if FDA determines that the products are misbranded or adulterated. This section provides that such misbranded or adulterated products are to be destroyed, reexported, or in appropriate cases, allowed admission if relabeling or other action can bring the product into compliance with the FD&C Act.

In addition to its authority under the FD&C Act, FDA has detention authority and authority to refuse admission of products offered for import into the United States under several other statutes. These include:

--Section 360(a) of the Radiation Control for Health and Safety Act of 1968 (42 U.S.C. 263h(a)) authorizes FDA to refuse admission of any radiation emitting equipment, such as microwave ovens, which are being imported into the United States, if it determines that the product certification is false or misleading. This section provides that such noncomplying electronic products are to be destroyed, reexported, or in appropriate cases, allowed admission if the product can be brought into compliance with the applicable standards.

--Sections 402 and 409(b) of the Federal Meat Inspection Act (21 U.S.C. 672 and 679(b)) authorize FDA to detain meat products found outside any premises where an inspection is being maintained under the Meat Inspection Act for purposes of enforcement of the FD&C Act.

--Sections 19 and 24(b) of the Poultry Products Inspection Act (21 U.S.C. 467a and 467f) authorize FDA to detain poultry products found outside any official establishment for purposes of enforcement of the FD&C Act.

--Sections 19 and 23(d) of the Egg Products Inspection Act (21 U.S.C. 1048 and 1052(d)) authorize FDA to detain egg products found at other than the inspected facility if it believes the products are in violation of the Egg Products Inspection Act.

Under the latter three statutes detention is for a period of up to 20 days, and the products cannot be moved from the place of detention until authorized by FDA.

ATTEMPTS TO OBTAIN DETENTION AUTHORITY FOR DRUGS HAVE BEEN UNSUCCESSFUL

FDA has sought authority to detain drug products on numerous occasions since 1974. All of these attempts have been unsuccessful. Administration bills were introduced in each Congress from the 93d in 1974 to the 96th in 1980.

Only one bill, S. 1075 (96th Congress, 1st session) received congressional action. The bill was passed by the Senate on September 26, 1979. Known as the "Drug Regulation Reform Act of 1979," S. 1075 proposed numerous changes in FDA's authority including increased civil penalties, subpoena authority, and administrative detention of drug products. Section 107 of the bill provided for amending section 304(g) of the FD&C Act by adding drugs to the detention authority FDA already had for medical devices. S. 1075 was referred to the House of Representatives in October 1979, but was not acted upon by the House.

DETENTION AUTHORITY COULD HAVE PREVENTED VIOLATIVE PRODUCTS FROM ENTERING THE MARKETPLACE

Many seizures are resulting in little or no violative products being recovered. We reviewed 35 recommended seizure actions in fiscal years 1979-81 by the five district offices included in our review. The 35 cases were selected from among those on which little or no violative products were recovered. We found that in most cases detention could have helped keep violative products off the market.

To seize a product believed to be adulterated or misbranded, FDA may request the manufacturer or distributor to voluntarily hold the product until seizure can be accomplished, request the State to embargo the product, request the manufacturer to recall the product, or wait for a seizure recommendation to be approved internally. Seizure recommendations must be approved by the district office, the regional office (in case of mass seizures), the Office of Drugs, ACRA, and the Office of General Counsel. For the 35 cases we reviewed, this process took, on the average, 61 days ranging from 6 to 154 days. Only 24 of the 35 cases were approved by the Office of General Counsel because these were the only ones where the products were believed to be still available for seizure. The General Counsel took no action on the other 11 cases because the products were not available for seizure.

After approval by the General Counsel, FDA must determine if the product is still available. This step could be eliminated if the product was already under FDA detention. If FDA finds that the product is still available, a complaint for seizure is filed by the U.S. Attorney's Office with the appropriate district court. The court then orders the U.S. Marshall to seize the violative product. In addition to the 61 days taken by FDA, we found that an average of 34 days was used to process the seizure orders through the U.S. Attorney's Office and the court and accomplish the seizure. Of the 24 cases approved by the General Counsel only 17 complaints for seizure were filed. The other cases were dropped because the violative product was no longer available. The U.S. Marshall successfully seized products in only nine cases. These seizures resulted in the recovery of about $1,220 in goods. While we could not determine the total value of the products available when the initial inspection was made in every case, the value of the available products for 27 of the 35 proposed seizure actions was estimated by FDA to be $192,000.

Seven of the proposed seizure actions we reviewed involved one manufacturer who had shipped to seven locations a product FDA believed was contaminated. FDA had requested the manufacturer to recall the product, but the manufacturer disagreed with FDA's analysis and refused to recall the product. Although FDA began seizure actions, none of the product was recovered.

We also found that FDA had limited success in obtaining a voluntary hold from distributors, and we found no cases in which a State embargo was requested. However, it should be pointed out that in some cases the products were moving so quickly that a State embargo may not have been possible.

We discussed FDA-State relations with district office officials and were told that cooperation varies from State to State. In the area covered by the five districts included in our review, one State does not have embargo authority for drug products, four others and the District of Columbia have never been asked to embargo drug products, and cooperation between FDA and the remaining eight States ranges from limited to very good. FDA officials in all five districts told us, however, that none of the States will embargo a product unless they can get an assurance from FDA that a seizure action will be accomplished.

An FDA official in one district office told us that his district generally would not ask a State to embargo a product until the General Counsel had approved the seizure. FDA officials in two other districts told us that they would not

request States to embargo drug products until they were reasonably sure concurrence would be forthcoming from the General Counsel. In the 35 cases we reviewed, nearly one-third were never approved by the General Counsel because the products were no longer available for seizure. Thus, under these conditions, the potential for State assistance becomes limited.

If FDA had detention authority, additional seizures could have been accomplished. For example, in one case FDA made an availability check on March 28, 1979, and found that a distributor had 146,000 tablets valued at nearly $6,000 available. Five days later, on April 2, 1979, the U.S. Marshall attempted seizure and found no product to seize. In another case, over $6,000 of unapproved new drugs were found at a drug distributor's facility. An Office of Drugs' memorandum to ACRA requesting approval of the seizure stated that "Since the dealer is not cooperatively holding, we ask that this action be expedited." Seizure was not attempted until 40 days later and the U.S. Marshall confiscated goods valued at $133.

In February 1980 FDA learned that two lots of a drug product had failed FDA-required testing. It also learned that one shipment of 1.3 million tablets valued at over $16,500 had been made to a distributor.

In an April 21 memorandum to ACRA, the Office of Drugs stated:

> "[This product] is a critical drug which should be promptly removed from the market if it is found to fail content uniformity requirements. We would like to point out that the firm was informed of the failing results by telephone on February 25, 1980 and follow-up TWX [communication] on February 27, 1980 by Certification Services Branch. The firm responded by letter dated March 17, 1980 in which they questioned our dissolution test results and ignored the content uniformity failures."

The seizure was approved by the Office of General Counsel on April 25, 1980. Seizure, however, was not attempted until June 18, 1980, at which time none of the product was available. FDA's lack of detention authority contributed to over 1.3 million violative tablets becoming available for public consumption.

CONCLUSIONS

Larger numbers of violative drug products could be kept out of the marketplace if FDA had authority to administratively detain such products. Although FDA has far-reaching detention authority under the FD&C Act and other statutes to detain various products, repeated attempts to obtain that authority for drug products produced in the United States have been unsuccessful. We believe that such detention authority could also speed up the process of approving and ultimately carrying out seizure actions because of the limited time products may be detained.

RECOMMENDATION TO THE CONGRESS

We recommend that the Congress amend section 304(g) of the FD&C Act by adding drug products to the language which gives FDA the authority to detain administratively medical devices. Suggested language to accomplish this recommendation follows.

> "Section 304(g) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 334(g), is amended by inserting the words 'drug or' before 'devise' wherever it appears and by inserting after 'misbranded' the words 'or otherwise subject to seizure.'"

AGENCY COMMENTS

In commenting on a draft of this report, HHS advised us that in the past, FDA has proposed legislation that would authorize administrative detention for regulated products and would consider such legislation for the fiscal year 1985 legislative proposals.

CHAPTER 4

FDA SHOULD TAKE ACTIONS TO REDUCE THE NUMBER OF DISAPPROVED REGULATORY RECOMMENDATIONS

FDA could reduce the number of district-proposed regulatory actions which are disapproved by FDA headquarters if (1) the Office of Drugs would develop definitive policies on actions to be taken on violations involving medically insignificant drugs and technical (insignificant) violations of the GMP regulations, (2) the districts were to submit recommendations in accordance with established policy and procedures, and (3) EDRO provided additional guidance to the districts on what constitutes sufficient evidence to support alleged violations. Each proposed regulatory action takes a considerable amount of time to prepare and review. To the extent the preparation of actions which are disapproved by headquarters can be avoided, the districts would have more time available to devote to other activities.

The disapproval of proposed regulatory actions is not in itself an indication of inefficiency or ineffectiveness. The district offices should not be discouraged from submitting proposed regulatory actions just because there is a chance that the proposed action will be disapproved. We agree with a comment by HHS in its comments on a draft of this report that:

> "investigators should be encouraged to identify apparent issues or problems and refer them to headquarters for determination of whether they should be considered as instances of non-compliance which should be pursued with regulatory action. It is through this mechanism that FDA investigators and compliance officers at all levels are encouraged to keep current in monitoring a rapidly changing, technologically advanced industry and to be alert to previously unidentified deficiencies that could have significant impact upon the quality of products and the public health."

However, if experience shows that proposed actions on a particular issue are repetitively disapproved, FDA should take action to advise its districts that those types of proposed actions will be disapproved and what other action, if any, the districts should take.

The preparation, submission, and review of a proposed regulatory action is a multistep process. At the district office, once an inspection of a drug firm is completed and the

violations indicate the need for possible regulatory action, the inspection report and associated evidence are reviewed by supervisory inspection personnel and the Director of the Investigations Branch who recommend what type of action should be taken against the firm. The proposed action is then reviewed by a compliance officer and the Director of the Compliance Branch who, upon concurrence, submit the recommendation to the District Director for review and approval. If approved, the District Director forwards the recommendation with the associated evidence to the Office of the Associate Director for Compliance, Office of Drugs. The recommended action is sent for review to one of four divisions that is responsible for the type of products and deficiencies noted in the district's recommendation. The division can recommend approval or disapproval of the district's proposed action. The final decision rests with the Associate Director for Compliance. When the Associate Director for Compliance approves a regulatory letter, the district office is notified and the letter can be issued by the district. Seizures, prosecutions, and injunctions approved by the Associate Director for Compliance must also be reviewed and approved by FDA's ACRA and the Office of General Counsel.

All actions disapproved by the Associate Director are returned to the district office with an explanation for the disapproval. If the district believes that the disapproval was not warranted, it may appeal the case through EDRO to ACRA and attempt to overturn the Associate Director's decision.

The following table shows the number of proposed regulatory actions submitted by the FDA district offices during fiscal years 1979-81 and the number of those proposed actions that were disapproved by FDA headquarters. The disapproved actions varied between 26 and 34 percent of proposed actions during those 3 years.

Proposed Regulatory Actions (note a)

	Fiscal year 1979		Fiscal year 1980		Fiscal year 1881	
	Sub-mitted	Disap-proved	Sub-mitted	Disap-proved	Sub-mitted	Disap-proved
Regulatory letters	173	63	141	38	96	26
Seizures	244	74	297	69	138	41
Injunctions	21	10	17	13	6	5
Prosecutions	5	2	6	1	2	-
Total	443	149	461	121	242	72

a/The proposed regulatory actions shown in this table represent only those actions submitted to the Office of Drugs for approval. It does not include "direct reference" actions taken by district offices because these actions do not require the Office of Drugs approval.

The five districts included in our review submitted 190 proposed regulatory actions in fiscal year 1979, 212 in fiscal year 1980, and 76 in fiscal year 1981. Of these, 60 were disapproved in fiscal year 1979, 44 in fiscal year 1980, and 29 in fiscal year 1981--about the same rate of disapproval as all the districts.

We reviewed 119 of the 133 disapproved regulatory actions submitted by the five district offices included in our review. Files on the other 14 cases were unavailable for review. We found that:

--Nineteen, or 16 percent, were disapproved because the proposed actions were not in accordance with present Office of Drugs' policy.

--Eighteen, or 15 percent, were disapproved because a clear policy had not been disseminated to all the district offices.

--Fourteen, or 12 percent, were disapproved because sufficient evidence was not submitted to support the recommended action.

--The other 68 proposed actions were disapproved for various reasons. Some of these disapprovals could have been avoided. For example, we found five cases that were disapproved due to lengthy time delays either in submitting the proposed action or in the Office of

Drugs review process. We found 11 cases that were disapproved because the proposed actions were based on the marketing of unapproved drugs which were approved by FDA subsequent to the submission of the proposed regulatory action. The status of these approvals could have been determined by a telephone call to the Office of Drugs before the recommended action was submitted.

We discussed the time required to prepare a recommended regulatory action with district officials. While most could not give us an estimate of the time required, one official estimated that his district used about 46 hours to review a regulatory letter, 28 hours for a seizure, between 53 and 61 hours for an injunction, and between 91 and 94 hours for a prosecution. This time does not include the time required to do the inspection, prepare the report, and discuss the possible actions to recommend. It also does not include the time required by the Office of Drugs' staff to review and respond to the proposed action.

NO CLEARLY ESTABLISHED POLICY REGARDING VIOLATIONS INVOLVING MEDICALLY INSIGNIFICANT DRUGS

Although there is no clearly established policy on violations involving medically insignificant drugs,[1] it appears that the Office of Drugs position has been to take no formal enforcement actions. During the 3-year period covered by our review, we found no cases involving medically insignificant drugs that were approved. Thus, district office staff time has been wasted developing recommended actions.

According to an FDA official, in early 1979, the Office of Drugs established a task force to develop a definitive policy on medically insignificant drugs. Because of the complexity of the problems encountered, the task force was unable to develop such a policy. Each division within the Office of Drugs was left to handle problems on a case-by-case basis. On August 20, 1979, the Division of Drug Manufacturing (now Division of Drug Quality Compliance), which is responsible for developing the basic Office of Drugs enforcement strategies for compliance programs regarding drug manufacturing practices, issued a memorandum establishing that Division's position. The memorandum stated that violations involving insignificant drugs which would pose no health hazard by reason of noncompliance with GMPs would not be enforced.

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[1]A medically insignificant drug is one which is sold over the counter, is used externally, and would not harm the user even if found violative.

Despite that Division's position, it appears that districts were confused since they continued to submit recommendations concerning medically insignificant drugs. We identified 12 subsequent recommendations--6 regulatory letters and 6 seizures--concerning medically insignificant drugs that were submitted by the 5 districts included in our review.

For example, one district recommended that a regulatory letter be issued to a firm that produced only one product, a medicated body powder. The district's recommendation included nine specific GMP violations. The district also pointed out that the firm had a history of these types of violations. The recommendation was disapproved by the Office of Drugs as contrary to policy. The disapproval memorandum issued by the Division of Drug Manufacturing stated that:

> "We are dealing here with a one product firm that manufactures an [over-the-counter] topical powder with little, if any, therapeutic significance. In the absence of some unusual problem, such as cross-contamination it would seem almost impossible that such a product could be manufactured faultily.
>
> "We note that your supervisory investigator recommended that no regulatory action be initiated. We agree with his conclusion."

Subsequent to this disapproval, the same district submitted four other recommendations for actions concerning medically insignificant drugs.

Another district proposed a seizure action against a firm that produced an over-the-counter topical ointment. In the disapproval memorandum the Office of Drug's Associate Director for Compliance stated:

> "* * * the potential benefits to be gained from initiating regulatory action against a firm must be weighed against the manpower (cost) necessary to correct [current good manufacturing practice] deviations. The resources expended to document, recommend and accomplish seizure/injunction/prosecution of a small firm manufacturing a limited number of topical [over-the-counter] drugs of little therapeutic significance do not, we believe, add significantly to the protection of the consumer's health. Such resources could be better utilized in the identification and correction of more egregious violations.

"Therefore, absent a showing of therapeutic significance or potential health hazard, we are not prepared to take regulatory action against the type of [over-the-counter] topical drugs/firms described above. We believe this position is consistent with the intent of Section 306 of the Act and with the Agency's charge to provide the maximum protection possible within the scope of our limited resources."

The district offices also proposed six regulatory actions based primarily on technical violations of the GMP regulations. According to FDA officials, technical violations are infractions of the GMP regulations which will have no adverse effect on manufactured drug products, such as the lack of a complete record for all returned products or the lack of formal written procedures for handling consumer complaints. The Office of Drugs has not developed a policy on this issue, but the position taken by the Associate Director of Compliance has been to take no enforcement action on only technical violations. This position, however, was not communicated to the districts. This resulted in recommendations being submitted by the districts that had little chance for approval and resources being wasted.

RECOMMENDATIONS SUBMITTED FOR ACTIONS CONTRARY TO THE OFFICE OF DRUGS' POLICY

In addition to the above cases, 19 recommendations were made for actions contrary to established Office of Drugs' policy. For example, drugs marketed before 1962 which are considered to be safe are currently being reviewed for efficacy by FDA. Until these drugs are proven to be ineffective, FDA policy precludes regulatory action unless a health hazard exists due to manufacturing problems. We found 10 cases submitted by the districts included in our review recommending regulatory action contrary to this policy. In addition, it is the Office of Drugs' policy to first inform a firm of a problem through a regulatory letter before taking seizure actions unless there is a serious health hazard. We found five cases in which seizure recommendations were submitted and subsequently disapproved because adequate prior warning was not given.

RECOMMENDATIONS DISAPPROVED BECAUSE OF A LACK OF EVIDENCE TO SUPPORT RECOMMENDED ACTION

Although guidance is given to the district offices in the Inspections Operations Manual and inspectors receive training

in what constitutes proper evidence, district offices are submitting some recommended actions that are subsequently disapproved because the evidence submitted is inadequate to support the recommended action.

We found 14 cases in which the lack of evidence was the primary reason or a contributing factor which resulted in disapproval by headquarters. For example, one district recommended a seizure action against a firm that advertised a product as a prevention and cure for such diseases as cancer, ulcers, and high blood pressure. The district contended the product was misbranded. The Office of Drugs disapproved the recommendation because materials needed to support the recommendation, such as the advertising materials and the product labeling--basic evidence needed to support a seizure in the courts--were not submitted for review.

In another case, which resulted in the disapproval of five separate seizure actions, headquarters informed the district that based on the evidence submitted it was not prepared to proceed with seizure action. The disapproval memorandum questioned the adequacy of much of the evidence submitted by the district. Headquarters also recommended that future visits to the establishment be made by a person who had sufficient experience to verify the manufacturer's testing procedures.

Finally, one district recommended a seizure action because finished products of the firm were thought to be nonsterile. Headquarters noted that the inspection report did not point out any reasons why a sterility problem existed and that there was no evidence that the inspector entered or reviewed the firm's sterile facility.

One reason for recommendations being submitted with insufficient evidence is a lack of internal coordination at the district level. In one district we found that five cases were disapproved or downgraded because investigators and compliance officers did not discuss the cases and coordinate their activities. For example, in one case involving a recommended seizure, the inspection report did not clearly identify which products were adulterated. Consequently, the Office of Drugs could not identify which products and how much of each were to be seized and disapproved the recommendation. In this case, the district's investigations branch recommended that a regulatory letter be issued and provided evidence to support that action. Although the Compliance Branch recommended a seizure action, we found no indication that the Compliance Branch requested the Inspections Branch to supply the additional evidence necessary to support a seizure action. We found similar coordination problems in another district.

CONCLUSIONS

Proposed regulatory actions require a considerable amount of district office and headquarters time to write, review, and approve or disapprove. To the extent proposed regulatory actions submitted by the districts that are subsequently disapproved by headquarters can be avoided, the districts and headquarters will have time available to devote to other duties.

We recognize that there will always be some cases disapproved by headquarters because of various reasons, such as the need to assure that all firms are treated equitably. However, time spent on many of the cases that have been disapproved could have been avoided if (1) headquarters had clearly delineated for the district offices its policy on taking regulatory action against firms who produce medically insignificant drugs and the policy regarding technical violations of the GMP regulations; (2) the district offices had done a better job in reviewing their proposed actions to assure they were consistent with the headquarters policy; (3) communications among district inspection officials, district compliance officials, and headquarters officials were improved; and (4) headquarters had provided additional guidance to the district offices on evidence required to support proposed regulatory actions.

In addition, the district offices need to review proposed regulatory actions more closely to assure that necessary evidence is submitted with the cases. The proposed actions that we reviewed which were disapproved by headquarters because of a lack of evidence did not contain the evidence needed to support the violation. A more thorough district office review should have detected this.

RECOMMENDATIONS TO THE SECRETARY OF HHS

The Secretary should require the Commissioner of FDA to:

--Develop and distribute to all districts definitive policies on actions to be taken on violations involving medically insignificant drugs and technical violations of GMP regulations.

--Provide additional guidance to the district offices on evidence required to support proposed regulatory actions.

--Encourage greater coordination and communications among district investigators, district compliance officials, and headquarters officials to better assure (1) district and headquarters officials agree on actions to be taken and (2) documentation to support recommended actions is appropriate.

AGENCY COMMENTS AND OUR EVALUATION

HHS agreed with our recommendation that FDA should develop and distribute to all districts definitive policies on actions to be taken on violations involving medically insignificant drugs and technical violations of GMP regulations. HHS said that FDA is currently evaluating its policy on drugs of lesser therapeutic significance and will be formulating new guidelines based upon the results of that evaluation. HHS added that FDA is also reviewing the agency's enforcement policy for over-the-counter drugs and for instances of quackery to determine whether a new policy is warranted.

In commenting on our recommendation to provide additional guidance to the district offices on evidence required to support proposed regulatory actions, HHS believes guidance currently available to the districts is adequate. Nevertheless, HHS said that FDA will review the guidance to determine if there are areas needing revision and updating. HHS pointed out that the element of judgment will always be an important part of the decisionmaking process and that the most detailed guidance will not eliminate variances in the individual assessment of the facts in similar or identical cases. While we agree that judgment will always play an important role in decisionmaking, we continue to believe that proposed actions which in some cases lack even the most basic types of evidence need to be avoided and additional guidance in this area may be needed.

HHS concurred with our recommendation to encourage greater coordination among district investigators, compliance officials, and headquarters officials. HHS informed us that in a December 1982 memorandum, FDA's Deputy Commissioner had directed ACRA and EDRO to initiate various activities intended to foster improved field/headquarters communications. The memorandum also addresses other activities intended to strengthen the agency's compliance enforcement programs and policies in keeping with the longstanding philosophy of encouraging voluntary compliance and voluntary correction of deficiencies and taking appropriate regulatory action should it become necessary.

CHAPTER 5

NO EVIDENCE IN THREE FDA DISTRICTS THAT INVESTIGATORS ARE FOLLOWING UP ON ALL PRIOR VIOLATIONS

Our review of a sample of inspections made by the Boston, Chicago, and Newark District Offices showed that many of the violations noted were not followed up in subsequent inspections. Our sample included inspections of 82 firms, which is over 10 percent of the registered firms in the three districts. By following up on prior violations FDA can determine whether firms are correcting previously identified violations and compile a history of firms' compliance with the law and regulations.

We reviewed 29 inspection reports in the Baltimore District and did not note a similar problem. FDA's regional manager had issued instructions in November 1978 to districts under his jurisdiction that all inspections and reports must discuss the status of prior violations in a separate section and state reasons why any corrections had not been made. We did not examine inspection reports for followup on prior violations during our work in the Philadelphia District Office because we completed our work in that district before identifying followup of prior deficiencies as a problem.

FDA procedures require that inspectors review the results of prior inspections before beginning an inspection, but there is no clear requirement that inspectors determine whether prior violations have been corrected or comment on the current status of these prior violations in the inspection report.

INSPECTION REPORTS FREQUENTLY DID NOT INDICATE FOLLOWUP OF PRIOR VIOLATIONS

Inspection reports in three of the five district offices visited frequently did not indicate whether FDA inspectors had followed up previously identified deficiencies. In Chicago we found that of 28 inspection reports that had identified deficiencies and where comprehensive follow-on inspections had been conducted, there was no evidence for 14 of these inspections that inspectors had followed up on the status of deficiencies previously reported. In Boston we reviewed 25 inspection reports which discussed 247 deficiencies and found that 153 of these deficiencies (62 percent) were not discussed

in the following inspection reports. In Newark we found that of 21 inspection reports with 196 identified deficiencies, the follow-on inspection did not show the current status in 106 (54 percent) of the deficiencies.

In those three district offices, over 50 percent of the deficiencies cited in the reports we reviewed were not mentioned in the subsequent inspection reports. There was no information in the files as to whether these deficiencies had been corrected. The chief of the Investigations Branch in Newark said that the inspection report format is exception oriented. There is no requirement to document in the inspection report the status of problems cited in previous inspections. According to this official, when an inspection report does not mention deficiencies found in previous inspections, the assumption is that the problem no longer exists because it was not cited again.

The Directors of the Investigations Branches in Boston and Chicago expressed similar sentiments. They said the emphasis in conducting an inspection is on identifying current violations rather than on reporting corrective actions or identifying prior violations that were not corrected. The three districts believe that recent inspection reports will contain more documentation on prior violations due to the current emphasis FDA is placing on voluntary correction of deficiencies.

The following examples are from the inspection files of the three districts.

In Chicago, three inspections made between 1977 and 1980 of one firm, a manufacturer of human drugs in aerosol cans, deodorants, and various cosmetics, noted similar deficiencies. The firm's promised corrective actions were not implemented and the violations continued.

In July 1976, the district had issued the firm an information letter, the predecessor to FDA's Notice of Adverse Findings, concerning its GMP deficiencies. The March 1977 inspection report did not indicate whether corrections had been made. At the conclusion of the 1977 inspection, the investigator noted his observations regarding the firm's questionable sanitation and storage practices. The December 1978 inspection report only noted the date of prior inspection, with no discussion of prior deficiencies. At the conclusion of the 1978 inspection, the investigator noted that he had observed sanitation and recordkeeping deficiencies. The September 1980 inspection report only noted the date of the prior inspection, with no discussion of prior deficiencies. The 1980 inspection report again cited recordkeeping deficiencies.

In Boston, three inspections conducted between 1980 and 1982 of a small manufacturer of topical over-the-counter drug products noted similar deficiencies.

The January 1980 inspection report identified eight deficiencies. No regulatory action was taken because the firm only produced medically insignificant (for definition see footnote 1, p. 19) products. The December 1980 inspection report identified seven deficiencies, of which four were new and three had been identified during the prior inspection. Five deficiencies previously identified were not mentioned. The January 1982 inspection report identified six deficiencies, of which three were new and three had been noted during prior inspections. The status of four deficiencies previously identified was not discussed in the January 1982 inspection report. At the conclusion of the 1982 inspection, the investigator advised the district that a Notice of Adverse Findings letter should be issued to the firm. The investigator's supervisor concluded that because of the nature of the products being produced, i.e., medically insignificant products, a routine followup inspection would be the appropriate action to take.

In Newark, two inspections in 1979 and 1980 of a contract manufacturer of over-the-counter drugs, vitamins, and health foods noted similar deficiencies. The August 1979 inspection report identified seven significant deficiencies. Correspondence from the firm indicated that deficiencies cited in the August inspection report had been corrected. Nine of the 12 deficiencies in the October 1980 inspection report were new and three were carried over from the previous inspection. Four deficiencies previously identified were not mentioned. In a November 1980 letter the firm again promised to correct the cited deficiencies. Based on this letter, the investigator recommended that regulatory action not be taken at this time.

CONCLUSIONS

In many cases, FDA inspectors in three FDA districts were either not following up on prior deficiencies on establishments being inspected or were not documenting the followup. This did not happen in a fourth district where the regional manager had issued specific instructions requiring followup and documentation. Such followup and the documentation thereof are important to assure that firms take necessary corrective action and that an accurate record is developed regarding compliance with the FD&C Act and FDA regulations. For problem firms, such documentation would also help in determining whether more aggressive action by FDA is needed. We be-

current status of previously identified deficiencies as part of their current inspection report.

RECOMMENDATIONS TO THE SECRETARY OF HHS

We recommend that the Secretary direct the Commissioner of FDA to revise the Inspection Operations Manual to require inspectors to (1) determine the current status of all prior unresolved deficiencies and (2) discuss the status of these deficiencies in subsequent inspection reports.

AGENCY COMMENTS AND OUR EVALUATION

HHS advised us that while it would revise the Inspection Operations Manual to more explicitly spell out the requirement for inspectors to determine the current status of previously identified deficiencies and document their findings, it believes the inspectors do, in fact, follow up on such deficiencies. HHS added that it is its understanding that whenever the inspection report does not discuss a previously identified deficiency it is because the deficient condition no longer exists, presumably because it was corrected. We could not determine from our review of the inspection files whether the previously identified deficiencies which had not been discussed in subsequent inspection reports had actually been corrected. However, we do not believe that it can be presumed that the deficiencies had been corrected just because they were not mentioned in the subsequent inspection report. If the inspectors are following up on the deficiencies, it would not require much additional effort to record this fact on the inspection report. If the deficiencies are not being followed up on, they should be.

APPENDIX I

DEPARTMENT OF HEALTH & HUMAN SERVICES — Office of Inspector General

FEB 14 1983

Mr. Philip A. Bernstein
Director, Human Resources
Division
United States General
Accounting Office
Washington, D.C. 20548

Dear Mr. Bernstein:

The Secretary asked that I respond to your request for our comments on your draft of a proposed report "Legislative and Administrative Changes Needed to Improve Regulation of Drug Industry." The enclosed comments represent the tentative position of the Department and are subject to reevaluation when the final version of this report is received.

We appreciate the opportunity to comment on this draft report before its publication.

Sincerely yours,

Richard P. Kusserow
Inspector General

Enclosure

COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES ON THE GENERAL ACCOUNTING OFFICE'S DRAFT REPORT, "LEGISLATIVE AND ADMINISTRATIVE CHANGES NEEDED TO IMPROVE REGULATION OF DRUG INDUSTRY", REPORT NO. HRD-83-24, DATED JANUARY 12, 1983

General Comments

In general, we find this report to be fair and constructive in its presentation of FDA's regulation of the drug industry. There are, however, a few aspects of the report that require clarification. We have addressed these in the context of commenting on the recommendations where possible.

One aspect that needs to be discussed, however, is not related to any particular recommendation. The report implies that a desirable goal would be to reduce dramatically the number of headquarters disapprovals of regulatory actions suggested by the field. We believe that, to the contrary, investigators should be encouraged to identify apparent issues or problems and refer them to headquarters for determination of whether they should be considered as instances of non-compliance which should be pursued with regulatory action. It is through this mechanism that FDA investigators and compliance officers at all levels are encouraged to keep current in monitoring a rapidly changing, technologically advanced industry and to be alert to previously unidentified deficiencies that could have significant impact upon the quality of products and the public health.

We believe it is incorrect to equate disapprovals of proposed regulatory actions with inefficiency or ineffectiveness. A desirable goal would be to reduce repetitive disapprovals of issues that have been resolved by previous referrals. FDA headquarters units should be sensitive to those issues and, when they arise, prepare new instructions to the field delineating an appropriate approach.

GAO Recommendation

We recommend that the Secretary of HHS, direct the FDA Commissioner to:

1. --develop a system to measure the effectiveness of the voluntary compliance process.

Department Comment

FDA concurs in principle with the recommendation. However, we have reservations about this recommendation. FDA has in the past attempted to do focused evaluations of its effectiveness in obtaining compliance. However to truly measure the effectiveness of a particular policy, all other factors that could affect compliance would have to be identified

and controlled. We believe this would be especially difficult in today's world because of the many changes that have occurred, such as technological improvements in the industry that make compliance with the law more attainable, publication of regulations and guidelines to give industry management better guidance about what is expected of them, and changes in FDA policies regarding actionable inspection findings. All these factors have contributed to the current state of compliance and to the problems associated with singling out any one factor to measure its effectiveness.

The recommendation also implies that FDA has significantly altered its compliance policies in the recent past and therefore could make meaningful effectiveness comparisons between the past enforcement activities and current activities. We do not believe this to be the case. FDA's policy has always been to seek voluntary corrections of deficiencies to the maximum extent possible and to use more formal enforcement approaches only when voluntary action is not forthcoming. There is, therefore, no historical baseline for making a comparison of the type that could indicate effectiveness.

However, we understand GAO is revising this recommendation in their final report to read that the Secretary direct the Commissioner to develop a mechanism to measure the extent to which voluntary corrective actions result in compliance. We find such a revision acceptable and would take the action necessary to develop the recommended mechanism.

GAO Recommendation

2. --Develop and distribute to all districts definitive policies on actions to be taken on violations involving medically insignificant or innocuous drugs and technical violations of GMP regulations.

Department Comment

We agree. FDA is currently evaluating its policy on drugs of lesser therapeutic significance and will be formulating new guidelines based upon the results of the evaluation. FDA is also reviewing the agency's enforcement policy for over-the-counter drugs and for instances of quackery to define a new policy if it is warranted. It should be noted that FDA does not consider medically insignificant drugs to be innocuous drugs. We would suggest that that term be changed in the report and deleted from this recommendation.

GAO Recommendation

3. --Provide additional guidance to the district offices on evidence required to support proposed regulatory actions.

Department Comment

While we believe adequate guidance is available to the districts regarding evidence necessary to support regulatory actions, FDA will review the guidance to determine if there are areas needing revisions

and updating. It should be recognized, however, that the element of judgment will always be an important part of the decision-making process and that the most detailed guidance will not eliminate variances in practice brought about by individual assessments of the facts in similar or identical cases.

GAO Recommendation

4. --Encourage greater coordination and communications among district investigators, district compliance officials, and headquarters officials to better assure (1) district and headquarters officials agree on actions to be taken and (2) documentation to support recommended actions is appropriate.

Department Comment

We concur. In a memorandum dated December 10, 1982, the Deputy Commissioner of Food and Drugs directed the Associate Commissioner for Regulatory Affairs and the Executive Director of Regional Operations to initiate various activities intended to foster improved field/headquarters communications. The memorandum also addresses other activities intended to strengthen the agency's compliance enforcement programs and policies in keeping with the longstanding philosophy of encouraging voluntary compliance, voluntary correction of deficiencies, and taking appropriate regulatory action should it become necessary.

GAO Recommendation

5. --revise the Inspection Operations Manual to require inspectors to (1) determine the current status of all prior unresolved deficiencies and (2) discuss the status of these deficiencies in subsequent inspection reports.

Department Comment

While we agree to revise the Inspection Operations Manual (IOM) to more explicitly spell out the requirement for inspectors to determine the current status of previously identified deficiencies and document their findings, we believe the current IOM addresses this issue; and that investigators do, in fact, follow up on such deficiencies. Since FDA's IOM directs investigators to document all their findings, it is our understanding that whenever the Establishment Inspection Report (EIR) does not discuss a deficiency observed in a previous inspection, it is because the deficient condition no longer exists, presumably because it was corrected. We interpret GAO's statements to be more a problem of the investigators adequately documenting their audit trail than one of failure to followup deficiencies. FDA will, nevertheless, revise the IOM to explicitly require documentation of followup.

GAO Recommendation to the Congress

We recommend that the Congress amend Section 304(g) of the FD&C Act by adding drug products to the language which gives FDA the authority to administratively detain medical devices.

Department Comment

In the past, FDA has proposed legislation that would authorize administrative detention for regulated products and would consider such legislation for the FY 85 legislative proposals.

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