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BY THE COMPTROLLER GENERAL

Report To The Congress

OF THE UNITED STATES

FDA's Approach To Reviewing Over-The-Counter Drugs Is Reasonable, But Progress Is Slow

Federal law requires the Food and Drug Administration to ensure that drugs sold over the counter are safe and effective. FDA has designed a reasonable approach to regulating this large market, where retail sales are estimated to be $5.2 billion annually.

However, despite reports by scientific panels that many drug ingredients currently marketed are unsafe or ineffective, FDA has been slow in developing and publishing regulations, called monographs, for the formulation and labeling of these drugs. After 10 years, regulations for only 4 of 64 categories of drugs have been issued. Enforcement of monographs may also become a problem.

This report discusses actions that could help speed the review process and improve enforcement.

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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 evaluation of the safety and effectiveness of over-the-counter drugs--a review which began in 1972 and which is not expected to be completed until 1990. The report (1) describes the strategy used to review these drugs, the reasons for taking so long, and the benefits realized to date and (2) contains suggestions for completing the review in a more timely manner and for improving enforcement efforts. Our review was made because our earlier work indicated that the Food and Drug Administration was taking an inordinate amount of time to complete this project.

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

FDA'S APPROACH TO REVIEWING OVER-THE-COUNTER DRUGS IS REASONABLE, BUT PROGRESS IS SLOW

D I G E S T

Are the 200,000 to 300,000 products marketed as over-the-counter (OTC) drugs safe and effective? Although the Food and Drug Administration (FDA) has been reviewing these products since 1972, it has published regulations--called monographs--for only 4 of 64 categories of drug products. FDA estimates that it will be 1990 before all the monographs are published.

In view of the size of the task it faced, FDA adopted a reasonable review process, but it is taking much longer than planned. GAO's review found problems similar to those found in earlier reviews of FDA's procedures for approving new drugs. Some of the same type of actions taken by FDA to speed up new drug approvals could be applied to the OTC drug review.

FDA'S APPROACH-- REASONABLE BUT TIME CONSUMING

FDA's strategy for reviewing OTC drugs is reasonable. It involves making a scientific analysis of available data and setting standards of safety and effectiveness for each ingredient used in classes of drugs, such as antacids or internal analgesics (pain relievers), instead of reviewing each OTC product individually. (See p. 5.)

The OTC review process consists of three phases: review of scientific data by expert advisory panels, review of panel findings and drafting and publishing of monographs by FDA, and enforcement of the monographs by FDA. (See p. 1.)

In 10 years, FDA has completed only 4 of 64 planned final regulations. Average processing time has risen despite greatly increased staff. In 1975, FDA estimated that it would take 15 months to publish a final monograph after the panel report was received. In 1980, this estimate had increased to 72 months for a short monograph and 108 months for a long monograph. (See p. 7.)

The review has resulted in unsafe or ineffective products--such as those containing methapyrilene, a potential carcinogen--being removed from the market. Also, products have been voluntarily reformulated and relabeled, and some drugs that previously were available only by prescription are now sold over the counter. (See p. 11.)

However, most of the review's expected benefits have not yet been realized. Having reviewed the safety and effectiveness of 731 ingredients with 1,393 uses (see footnote, p. 12), the panels concluded that a third of the ingredient uses were unsafe or ineffective and another third lacked sufficient evidence that the ingredients were safe and effective. Many of the drug products containing those ingredients will have to be relabeled or reformulated. (See p. 12.)

FACTORS DELAYING COMPLETION OF THE OTC REVIEW

The review turned out to be a much larger task than anticipated. But other factors related to planning and managing the monograph process have contributed to the delays. Specifically:

--Milestone dates for completing monograph documents were not based on priorities, not sufficiently detailed, and not based on actual experience. Priorities that were set had little meaning.

--Status reports either were not used to track progress in completing monograph documents or did not compare results to projected milestones.

--Policy decisions often were not made promptly.

--The office of the Director of FDA's Division of Over-the-Counter Drug Evaluation had taken over functions related to monograph development that were supposed to be the responsibility of the division's four branches. As a result, the monograph documents got bogged down in the Director's office while staff in the branches were not effectively used. (See pp. 13 to 18.)

MONOGRAPH ENFORCEMENT HAMPERED BY LACK OF ACCURATE LISTING OF OTC DRUGS AND INADEQUATE MONITORING

FDA has implemented two pilot compliance programs. GAO's review of these programs indicated several potential problems for future OTC compliance efforts. For example, the antacid compliance effort was begun in 1976, yet as of January 1982, FDA had not completed its initial review of the identified products. It took FDA about 3 years to identify products subject to the monograph, but it still does not know if it has identified all the products on the market.

The problems were caused by (1) the lack of an accurate listing of OTC drugs, which caused FDA to use the lengthy process of searching catalogs and visiting manufacturers to locate products, and (2) FDA's failure to adequately monitor or evaluate enforcement efforts. (See p. 22.)

RECOMMENDATIONS TO THE SECRETARY OF HEALTH AND HUMAN SERVICES

The Secretary should direct the Commissioner of FDA to:

--Establish priorities for completing individual monographs based on objective criteria, such as consumer sales or market impact, and establish detailed milestones for completing the development of monographs and the publication of final regulations based on actual experience, staff skills and experience, the work required, and the priority of the monograph document.

--Establish goals for expediting the OTC review and develop a system for measuring progress in completing all monograph documents which measures progress against projected milestones and provides feedback to FDA and the Department.

--Develop a mechanism for high-level agency officials to promptly identify and resolve policy issues.

--Review, and revise where appropriate, procedures for reviewing draft monograph documents to ensure that branch personnel are given necessary supervision and authority to develop the products for which they are responsible.

--Determine, based on the anticipated cost and timeliness of alternative approaches, whether the OTC drug listing files are needed. If the listing is not needed, FDA should propose legislation to amend the Drug Listing Act to eliminate the reporting requirement. If it is needed, FDA should assess the relative efficiency of updating the entire system in the next few years or updating the system by drug category as monographs are published.

--Establish measurable objectives for the OTC enforcement effort and the expected timetables for performing the work.

--Maintain for each category of drug product a complete master list of firms manufacturing the drug and a list of products as they are identified for each monograph.

--Track the progress made in reviewing and following up on products subject to the monographs and highlight, through written reports or regular meetings with district representatives, problems encountered in enforcing monographs. (See pp. 19 and 28.)

AGENCY COMMENTS
AND GAO EVALUATION

The Department of Health and Human Services (HHS) agreed with the intent of the GAO recommendations and pointed out a number of corrective actions that had been or were being taken.

HHS did not, however, respond to a major portion of one recommendation which would establish detailed milestones for completing the development of monographs. GAO believes that FDA management needs such milestones to assess progress being made in developing the monograph documents.

GAO also believes that FDA needs to take additional action on several of the recommendations. For example, on the recommendation that goals be established for completing the OTC review, FDA does have short-term goals for some of the monograph documents in the annual merit pay and senior executive service contracts of supervisors and managers.

While these goals are a step in the right direction, they do not include all the monographs. Moreover, additional long-term goals are needed. (See pp. 19 and 29.)

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This review was made because earlier GAO work indicated that FDA was taking an inordinate length of time to complete the project. GAO wanted to determine why the review was taking so long and what steps could be taken to expedite it.

Tear Sheet

Contents

ABBREVIATIONS

FDA	Food and Drug Administration
GAO	General Accounting Office
HHS	Department of Health and Human Services
OTC	over-the-counter

CHAPTER 1

INTRODUCTION

Over the years, several hundred thousand prescription and over-the-counter (OTC) drugs have been marketed by over 4,500 firms. The Food and Drug Administration (FDA), a constituent agency of the Department of Health and Human Services (HHS), estimates that 200,000 to 300,000 OTC drug products are on the market. Annual sales of OTC drugs are estimated by "Drug Topics," a drug industry magazine that performs an annual sales survey, to be about $5.2 billion.

The Federal Food, Drug, and Cosmetic Act of 1938 (21 U.S.C. 301) required that, before a new drug could be marketed, it had to be proven safe. Most OTC drugs, however, were already considered safe and did not require this preclearance. In 1962 the act was amended to add a requirement that drugs also be proven effective. "Safe" means a low incidence of adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use as well as low potential for harm which may result from abuse under conditions of widespread availability. "Effective" means a reasonable expectation that, in a significant proportion of the target population, the pharmacological effect of the drug, when used under adequate directions for use, will provide clinically significant relief of the type claimed.

In fulfilling the requirements of the 1962 amendments, FDA in 1966 began reviewing drugs that had previously been approved for safety only. This review, done by the National Academy of Sciences/National Research Council, covered about 3,500 prescription and 500 OTC drugs. Study results showed that only 25 percent of the OTC drugs reviewed were safe and effective for their intended uses. Therefore, FDA decided that all OTC drugs needed to be reviewed and in 1972 began its OTC drug review effort.

THE OTC DRUG REVIEW

FDA's OTC drug review encompasses all OTC drugs on the market. The review is intended to assure consumers that these medications are safe and effective for their intended uses and that the product labels provide all the information needed to use the drugs properly.

FDA's Bureau of Drugs has primary responsibility for the review, which is being conducted in three phases: (1) making a scientific analysis of available data and developing safety and effectiveness standards for each ingredient used in OTC drugs, (2) having public and agency reviews of the proposed standards and then issuing regulations--called monographs--for each category of ingredient, and (3) enforcing the regulations.

FDA created 17 panels of medical and scientific experts to review therapeutic categories of OTC drug ingredients. As explained more fully on pages 6 and 7, each panel was to issue one or more reports, which FDA would publish as proposed monographs. After considering additional information and comments, FDA would issue tentative final monographs. After an opportunity for objections and requests for public hearings, final monographs would be issued. FDA currently estimates that 64 1/ final monographs or final orders 2/ will be published.

The Bureau of Drugs' Division of Over-the-Counter Drug Evaluation is responsible for the first two review phases, although other offices, including the Office of New Drug Evaluation and Office of General Counsel, assist in the review. As of March 1982, the division had 41 staff members and an annual budget of about $2 million. The regulations are enforced by the Division of Drug Labeling Compliance through its OTC Compliance Branch. The Drug Listing Branch also contributes data for OTC compliance efforts. FDA's 21 district offices also help enforce OTC drug regulations.

By October 1981, the advisory panels had essentially completed the scientific review of OTC drug ingredients, and as shown in the table on page 8, FDA had received 63 panel reports as of March 1982. FDA has published two final monographs and two final orders. In addition, four other final orders were issued to address safety risks identified during the review but were not included in the total count of final monographs and orders because they dealt with individual ingredients rather than entire therapeutic categories. FDA has developed compliance programs to enforce one of the final orders and one of the monographs. A compliance program for the other monograph has been held in abeyance until several other monographs containing products with similar ingredients are published. The other final orders were handled through voluntary recalls of the products by the private firms.

OBJECTIVES, SCOPE, AND METHODOLOGY

This review resulted from a survey to determine whether FDA (1) is effectively implementing its OTC evaluation project, (2) has taken appropriate steps to remove ineffective or mislabeled

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1/The number of monographs FDA expects to publish has ranged over the years from 27 to about 98, depending largely on whether related categories of drugs were split or combined. The 64 monographs and final orders currently expected to be published do not include 17 categories of ingredients which were deferred for internal FDA review or other rulemaking processes.

2/The regulations are issued as final orders without monographs when no ingredients are found to be safe and effective.

drugs from the market, and (3) has taken adequate measures to warn consumers of an OTC drug's possible risks. We started a review of FDA's OTC drug review project because our survey indicated that FDA was taking an inordinate length of time to complete the project, and we wanted to determine why it was taking so long and what steps could be taken to expedite it. Our review was performed in accordance with GAO's current "Standards for Audit of Governmental Organizations, Programs, Activities, and Functions."

We made our review at FDA offices in Rockville, Maryland, and Philadelphia, Pennsylvania. Most of our work was concentrated in the Bureau of Drugs' Division of Over-the-Counter Drug Evaluation, which is responsible for the panel and monograph phases of the OTC review, and its Division of Drug Labeling Compliance, which is responsible for enforcing compliance with the monographs. We also either performed work or interviewed officials in the following offices:

--Bureau of Drugs:
  Office of the Director.
  Office of Planning and Evaluation.
  Office of Assistant Director for Regulatory Affairs.
  Office of Associate Director for New Drug Evaluation.
  Office of Associate Director for Drug Monographs.
  Office of Associate Director for Information Systems.

--Office of the General Counsel.

--Office of the Commissioner:
  Executive Director for Regional Operations.
  Philadelphia Regional Office.

We conducted a two-part review. The first part involved assessing FDA's rulemaking process. By examining agency records and conducting interviews, we assessed the status of the OTC review. We then reviewed the progress of each of the 64 potential monograph documents, quantifying the time spent at each stage of development and identifying reasons for delays. We interviewed the FDA staff and officials responsible for developing the monograph documents, reviewing the documents, and managing the program. We also reviewed the findings of a 1978 management study of the OTC division.

The second part of our review focused on FDA's plans and procedures for implementing the compliance program and the results of the two compliance programs undertaken. We interviewed staff responsible for OTC compliance activities, as well as officials responsible for planning and managing the program. We examined records in the Division of Drug Labeling Compliance for the antacid compliance program. We also reviewed the compliance

program guidance given to the field offices and inspected records on OTC compliance at the Philadelphia field office. At this office, we interviewed officials concerning the adequacy of the plans and guidance the Division of Drug Labeling Compliance had provided.

We chose the Philadelphia office because it is a district and a regional office and has a large number of firms for which compliance activities were required as a result of the antacid final monograph. Additionally, Philadelphia's Regional Director is chairman of the Field Drug Committee, which serves as a liaison between district/regional offices and headquarters; thus, he was able to give a regional perspective of what coordination is necessary between headquarters and regional and district offices to make OTC enforcement effective.

In assessing FDA's efforts to implement its compliance program, we interviewed FDA officials and examined records and reports pertaining to their listing of OTC drug products. We reviewed a study report prepared by an FDA contractor on the OTC drug listing file and interviewed Drug Listing Branch officials on the contractor's report. We also interviewed FDA officials responsible for preparing a task force report dealing with the OTC drug listing file.

We did not know of any criteria on how long it should take to complete a project this large and complex. FDA also did not have any such criteria. Therefore, we concentrated on attempting to determine what management actions could expedite the project.

CHAPTER 2

FDA'S REVIEW OF OTC DRUGS: A REASONABLE BUT TIME-CONSUMING PROCESS

FDA has developed a reasonable approach for reviewing OTC drugs. However, the review is taking a long time. Although the review was originally expected to be completed in 1977, FDA now estimates that it will not be completed until 1990. After 10 years, FDA has completed only 4 of an expected 64 final regulations.

The Commissioner and other FDA officials have expressed concern over how long the review is taking. We do not know, nor has FDA established, what a reasonable time should be for completing such a project.

The review's achievements thus far include removing some unsafe or ineffective ingredients from the market; allowing selected prescription drugs to be sold over the counter, thereby increasing their availability for self-medication; and relabeling and reformulating some products. However, most of the review's expected benefits have not yet been realized.

FDA'S STRATEGY IS REASONABLE

FDA's strategy for reviewing OTC drugs is reasonable, considering its estimate that there are 200,000 to 300,000 OTC products on the market. FDA could have used rulemaking procedures to write safety and effectiveness standards for various therapeutic classes of OTC drugs or reviewed each product individually and then by separate court action moved against each problem product. FDA selected the rulemaking approach because it provided for a consensus of scientific judgment, appeared to be more efficient and effective, offered greater consumer and industry input, required less litigation, and provided equal treatment of all manufacturers at a lower cost.

The rulemaking approach consists primarily of developing and enforcing regulations, called monographs, which define the conditions under which classes of OTC drugs are generally recognized as safe and effective and not mislabeled. Under this approach, drug products meeting the monograph standards can be sold over the counter without preclearance or approval by FDA, yet consumers can have a reasonable assurance of their safety and effectiveness.

Expert panels used to review and categorize ingredients in OTC drug products

FDA realized that, with 200,000 to 300,000 OTC drug products on the market, scientific analysis of individual products not only would be costly and time consuming but also could result in unequal treatment of manufacturers since standards might be imposed on one product or manufacturer before other similar products on the market were reviewed. Furthermore, a consensus of scientific judgment as to which products were "generally recognized as safe and effective" was required. Therefore, FDA created 17 panels of medical and scientific experts to review the active ingredients 1/ contained in therapeutic, or similar, categories of OTC drugs. The first panel was convened in February 1972. Each panel had seven voting members, plus nonvoting industry and consumer representatives. Appendix I lists the panels and the categories of OTC drugs they reviewed.

On the basis of evidence submitted by industry, the panels identified the ingredients used in each category of drug product and determined whether there was sufficient evidence to conclude that these ingredients were safe and effective in achieving claimed results. The panels also determined what should be put on labels to enable consumers to use the product properly. After open deliberation, the panels submitted reports to FDA, recommending that ingredients reviewed be placed in one of three categories: I (safe and effective for specified uses), II (not generally recognized as safe and effective), or III (data insufficient to classify in category I or II). 2/ In addition, the panels made recommendations concerning prescription drug ingredients which they thought could be used safely and effectively without medical supervision; i.e., as an OTC preparation.

Drug monographs used to maximize public exposure to proposed method of regulation

FDA recognized that expert panel reports could serve only as an informed basis for its judgment and that it had the legal responsibility for making final decisions. In the monograph phase, therefore, FDA established a mechanism for obtaining

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1/All subsequent references in this report to ingredients mean the active ingredients of the drug product.

2/FDA was later barred by court order from publishing final monographs which allowed marketing of category III ingredients because they have not been proven safe and effective. Cutler v. Kennedy C.A. 77-0734 (D.D.C., July 16, 1979).

and considering a maximum of public, industry, and agencywide input before issuing final rules for each drug category. Thus, each panel report is to be first issued for public comment as a "proposed monograph." After carefully considering comments and any additional information received, FDA would then issue its own proposed determination of findings as a "tentative final monograph," again providing an opportunity for comment and public hearings. With this open process, FDA reasoned that it could assure fair consideration of consumer and industry views before issuing the final monographs.

Use of therapeutic categories represents a cost effective approach to insure compliance with monographs

FDA has the authority and responsibility to enforce the final monographs it publishes. With well-considered determinations of safety and effectiveness, FDA reasoned that it would no longer be forced to review the safety and effectiveness of individual products and should be able to enforce standards more uniformly and efficiently. FDA also felt it would be able to avoid the costly and time-consuming product-by-product litigation that had been occurring before the OTC review. In the past, each time FDA won a lawsuit and the court ordered the product off the market, the manufacturer could change the drug and the label slightly and begin marketing it as a different drug. Although data were not available to estimate the cost of a product-by-product review, we believe FDA's use of a therapeutic category approach is more cost effective. In addition, this approach allows FDA to set standards across entire categories of OTC drug products, with significant cooperation and support from the drug industry.

OTC REVIEW IS TAKING A LONG TIME

The OTC review is taking a long time. The panel phase took much longer than originally estimated, and the monograph phase is now experiencing long delays even though total staff working on the project increased from 6 in 1973 to a peak of 46 in 1980.

When FDA began the OTC review in 1972, officials estimated that the panel phase would be completed by 1974 and the entire review by 1977. By 1978, the goal for completing the review had slipped by 7 years to 1984. In 1980, the completion milestones were again assessed, and the estimated project completion date was moved to 1990.

The review is taking a long time for a number of reasons. These include (1) the panel phase taking much longer than expected partly because there were more ingredients to review than originally anticipated, panel meetings were opened to the public, and scientific evidence was lacking on the effectiveness of many

ingredients; (2) a July 1979 court order, which prevented FDA from issuing any monographs which allowed marketing of ingredients classified as category III (insufficient evidence to classify as safe and effective); (3) FDA internal management problems; and (4) the 1981 freeze on the issuance of regulations.

The first panel was convened in February 1972; 14 months later in April 1973, FDA published the panel's report and a proposed monograph. The tentative final monograph was published 7 months later and the final monograph 7 months after that, well within the established 1977 goal for completing the review. It took 3 years to convene the other 16 panels, and over 9 years for the last panel to complete its work. Although FDA received a second panel report in July 1974, it was 1975 before the agency began receiving a significant number of panel reports.

The following table shows the number of panel reports FDA received each year and the documents' status as of March 1982. As shown, many panel reports have still not been issued as final monographs or orders, including one completed in 1974.

Panel Reports Completed by Year and Status as of March 1982

Calendar year in which panel reports completed	Number of reports completed by panels	Status as of March 1982 (note a)			
		Panel report adopted	Proposed monograph published	Tentative final monograph published	Final order/ monograph published
1972	-	-	-	-	-
1973	b/1	-	-	-	b/2
1974	1	-	-	1	-
1975	7	-	2	4	1
1976	8	-	8	-	-
1977	5	-	5	-	-
1978	15	2	12	-	1
1979	8	2	6	-	-
1980	16	7	9	-	-
1981	2	2	-	-	-
Total	b/63	13	42	5	4

a/The table is intended to show the March 1982 status of panel reports completed each year but not the year in which the documents moved to each stage of development. For example, seven panel reports were completed in 1975. As of March 1982, two were in the proposed monograph stage, four were in the tentative final stage, and one had been published as a final monograph.

b/The antacid panel submitted one report covering antacids. FDA later decided, based on comments received when the antacid proposed monograph was published, to issue a second monograph for antiflatulant products. Therefore, the number of panel reports is less than the number of monographs and final orders.

Only 1 (a final order for daytime sedatives) of the 54 panel reports completed after 1975 has been published as a tentative final or final monograph. Thirteen other panel reports have been adopted but not published as proposed monographs.

The estimated time frames for completing each phase of monograph development have increased appreciably. In 1975 FDA estimated it would take 3 months to publish a proposed monograph after the panel report was completed. By 1980, this estimate was increased to 12 months for a short monograph and 18 months for a long monograph. 1/ During the same period, the estimated time to publish a tentative final monograph, after publication of the proposed monograph, increased from 6 months to 25 months for a short monograph and 40 months for a long monograph. The estimated time to publish a final monograph, after publication of the tentative final monograph, increased from 6 months to 35 months for a short monograph and 50 months for a long monograph. The total estimated time to complete processing of monographs after the panel report was issued increased to 72 months for a short monograph and 108 months for a long monograph from an estimated 15 months.

The actual time to complete each phase has sometimes considerably exceeded these estimates. FDA estimates that 16 months will be required to respond to comments and resolve issues for a long monograph. The internal analgesic panel report, a relatively long document of about 1,200 pages, generated 128 sets of comments when it was published as a proposed monograph in 1977. A professional staff member worked full time for nearly 3 years to summarize and respond to those comments and resolve policy issues. The monograph was further delayed by 4 months as policy issues arose after the draft was finished and circulated for FDA review outside the OTC division. Publication of the monograph has also been delayed because other monographs have had a higher priority. As a result, activities on the monograph, which according to FDA estimates should have taken about 16 months, have taken nearly 5 years as of March 1982.

The timeliness of the OTC review has been of concern to FDA and others for several years. In 1977 the Commissioner voiced concern over the increasing delays and problems in the OTC review and asked that immediate attention be directed to resolving them. These delays and problems were also acknowledged by the Deputy Commissioner during hearings before the Subcommittee on Oversight and Investigations, House Committee on Interstate and Foreign Commerce (now Committee on Energy and Commerce), in June 1979.

1/FDA did not define what it would consider "long" or "short" monographs.

Review is now at most labor-intensive phase

FDA is now at the most labor-intensive phase of the OTC review. Therefore, FDA should carefully plan the work, set priorities, and monitor the process to ensure that the review is completed as efficiently and promptly as possible.

As shown in the table on page 8, FDA has published four final regulations (two monographs and two final orders) and has five regulations at the tentative final monograph stage. Of the remaining 55 documents, 13 are in the panel report phase and 42 are in the proposed monograph phase. Of the 42 documents in the proposed monograph phase, 10 were moved to that phase in January and February 1982.

Much more staff time is required to process tentative final and final monographs than to process proposed monographs. As a result, the more documents that are concurrently in this phase, the more difficult the effort becomes to manage. Tentative final and final monographs each require, according to FDA's estimated time frame, 16 months in the OTC division plus 6 months elsewhere in FDA to resolve issues and review and comment on the document. In contrast, FDA records show that it should take about 5 months of OTC division time to publish a proposed monograph after the adoption of a panel report. As pointed out on page 9, these estimates are sometimes considerably exceeded. The 5-month period does not include time spent by FDA staff in assisting the panels before completion of the panel reports.

As a result, by the end of fiscal year 1982, most of the unpublished documents are expected to be in the most labor-intensive phases of the monograph process. As of March 1982, FDA had about 130 documents yet to publish and a staff of about 20 professionals in the four branches to work on them. Since each monograph must be published in the Federal Register at three stages of development--as a proposed monograph, as a tentative final monograph, and as a final monograph--that effort will require FDA to carefully plan, set priorities, and monitor the process to ensure the OTC review's goals are achieved as efficiently as possible.

MOST EXPECTED OTC REVIEW BENEFITS NOT YET REALIZED

Although the OTC review effort has produced some benefits, the panel findings and recommendations indicate that most expected benefits are still to be realized as FDA publishes and enforces additional final monographs. Although FDA may not concur with all panel recommendations, our review of panel findings and recommendations indicates that extensive changes in OTC drug product formulation and labeling are likely to be required.

Benefits achieved to date

Benefits achieved include the removal of a number of unsafe ingredients from OTC drug products, the conversion of some prescription drugs to OTC drugs, and the voluntary reformulation and relabeling of some products.

The final antacid monograph, published by FDA in 1974 and amended in 1979, classified 30 ingredients as safe and effective and 9 ingredients as unsafe or ineffective for use in these products, defined the allowable indications for some ingredients, and contained standards regarding the required acid-neutralizing capacity of the active ingredients. Drug manufacturers must now comply with these standards in formulating and labeling products.

As of March 1982, six final regulations or final orders had been issued as a result of the OTC review. These issuances have resulted in the removal of unsafe or ineffective ingredients from the market. In addition, FDA requested manufacturers to voluntarily remove from the market over 700 products containing methapyrilene, after this ingredient was found to be a potential carcinogen. Examples of ingredients removed from the market include zirconium, which was removed from aerosol antiperspirants and other drug and cosmetic products because of its potential for causing lung disease, and hexachlorophene, which was removed from OTC products when toxic levels were found to be absorbed in infants' blood. In addition, FDA issued a final order to remove from the market daytime sedatives, for which consumers annually spent about $7 million, after FDA concluded that the antihistamines, bromides, and scopolamine compounds used in these products were not effective as daytime sedatives.

Some products previously marketed as prescription drugs are now available for sale as OTC preparations, making them more accessible to consumers. Advisory panels recommended that 37 ingredients be switched from prescription to OTC products. As of March 1982, FDA had allowed 17 of the 37 ingredients to be sold over the counter. For example, since FDA published the external analgesic proposed monograph covering hydrocortisone--an anti-inflammatory skin care ingredient--OTC sales of products containing this ingredient have grown to $50 million annually, and industry officials expect them to grow to $300 million by 1985.

FDA and industry officials advised us that significant actions have been taken to relabel and reformulate products in anticipation of final published monographs. However, FDA has no comprehensive record of these changes. We did become aware, during our review, of a number of these actions. A notable example is the labeling of sunscreen products, which now contain a rating factor that informs consumers of the amount of protection they can expect. Other examples include the reformulation of two leading pain

reliever products to remove ingredients not shown to be safe and effective, the modification of directions for use of a sleep-aid product, and the addition of warnings regarding accidental ingestion in many OTC products.

Many additional products will require reformulation, relabeling, or removal from the market

As of January 1981, FDA had listed and categorized 1,393 product uses 1/ for the 731 OTC ingredients reviewed by the panels. The following table shows that 69 percent of the uses may require some change. Of these, 33 percent are in the not generally recognized as safe and effective category, and products containing these ingredients will require some reformulation, relabeling, or removal from the market.

	Number	Percent of total
Category I (safe and effective)	428	31
Category II (not generally recognized as safe and effective)	461	33
Category III (insufficient information)	504	36
Total	1,393	100

Ingredients in category III must be reclassified as category II if acceptable data about their safety or effectiveness are not received by FDA before the final monograph is published (see footnote on p. 6). Therefore, once these monographs are published, products containing ingredients classified by the panels as category II or III may be required to be reformulated, relabeled, or removed from the market.

1/The term "product uses" recognizes ingredients that have more than one use. For example, aspirin is one ingredient in the 731 but is counted four times for ingredient uses (analgesic, fever reducer, antirheumatic, and buffered analgesic).

CHAPTER 3

FDA CAN EXPEDITE THE OTC REVIEW

FDA can take several actions to expedite the OTC review. It can (1) improve its planning through better use of priorities and milestones, (2) make more timely policy decisions, and (3) make better use of the OTC division staff. This situation appears similar to what we found when we reviewed the time FDA takes to approve new drugs. In a May 1980 report, 1/ we noted that the drug approval process was lengthy and delayed the availability of important new drugs. After that report was issued, FDA took a number of actions and established goals for reducing the time required to approve new drugs. Although progress has been slow, as indicated in our followup review, 2/ FDA has reduced the time required to approve new drugs. We believe that similar action is needed to expedite the OTC review.

PRIORITIES AND MILESTONES HAVE NOT BEEN USED EFFECTIVELY

Although FDA has established priorities and general milestones for completing the OTC review, the milestones are not based on actual experience, are not sufficiently detailed, and are rarely met. FDA's ability to accurately measure its progress in completing the OTC effort and identify causes of delays appears to be hampered by a lack of more detailed milestones against which progress can be measured. Also, milestones are generally set without considering a monograph's current status, the priority assigned to it, or the complexity or number of issues involved.

Priorities and milestones are valuable planning tools. FDA has used both--but not effectively. Priorities define the most important objectives of an organization and provide the basis for allocating limited resources among competing demands. Milestones provide the time-based road map for completing individual monographs and a basis for quickly identifying delays so that their causes can be analyzed.

Priorities have little meaning

As a result of a 1978 management study of the OTC project by the Bureau of Drugs' Office of Planning, Evaluation, and Management, FDA designated 10 monographs as high priority based on such

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1/"FDA Drug Approval--A Lengthy Process That Delays the Availability of Important New Drugs" (HRD-80-64, May 28, 1980).

2/"Speeding Up the Drug Review Process: Results Encouraging--But Progress Slow" (HRD-82-16, Nov. 23, 1981).

criteria as market sales of the products that would be regulated by the monograph. FDA has since abandoned that concept, apparently because it was not being followed, and now sets priorities based on which monographs can most easily be moved to the next stage of their development.

The 1978 management study report emphasized the need to establish priorities to guide the division's efforts. It recommended that such criteria as product sales volume be the basis for assigning priorities. Following these recommendations, in June 1978 the Director of the OTC division developed a list of the 10 top priority monographs. However, as of March 1982, only one of these had been published as a final order and two others as tentative final monographs. The other seven remain in the same development stage as when they were designated top priority. For example, the proposed monographs for laxatives and topical antibiotics were published in March 1975 and April 1977, respectively, yet neither had reached the tentative final monograph stage as of March 1982. FDA staff pointed out that, although these documents have not progressed to the next stage, a considerable amount of work has been performed on the documents and most are nearing completion.

In fiscal year 1981, the OTC Director established a new list of priorities. It included 16 panel reports, 5 proposed monographs, and 1 tentative final order which he thought could be processed to the point where the Director of the Bureau of Drugs could approve them for publication. Moving these monograph documents was included as a performance objective in the branch chiefs' 1981 merit pay performance contracts.

Milestone dates are seldom met

The OTC division periodically estimates milestone completion dates for each stage of monograph development. However, its projections have seldom been met, and they have not included such important details as when the first draft will be completed or when the monograph should be forwarded to the division's Office of Director for review.

The list of milestone dates generally shows for each monograph the estimated or actual date when the document was or will be approved by the panel or published in the Federal Register as a proposed, tentative final, or final monograph. The OTC division used to update its milestone estimates quarterly; however, in 1980 the division changed the updating from quarterly to annually. Despite frequent efforts to update milestones, milestones were rarely met. For example, in March 1975, the 10 product categories that were later designated as high priority in 1978 were all estimated to be completed during 1976. A final order (see footnote 2, p. 2) was issued for one of these in 1979, but the most recent estimate, prepared in December 1980, showed expected completion dates for

final monographs for the other nine ranging from 1981 to 1986. At least some of these dates will not be met since OTC division officials do not expect to issue another final monograph until fiscal year 1983 or later.

One reason milestones are not being met is because the OTC division is not drawing on past experience to establish realistic milestones. The various estimates prepared by the division showed the number of months required for each major step in the process for long and short monographs. For example, the December 1980 estimate showed a 40-month time frame for processing a long monograph from the proposed to the tentative final monograph stage, including 19 months of OTC division processing time and 21 months of nondivision time. Sixteen months of the division time was for reviewing, summarizing, and responding to industry and consumer comments. However, the problem is that the time frames apply equally to monographs that receive a large number of comments and those that do not. For example, FDA used the same 16-month estimate of division time for the internal analgesic monograph, which had 128 sets of comments; the opthalmic monograph, which had 917 sets of comments; and the anorectal monograph, which had 17 sets of comments. It took FDA about 3 years--2-1/2 times the standard estimate--to summarize and respond to the 128 sets of comments on the analgesic monograph.

Program management system and monthly document status reports not used as management tools

FDA did not use its agencywide program management system and monthly OTC review document status reports to monitor whether review milestones were being met or analyze where delays were occurring.

The program management system provides for periodically evaluating each agency project. These evaluations, conducted by an independent team, are intended to assess past performance and current strategies as well as to establish future priorities and identify areas needing more evaluation. Program management system goals called for the OTC division to publish at least 20 proposed monographs, 9 tentative final monographs, and 4 final monographs in fiscal year 1980. In contrast, FDA published 11 proposed monographs, no tentative final monographs, no final monographs, and 1 final order. Nevertheless, no evaluation or analysis was made under the program management system to determine why these delays had occurred or what action was needed to complete the OTC project in a timely manner. FDA officials pointed out, however, that the court decision on category III ingredients (see footnote, page 6) delayed issuance of tentative final and final monographs.

The OTC division's monthly document status report was designed to inform management of progress made in developing monographs. The reports were of little value, however, because they failed to highlight issues needing resolution, were not used for planning and decisionmaking, and did not measure progress against predetermined milestone dates. As a result, the Director, OTC division, discontinued the reports in July 1981 in favor of weekly written status reports from the branch chiefs.

POLICY ISSUES SHOULD BE RESOLVED MORE PROMPTLY

FDA has frequently not resolved OTC policy issues in a timely manner. Because the OTC review is complex and controversial, FDA is often faced with policy decisions which significantly affect one or more monographs and which need to be resolved promptly before they create delays.

Examples of policy issues facing FDA include:

--How many active ingredients may be included in an OTC drug product?

--When is a cosmetic actually a drug, subject to the requirements of the OTC review?

--How much and what type of evidence is needed to classify an OTC drug ingredient as safe and effective?

The OTC division generally becomes aware of such issues before completion of the panel phase of monograph development. Nevertheless, they are usually not resolved until many months later, when the monograph is circulated within FDA for comment and the OTC division has wasted months waiting for decisions.

FDA has two mechanisms for resolving policy issues. The first is the Bureau of Drugs' drug monograph meetings, which are attended by various associate directors in the Bureau of Drugs (such as Regulatory Affairs, Compliance, Drug Monographs, and New Drug Evaluation). At these meetings, attempts are made to resolve policy issues through consensus.

When the drug monograph meetings fail to resolve policy issues or when the Office of General Counsel disagrees with a policy position in the monographs, the matter is brought before the OTC Drug Steering Committee, which includes the attendees of the drug monograph meetings, the General Counsel, and the FDA Commissioner.

Delays resulting from FDA's failure to resolve policy issues usually occur when a reviewer in another office, such as General Counsel, disagrees with the way the OTC division has handled

an issue. For example, the topical otic (earwax products) monograph was delayed about a year because the Office of the General Counsel disagreed with the way the division responded to a comment on the panel report. The proposed monograph was approved in the Bureau of Drugs in August 1980 and sent to the Office of General Counsel. The issue involved classifying carbamide peroxide, an ingredient in topical otic products, as safe and effective. The OTC division redrafted the monograph and returned it to the General Counsel in December 1980. The issue was resolved in December 1981, when the General Counsel accepted the original version circulated in August 1980. Other monographs that were delayed pending resolution of policy issues included (1) the oral cavity (mouthwash) proposed monograph, delayed about 8 months, (2) the relief of oral discomfort proposed monograph, delayed about 12 months, and (3) the weight control proposed monograph, delayed about 12 months.

OTC STAFF CAN BE USED MORE EFFECTIVELY

The OTC division is not using its staff effectively. Despite tripling the number of staff working on the review since 1976 and revising its organizational alignment to streamline the review process, establish clearer lines of responsibility, and better use the division staff, the time to process proposed and tentative final monographs has increased dramatically because the organizational realignment has been implemented on paper but not in practice.

The 1978 management study of the OTC program (see p. 13) concluded that the OTC division's flat organization created a situation in which there was no readily identifiable delegation of authority, clearly defined areas of responsibility, or specific chain of supervisory control and review. As a result, staff time was wasted.

However, in spite of the new organizational structure, staff time is still being wasted by officials who usurp the functions delegated to others. For example, the deputy director, along with two special assistants from the quality control group, has assumed responsibility for developing specific monographs, for assigning and supervising professional staff assigned to various monographs, and for tracking the status of monograph documents sent outside the division--responsibilities that, according to delegations of authority approved by the Director of the Bureau of Drugs, belong to others.

The deputy director and special assistants are also part of a lengthy, repetitive review process in which they review and approve all interim and final monograph documents. Once a document is drafted by a document manager in one of the four branches, it is reviewed and approved by the branch chief, then sent to the Office of the Director. The deputy director reviews the document

and assigns it to the two special assistants, who review it and return it to him for a final review and consolidation of comments and changes. The document is then returned to the document manager, where the changes are incorporated and the review cycle begins again. This process continues until the deputy director and both special assistants are satisfied with the document.

While this is going on, the branch chief and document managers--who have been delegated responsibility for doing the reviewing and approving--have little direct involvement in the process except to ensure that the reviewers' changes are incorporated in the draft. The impact of this process on a monograph can be significant. For example, the skin bleaching proposed monograph was published in November 1978. FDA received seven sets of comments, which raised 19 issues regarding the monograph. The branch document manager prepared responses which summarized the issues and presented reasons why the comments were accepted or rejected. The discussion of each issue and response averaged about 1-1/2 pages in length, yet 15 of the 19 issues took 10 months or more for review. Also, a count of each time the packages were processed or reviewed by one of the five people in the review chain showed that the 19 packages were handled 375 times, an average of about 20 cycles per issue. The review of the antiperspirant tentative final monograph also required about 20 processing steps for each of the 32 issues and responses--a total of 637 processing steps.

CONCLUSIONS

We believe that FDA can take a number of actions to expedite the OTC review. These include improving its planning through better use of priorities and milestones as tools in managing the review, making more timely policy decisions, and better using the OTC division staff.

Because the monograph development process is lengthy, FDA must carefully plan, manage, and evaluate the review so that delays are quickly identified and management attention can be focused on solving problems or adjusting workloads and schedules.

The OTC project's management problems are similar to those we identified when we reviewed the time required by FDA to approve new drugs. After our May 1980 report was issued, FDA took a number of steps and established goals for reducing the time required to approve new drugs. A similar approach to the OTC review would expedite the project.

RECOMMENDATIONS TO THE SECRETARY OF HHS

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

--Establish priorities for completing individual monographs based on objective criteria, such as consumer sales or market impact, and establish detailed milestones for completing the development of monographs and the publication of final regulations based on actual experience, staff skills and experience, the work required, and the priority of the monograph document.

--Establish goals for expediting the OTC review and develop a system for measuring progress in completing all monograph documents which measures progress against projected milestones and provides feedback to FDA and HHS.

--Develop a mechanism for high-level agency officials to promptly identify and resolve policy issues.

--Review, and revise where appropriate, procedures for reviewing draft monograph documents to ensure that branch personnel are given the necessary supervision and authority to develop the products for which they are responsible.

AGENCY COMMENTS AND OUR EVALUATION

HHS agreed with our recommendation that FDA establish priorities for completing individual documents for publication and stated that priorities have been established and are being used. HHS said the top priority is panel reports and proposed monographs followed by tentative final monographs and final monographs. According to HHS, current priorities for publishing documents consider the current status of documents, the number and complexity of issues requiring resolution, and the impact that issues in one monograph may have on policies related to other monographs and to prescription drugs. HHS added that staff may work on lower priority documents while issues relating to a higher priority document are resolved, and in some cases the lower priority document may progress faster because it has fewer or less severe problems. HHS did not comment on the portion of our recommendation that FDA establish detailed milestones for completing the development of monographs and the publication of final regulations.

We continue to believe that monographs on products with high-volume consumer sales and market impact, such as internal analgesics and cough and cold remedies, should be given priority over monographs on products having far less consumer sales and market impact. We recognize that some of these documents may be more

difficult to process and face obstacles not present in other documents, but this should not preclude establishing them as priorities.

Although HHS did not respond to our recommendation concerning detailed milestones, we believe that establishing such milestones is very important for FDA management in assessing progress in developing monograph documents. We believe that, in establishing these milestones, a system of reporting should be adopted so that FDA management can determine whether the detailed milestone dates are being achieved. Such a system could be used to identify issues needing to be resolved or other problems being experienced.

HHS agreed with our recommendation that FDA establish goals for expediting the OTC review and develop a system for measuring progress in completing monograph documents. HHS pointed out that goals for completing specific documents are included in the merit pay and senior executive service plans of FDA supervisors and managers and in employee performance plans. According to HHS, progress toward those goals is being tracked through a new system designed to give management current information on the status of each document and the amount of time elapsed at each stage of the review, which should help FDA managers identify and resolve potential problems. HHS added that progress is measured through regular meetings at various levels in FDA.

FDA's action is not fully responsive to our recommendation. The merit pay and senior executive service plans we reviewed contained goals for those documents that appeared most likely to be met by the end of the year. They did not contain goals for all documents. In addition, although the new system for tracking the progress of documents does show how long a document has been in each office, it does not show whether the document is proceeding on or ahead of schedule or whether problems are being encountered. This is especially true for the OTC division, which requires most of the processing time. For example, the system's February 26, 1982, status report showed that the antidiarrheal and laxative monographs had been in the OTC division 2,395 days but did not provide any information on the status of these documents within that division.

Concerning our recommendation that FDA develop a mechanism for identifying and resolving policy issues, HHS advised us that the Bureau of Drugs holds biweekly meetings at which technical and policy issues are presented to Bureau management for resolution. Issues that cannot be resolved at this level are discussed and resolved at meetings of the OTC Drug Steering Committee. (See p. 16.) HHS also pointed out that the Bureau's Deputy Director has

initiated meetings with the Director of the OTC division to identify issues needing resolution. Our concern in making this recommendation was that policy issues were not being brought to the attention of FDA management. The mechanism for resolving those issues, once identified, appeared to be appropriate. We believe that the meetings between the Bureau's Deputy Director and the Director of the OTC division could be a useful mechanism for identifying issues needing resolution if the staff and OTC division officials raise the issues.

HHS agreed with our recommendation to review, and revise where appropriate, procedures for reviewing draft monograph documents. HHS advised us that FDA is reviewing the OTC program to determine what, if any, procedural and policy changes may be appropriate. This review will include an evaluation of the organizational structure and placement of the review division, the skills required to complete the review versus those available within the division, and mechanisms for resolving issues that arise in preparing documents for publication.

CHAPTER 4

MONOGRAPH ENFORCEMENT HAMPERED BY LACK OF ACCURATE LISTING OF OTC DRUGS AND INADEQUATE MONITORING

The lack of an accurate listing of OTC drugs and inadequate monitoring and evaluation of the enforcement effort have hampered the initial efforts to enforce the published monographs and final orders. Unless actions are taken to correct these problems, enforcement will become more difficult as more monographs are published.

FDA DOES NOT HAVE AN ACCURATE LISTING OF OTC DRUG PRODUCTS SUBJECT TO ENFORCEMENT

The lack of an accurate listing of OTC drugs has contributed to FDA's inability to determine to what extent the OTC market is complying with published monographs. The Drug Listing Act of 1972 (21 U.S.C. 360) gave FDA a tool to effectively identify OTC drug products subject to the monographs. However, because FDA never allocated sufficient resources to keep the listing accurate and up to date, it has not been used in monograph enforcement. Instead, to identify products subject to monographs, FDA has had to rely on field staff visits to firms which might manufacture them. This approach is time consuming and inefficient in that it does not give FDA an accurate means of assessing the extent to which it has identified all of the OTC products subject to monograph enforcement.

Drug listing intended to aid FDA in identifying products

The Drug Listing Act of 1972 requires all manufacturers and distributers of human drugs--both prescription and OTC--to register their establishments and products with FDA. All new establishments must register their products within 5 days of starting operations and must update product listings whenever there is a change in the product's name, the quantity or identity of active ingredients, or the labeling. The act states that a major purpose of the listing is "to permit timely and effective regulation of drugs and alleviate the burden of reviewing drugs that have been removed from the market." After the act was passed, FDA reported to the Congress that the act provided important new consumer protection because it enabled FDA to identify, by name or manufacturer, drugs that should be relabeled, taken off the market, or checked for compliance with quality standards.

OTC drug listing not maintained or fully used

FDA's drug listing files contain about 200,000 OTC products, and each year drug companies submit over 11,000 forms to FDA, reporting new OTC products, discontinued products, and labeling or ingredient changes. However, the agency has not provided a staff large enough to keep track of these changes.

From its inception in 1972, the OTC drug listing program has not had enough staff because FDA has given a higher priority to the files for firm registration and prescription drugs. As a result, the OTC file is out of date and inaccurate. From 1972 through 1976, sporadic attempts were made to automate and maintain the OTC drug data, but staff turnover averaged about 100 percent annually and several vacant positions were not filled. In 1978, FDA stopped entering data in the automated OTC file because of pressure to publish the National Drug Code Directory. 1/ Meanwhile, the staff shortages continued.

As a result, the OTC drug listing currently includes:

--Two automated files, which contain manufacturer, product, and ingredient data on about 200,000 products:

  (a) An "old file," automated between 1972 and 1976, in an initial attempt to create an OTC drug list.

  (b) A "new file," automated between 1976 and 1978, when resources were available to update the system. The new file was started with the intention of merging the files once the new file was in operation.

--A manual file containing about 25,000 forms received since 1978. Drug listing forms are filed in bins by drug firm. Bureau of Drugs officials estimated that 30 to 40 percent of these forms report changes to the 200,000 products listed in the "old" and "new" automated files.

Any use of the OTC file requires FDA to search the two automated files and manually search the 25,000 drug listing forms. This process is further complicated by the fact that products have not been listed by therapeutic category, although the system allows for such a classification. Further, the director of the drug listing program estimated that, with such problems as data duplications, inaccurate reporting, errors in data entry, and errors resulting

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1/An FDA compendium of all prescription drugs by manufacturer and national drug code number that is compiled from the prescription drug listing file.

from the manual search of detailed data, a search of the OTC files would produce data that were only about 50-percent accurate.

In 1980 the Bureau of Drugs contracted with a consulting firm to provide a "comprehensive evaluation of the resource options which could be utilized to implement the drug listing." The contractor concluded that the primary use of the listing was in planning compliance activities but that additional resources were needed to update and maintain the system. The contractor estimated that over 36 staff years of effort would be required to update the OTC drug listing file, based on FDA's experience with the prescription drug file and considering the larger volume of OTC products. In addition, the contractor estimated that almost 13 staff years would be needed annually to maintain the file. Bureau of Drugs officials considered this estimate to be very high; they believed the file could be maintained with considerably less staff.

Bureau of Drugs officials advised us that, even if additional resources were available, they would not be used on the OTC drug listing because the officials believe the listing is not needed. They believe that, when compliance with monographs is achieved among major firms, the smaller firms will also comply. They indicated that, when a monograph is published, they will identify products based on their knowledge of companies and the information available in trade publications.

We believe that FDA should update the system as a whole or by drug category as monographs are published. If the drug listing is not needed, FDA should propose legislation to amend the Drug Listing Act to eliminate the requirement that such reports be filed.

ENFORCEMENT EFFORTS HAVE BEEN TIME CONSUMING

FDA has used the antacid final monograph and, to a lesser extent, the daytime sedative final order to develop and test procedures for assuring compliance with OTC monographs. These efforts proved to be very time consuming--partly because the drug listing could not be used efficiently or effectively to identify all drug products subject to enforcement.

Antacid monograph enforcement

The antacid final monograph was published in 1974, but 7 years later FDA still did not know how many antacid products were on the market. Also FDA has not reviewed, for compliance with the monograph, all the antacid products it has identified. Because it was the first monograph to be published, there were delays in designing the enforcement approach. As a result, the antacid compliance program was not initiated until October 1976--2 years after publication of the monograph.

Although FDA maintains the OTC drug listing file to identify products subject to the monograph, the Bureau of Drugs compliance staff did not use the file because data were not up to date. Instead, the compliance staff used trade publications to identify 80 "high-priority" firms--the market leaders--and directed their district offices to collect labels from the antacid products these firms manufactured. A total of 192 high-priority products were identified this way. From 1976 through 1978, district offices continued to collect labels from another 278 antacid products manufactured by 124 "low-priority" firms.

According to Bureau of Drugs officials, FDA reasoned that, by requiring the market leaders to adhere to the regulations, it could achieve compliance throughout the market. They stated that, once the rules were enforced, the affected firms would demand that others be held to the same rules and would report violations to FDA. The market would thus become self-regulating, and compliance would be achieved with a review of only a few products. Therefore, the Bureau of Drugs reviewed the 192 products manufactured by the high-priority firms for compliance with monograph requirements, but did not review most of the products manufactured by low-priority firms.

After FDA headquarters reviewed the products manufactured by high-priority firms, enforcement priorities for violations were set as follows: (1) nonpermitted ingredients, (2) improper labeling claims, (3) insufficient or inaccurate warnings, and (4) other label violations. FDA's review of 146 1/ products manufactured by high-priority firms showed that 77 complied with FDA's monograph requirements and the other 69 had a total of 84 violations. Six products contained nonpermitted ingredients, 17 had improper indications for use of the product, 33 had insufficient or inaccurate warnings, and 28 had improper directions for use.

Some firms marketing products that did not comply with FDA's monographs indicated that they would comply voluntarily and were not sent regulatory letters. 2/ However, FDA issued 13 regulatory letters from September 1977 to May 1979 to firms that manufactured products found to be in violation. According to FDA records, these firms eliminated the violations. We could find no evidence that FDA followed up with firms that indicated they would comply voluntarily.

1/Although FDA officials said they reviewed 192 products, the product listing we reviewed contained only 146.

2/A letter notifying the drug company that a product is in violation of FDA requlations and requesting a written response within 10 days.

In 1980, FDA delegated authority to the district offices to review the products manufactured by low-priority firms identified from 1976 to 1978 and to take regulatory action as appropriate. The district offices were also given authority to enforce a 1978 amendment to the monograph which classified some ingredients as category II (not generally recognized as safe and effective) that had been originally classified as category III (data insufficient to classify as safe and effective). However, officials in the district office we visited (Philadelphia) indicated that products had not yet been reviewed for the additional category II ingredients, and a Bureau of Drugs compliance official indicated that no attempt had been made to identify products containing these ingredients.

FDA has spent 5 years identifying and reviewing products subject to the antacid monograph, yet consumers still cannot be sure that all the antacid products they purchase are safe and effective and meet the monograph's requirements. For example, FDA still does not know how much of the total antacid market the 470 identified products (192 manufactured by high-priority firms and 278 manufactured by low-priority firms) represent.

Enforcement of daytime sedatives final order

FDA took less time to issue the compliance program for daytime sedatives, but again it had problems identifying all of the products subject to the order. The final order was published in June 1979, and the compliance program was published in April 1980. The Bureau of Drugs identified 18 products from materials submitted by firms. District offices were then given total authority for identifying additional products, reviewing them, and enforcing the monograph. In the district we visited, an extensive search through trade publications and investigations was halted in March 1981 because no products were identified. FDA officials concluded that, since few products were identified nationally, the products had been voluntarily discontinued before the order's effective date.

IMPLEMENTATION OF COMPLIANCE PROGRAMS NOT ADEQUATELY MONITORED

Although FDA issues detailed compliance programs for OTC monograph enforcement, its monitoring of enforcement activities is inadequate. Information routinely compiled on the status of initial enforcement efforts has not been sufficient to evaluate the status of OTC monograph compliance. Consequently, FDA cannot easily assess the status of the program, and gaps and delays in enforcement have not been easily or quickly identified.

FDA has routinely collected information on OTC monograph enforcement, including:

--Hours charged by district investigators to the OTC compliance program (i.e., time spent collecting or reviewing labels or investigating specific products).

--Labels of products and investigation reports submitted by district offices to headquarters for review and enforcement (when authority for enforcement rests in headquarters).

--Regulatory letters issued to firms in violation of the monograph, and the status of responses to the letters.

The Bureau of Drugs, however, has not systematically compiled information on:

--Firms visited at which no relevant products were found, which would help assess the extent of market coverage.

--Products reviewed by districts that were found to be in compliance with the monograph, which would help assess the degree of voluntary compliance.

--The status of headquarters review of products identified, which would help direct followup on product compliance.

Further, although collected antacid labels were kept on file and informal counts of products were maintained, FDA's official lists of firms and products investigated are not complete. For example, of the 192 products identified as being manufactured by high-priority firms, only 146 are listed in the compliance program; of the 278 products identified as being manufactured by low-priority firms, only 97 are listed. It is difficult, therefore, for either headquarters or district offices to assess the current status of compliance with the antacid program.

Without routine collection and review of these data in initial enforcement programs, some segments of the compliance programs have "fallen through the cracks." Staff years assigned to district offices for OTC enforcement have been consistently underused, and FDA has not been able to complete the compliance effort in a timely manner. For example, FDA:

--Has not maintained a record of the extent to which antacid products have been reformulated to remove ingredients classified as ineffective pursuant to the 1978 amendments to the antacid monograph.

--Did not review low-priority antacid products for compliance with the monograph until 1980 and 1981, several years after collecting labels for these products.

--Did not follow up on high-priority antacid products not in compliance with the monograph but not sent regulatory letters, until 1980 and 1981.

During our review FDA acted to improve the monitoring of its enforcement efforts. In April 1981, the Bureau of Drugs compiled and issued a list of antacid products not yet reviewed to guide district office followup. The Bureau is also revising the general compliance program to include quarterly reporting of firms visited and products reviewed under the monograph.

CONCLUSIONS

FDA efforts to enforce the one published OTC monograph have taken a long time and are still not complete. We recognize that some of the problems encountered were the natural result of starting up a new program. However, unless corrective actions are taken, the problems we identified are likely to affect future monograph enforcement efforts. FDA can use this experience to improve its enforcement process and provide more timely and complete assurance to consumers that OTC products are safe, effective, and properly labeled.

Since the intent of the OTC program is to cover the market by classes of drugs, we believe FDA should improve its capacity to identify products affected by the monographs more promptly. FDA should determine whether the OTC drug listing is needed for this identification process. If it is not, FDA should propose legislation to amend the Drug Listing Act to eliminate the requirement for reporting and save the Government and industry time and money. If, on the other hand, the drug listing will be needed as additional monographs are published, FDA should assess the relative efficiency of (1) updating the entire system in the next few years or (2) updating the system by drug category as monographs are published.

RECOMMENDATIONS TO THE SECRETARY OF HHS

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

--Determine, based on the anticipated cost and timeliness of possible alternative approaches, whether the OTC drug listing files are needed. If the listing is not needed, FDA should propose legislation to amend the Drug Listing Act to eliminate the reporting requirement. If it is

needed, FDA should assess the relative efficiency of updating the entire system in the next few years or updating the system by drug category as monographs are published.

--Establish measurable objectives for the OTC enforcement effort and the expected timetables for performing the work.

--Maintain for each category of drug product a complete master list of firms manufacturing the drug and a list of products as they are identified for each monograph.

--Track the progress made in reviewing and following up on products subject to the monographs and highlight, through written reports or regular meetings with district representatives, problems encountered in enforcing monographs.

AGENCY COMMENTS AND OUR EVALUATION

Regarding our recommendation that FDA determine, based on the anticipated cost and timeliness of possible alternative approaches, whether the OTC drug listing files are needed, HHS agreed that a complete and accurate listing of OTC drug products would help FDA determine the extent to which the OTC market is in compliance with published monographs. HHS said that FDA is exploring the possibility that an outside contractor may be interested in developing and maintaining the drug product listing as an economic venture with FDA having access to information it requires for program purposes, thus substantially reducing or eliminating FDA's cost. HHS added that, if this approach is not feasible, FDA will review and make recommendations on the Drug Listing Act requirement for reporting information on OTC drug products.

Concerning our recommendation that FDA establish measurable objectives for the OTC enforcement effort and the expected timetables for performing the work, HHS agreed and said it considered this recommendation implemented. HHS pointed out that the strategy followed is for the Bureau of Drugs to identify high-priority producers and determine their compliance status and leave followup on the other products to the field. A specific timetable is not required for district office followup of lower priority products. The compliance program for OTC drugs, which was revised in September 1981 to include a required quarterly report from district offices, directs the offices to bring to the Bureau's attention any problems encountered in implementing the program. As we state in our comments on the HHS response to the recommendation to track the progress made in reviewing and following up on products subject to the monographs (see p. 30), we believe that these actions will be helpful. However, since district officials were uncertain about how much time they should devote to searching for products, headquarters officials need to monitor the compliance programs closely to assure that the district office efforts are not being wasted.

Regarding our recommendation that FDA maintain for each category of drug product a complete master list of firms manufacturing the drug and a list of products as they are identified for each monograph, HHS advised us that its present system permits the identification of products subject to the program. According to HHS, the system, which consists of reviewing catalogs and product files of drug manufacturers and distributors in each district, is admittedly slower and less efficient than use of a drug listing file. On the basis of our review, the system not only is less efficient, but also fails to identify many OTC products subject to the FDA monographs. Consequently, we believe our recommendation should be implemented if the drug listing file is continued in some form. If the file is not continued, HHS needs to be aware of the shortcomings of the present system and be prepared to improve its existing manual process.

HHS agreed with our recommendations to track the progress made in reviewing and following up on products subject to the monographs and to highlight, through written reports or regular meetings with district representatives, problems encountered in enforcing monographs. HHS noted that the compliance program for OTC drugs has been revised to include a required quarterly report from each district office on all compliance activities. The program also directs the district offices to bring to the Bureau of Drugs' attention any problems it is encountering in implementing the program. Although we agree that these actions will be helpful, we found during our visit to a field office that these officials are not always aware that a problem is being encountered. Therefore, we believe that headquarters officials should identify through their monitoring efforts any problems that are being encountered, but not being brought to their attention by the district offices.

APPENDIX I

OTC ADVISORY REVIEW PANELS AND STATUS OF MONOGRAPH DOCUMENTS AS OF MARCH 1, 1982

Panel/categories of OTC drugs	Panel convened	Panel report adopted	Proposed monograph published	Tentative final monograph published	Final monograph/ order published
Antacid:	2/22/72				
Antacids		1/23/73	4/5/73	11/12/73	6/4/74
Antiflatulents		1/23/73	4/5/73	11/12/73	6/4/74
Antimicrobial I:	6/29/72				
Topical antimicrobials		7/24/74	9/13/74	1/6/78	
Antimicrobial II:	7/26/74				
Topical antibiotics		10/28/76	4/1/77		
Topical antifungals		2/23/80			
Topical acne		11/15/80			
Antiperspirant:	3/15/74				
Antiperspirant		1/26/78	10/10/78		
Contraceptive and Vaginal:	8/2/73				
Vaginal contraceptives		12/8/78	12/12/80		
Vaginal drugs		12/8/78			
Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic:	11/6/72				
Anticholinergics		3/3/76	9/9/76		
Expectorants		3/3/76	9/9/76		
Antihistimines		3/3/76	9/9/76		
Antitussives		3/3/76	9/9/76		
Bronchodilators		3/3/76	9/9/76		
Nasal decongestants		3/3/76	9/9/76		
Combinations/general comments		3/3/76	9/9/76		
Dentifrices and Dental Care:	4/24/73				
Anticaries		7/13/78	3/28/80		
Oral mucossal injury		4/28/78	11/2/79		
Relief of oral discomfort		7/13/78			
Hemorrhoidal:	7/9/73				
Anorectal		1/24/78	5/27/80		
Internal Analgestic and Antirheumatic:	10/24/72				
Internal analgesic antipyretic, and antirheumatic		4/5/77	7/8/77		

APPENDIX I

Panel/categories of OTC drugs	Panel convened	Panel report adopted	Proposed monograph published	Tentative final monograph published	Final monograph/ order published
Laxative, Antidiarrheal, Antirheumatic and Emetic:	4/20/73				
Antidiarrheals		2/10/75	3/21/75		
Antiemetics		2/10/75	3/21/75	7/13/79	
Emetics		2/10/75	3/21/75	9/5/78	
Laxative		2/10/75	3/21/75		
Ophthalmic:	9/10/73				
Ophthalmic		3/10/79	5/6/80		
Oral Cavity:	2/26/74				
Oral cavity		12/14/79			
Sedatives, Tranquilizer and Sleep-Aid:	11/15/72				
Nighttime sleep-aid		10/21/75	12/8/75	6/13/78	
Stimulants		10/21/75	12/8/75	6/13/78	
Daytime sedatives		10/21/75	12/8/75	6/13/78	6/22/79
Topical Analgesic:	3/6/73				
External analgesics		5/23/78	12/4/79		
Topical otic		8/23/77	12/16/77		
Skin protectants		12/14/77	8/4/78		
Sunscreens		12/14/77	8/25/78		
Miscellaneous External:	1/13/75				
Antiseptic mercurials		10/6/80	1/5/82		
Camphorated oil		3/7/80	9/26/80		
Corn and callus removers		6/23/80	1/5/82		
Dandruff, seborrhea, and psoriasis		12/15/80			
Hormone creams		12/14/79	1/5/82		
Hair growers		12/10/79	11/7/80		
Ingrown toenails		4/20/80	10/17/80		
Insect bite neutralizer		12/15/80			
Parasiticides		12/15/80			
Poison (ivy, oak, and sumac) prevention		12/15/80			
Nailbiting and thumb-sucking deterrents		3/12/79	10/17/80		
Male genital desensitizers		4/20/80			
Skin bleaching		12/12/77	11/3/78		
Wart removers		12/11/79	10/3/80		

APPENDIX I

Panel/categories of OTC drugs	Panel convened	Panel report adopted	Proposed monograph published	Tentative final monograph published	Final monograph/ order published
Miscellaneous Internal:	1/13/75				
Anthelmintics		6/23/78	9/9/80		
Antidotes for treatment of acute toxic ingestion		6/24/78	1/5/82		
Aphrodisiacs		7/21/79			
Cholecystokinetics		6/23/78	2/12/80		
Digestive aids		1/19/79	1/5/82		
Diuretics/menstrual products		10/17/81			
Exocrine pancreatic insufficiency		11/19/78	12/21/79		
Hypophosphatemia and hyperphosphatemia		9/30/78	12/9/80		
Insect repellants		6/7/80	1/5/82		
Internal product for fever blisters and canker sores		9/28/80	1/5/82		
Overindulgence in food		8/23/81			
Deodorants for internal use		6/7/80	1/5/82		
Smoking deterrents		2/23/80	1/5/82		
Stomach acidifiers		6/23/78	10/19/79		
Sweet spirits of nitre		6/23/78	2/22/80	N/A	6/27/80
Weight control		3/2/79	2/26/82		

The following drug categories were not reviewed by the Miscellaneous Internal Panel and were deferred to the Office of New Drug Evaluation for review:

Ammonia inhalants
Appetite stimulants
Common kidney and bladder irritation remedies
Glucose tolerance
Increased caloric intake
Lactose tolerance
Leg muscle cramps
Oral electrolyte replacement
Poison oak and poison ivy (treatment)
Salt substitutes and salt tablets
X-ray contrast

The following drug categories were reviewed by the Miscellaneous External Panel, but will be included in other monograph documents (e.g., the panel recommended that diaper rash be included under the skin protectant monograph).

Boil ointment
Diaper rash
External product for fever blister and cold sores
Antiseptic alcohols
Astringents

The following products were reviewed by the Vitamin, Mineral, and Hematinic Panel, but responsibility for these products was transferred to FDA's Bureau of Foods on November 27, 1981.

Vitamins and minerals

APPENDIX II

DEPARTMENT OF HEALTH & HUMAN SERVICES

March 18, 1982

Mr. Gregory J. Ahart
Director, Human Resources
Division
United States General
Accounting Office
Washington, D.C. 20548

Dear Mr. Ahart:

The Secretary asked that I respond to your request for our comments on your draft of a proposed report "FDA's Approach to Reviewing the Safety and Effectiveness of Over-the-Counter Drugs Is Reasonable But Progress Is Slow." 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

APPENDIX II

COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES ON THE GENERAL ACCOUNTING OFFICE'S DRAFT REPORT, "FDA'S APPROACH TO REVIEWING THE SAFETY AND EFFECTIVENESS OF OVER-THE-COUNTER DRUGS IS REASONABLE BUT PROGRESS IS SLOW," DATED FEBRUARY 16, 1982

General Comments

We appreciate the opportunity to comment on the draft report. Generally, we find the report to be well balanced in tone and constructive in its analysis of the Food and Drug Administration's (FDA) over-the-counter (OTC) drug evaluation program. The report points out that the policies and procedures for conducting the over-the-counter drug review are logical and reasonable, although the review is taking significantly longer to complete than had been anticipated. We agree with both these observations. We also generally agree that the report has identified some areas of program operation requiring corrective action. In fact, FDA has already initiated some corrective measures as a result of discussions with the auditors and the agency's own assessment of the program. We believe, however, the report could be improved by including some discussion of the rationale upon which the OTC review was originally planned and subsequent events outside FDA's control that have influenced both the length of time required for the review and the nature of the decisions made.

The OTC drug review has proven to be one of the largest, most complex projects ever undertaken by the FDA. Over a nine-year period, 17 expert advisory panels involving 200 persons were involved in the review of 731 active drug ingredients for 1,393 uses in over 300,000 drug products. The panels met 522 times and submitted reports on 64 classes of drugs which included the panels' evaluation of whether the active drug ingredients and the marketing conditions were Category I (generally recognized as safe and effective), Category II (not generally recognized as safe or effective), or Category III (insufficient evidence for the panel to reach a conclusion). In the absence of accurate estimates of the enormity of this project, and with a sincere desire to complete the project as expeditiously as possible, the three-year period originally planned appeared ample. In retrospect it was grossly over optimistic.

One major problem that emerged in this process was the paucity of quality scientific evidence available for review by the panels in reaching final conclusions on the general recognition of safety and effectiveness. The scope of the review and the inadequacy of the evidence in the medical literature were among the numerous important factors in extending the review well beyond the originally anticipated time.

A number of other factors have also contributed to the lengthy review time. Paramount among them were events leading to changes in the legal climate surrounding the review. Some of these events added new steps

APPENDIX II

to the review process. Others required careful consideration (with a concomitant expenditure of resources) of troublesome and unexpected issues bearing on how the OTC review process should function. The following events are significant in this respect:

1. Questions arose concerning the need for transcripts of the entire proceedings and whether they should be part of the administrative record. As a result, FDA amended the OTC drug review procedural regulations to provide that transcripts were not part of the record. In subsequent litigation under the Freedom of Information Act (FOI), FDA was directed to release transcripts of portions of panel meetings that had been closed to the public. The resultant impact of this decision was a temporary diversion of resources to respond to lengthy FOI requests.

2. The enactment of the "Government in the Sunshine Act" in 1976 required FDA to open virtually all portions of the OTC review panel meetings to the public. An outgrowth of this occurrence was more extensive participation by industry and consumer groups and a related decline in the speed of the panels' deliberative process. We believe that, on balance, the process benefited by this decision and the increased public scrutiny of and participation in panels' deliberations. We believe the panels' reports have generally been better because of this input. Some actions to reformulate products or take other corrective measures were initiated immediately because of the participation of industry representatives.

3. Issues relating to the marketing status of prescription drugs that were also under consideration in the OTC review resulted in protracted administrative proceedings and related litigation.

4. The OTC drug review regulations permitting firms to continue marketing products in Category III while testing them for safety and effectiveness were successfully challenged in court (the "Category III Lawsuit"). As a result of the court's decision, FDA was required to change substantially the procedures for developing monographs and to create an administrative procedure for firms to submit the results of their product testing to FDA. These amended procedures have recently been challenged by litigation that is still pending.

5. Recent legislation and Executive Orders direct FDA to consider economic matters, as well as safety and effectiveness, in the course of its administrative proceedings.

Any one of these events alone would not necessarily have had a significant impact on the review. Taken together and with other similar events, however, they have had an adverse impact on the progress of the review.

It is important to underscore the fact that although the OTC review is incomplete, benefits have already been realized, particularly in the quality of OTC drugs available to the public. In their deliberations, the advisory panels recommended that more than 30 drugs be converted from prescription use to OTC use. FDA has agreed with most of these recommendations and, indeed, has permitted the marketing of new OTC products containing drugs formerly limited to prescription use even though the final monographs have not been published. In addition, FDA is suggesting that some prescription drugs other than those considered by the panels be made available for self-medication by the general public. Also, although only one final monograph has been published, the industry has already adopted many of the recommendations of the panels and has reformulated many products to delete those ingredients which were classified as Category II or to replace those ingredients that were classified as Category III with other ingredients classified as Category I. The precise number of these reformulations and relabelings is not available, but it is estimated to affect thousands of products. Further, and perhaps more significantly, in several instances where ingredients were identified as being unsafe, prompt enforcement by FDA has resulted in their being removed from the OTC marketplace promptly. Notable examples include methapyrilene an antihistamine which was used in the many OTC cough, cold and nighttime sleep aid products; hexachlorophene which had been in topical antimicrobial skin cleanser products; zirconium in antiperspirants; and sweet spirits of nitre. FDA intends to continue this practice to asssure that any ingredients which may present safety concerns are properly identified and removed from OTC products in the marketplace.

In addition, we want to stress two aspects of the OTC review and enforcement activities that we believe the report should recognize:

1. The OTC review has been conducted under a stated philosophy that the first priority was to complete the advisory panel reviews and publish their reports as proposed monographs. This is explained more fully in our response to the first recommendation.

2. As described more fully in our response to the specific recommendations, resource constraints have prevented maintenance of the OTC drug listing for a number of years. FDA has been forced to employ less efficient, but nonetheless effective methods of identifying products subject to the monographs and taking enforcement action when necessary. This practice is consistent with the enforcement activities relevant to other products for which there are no

requirements to list. We do not anticipate that FDA will be able to expend resources to maintain the OTC drug listing file for the forseeable future.

GAO Recommendation

We recommend that the Secretary direct the Commissioner of FDA to take steps to complete the OTC review in the most timely manner possible. Specifically he should direct the Commissioner to:

1. —Establish priorities for completing individual monographs based on objective criteria such as consumer sales or market impact and establish detailed milestones for completing the development of monographs and the publication of final regulations based on actual experience, staff skills and experience, the work required, and the priority of the monograph document.

Department Comment

We agree that FDA should establish priorities for producing individual documents for publication. Priorities are established and are being used. The top priority is Panel Reports and Proposed Monographs followed by Tentative Final Monographs (TFM) and Final Monographs (FM). Important safety issues are taken immediately and do not wait in queues. As early as 1978 FDA had designated 10 monographs as having a high priority. However, within the total framework of the OTC review with respect to publishing panels' reports and developing monographs, factors other than market impact or consumer sales have determined which documents were published first. Early during the review FDA determined that the first priority was to complete all the panel reviews and publish the reports. Following completion of the panel phase, FDA would move to the subsequent stages of the process, i.e., publishing Tentative Final Monographs and then Final Monographs. However, with this concerted effort to bring to a close the initial stage of review, work on TFMs and FMs was begun on documents that were already in later stages of development in order not to delay unnecessarily those monographs for which comments had been submitted on earlier publications. Current priorities for publishing documents take into consideration the current status of documents, the number and complexity of issues requiring resolution, the impact that issues in one monograph may have on policies relative to other monographs (many ingredients are included in more than one monograph) and to policies relative to the regulation of prescription drugs.

It should also be recognized that while documents may be assigned a high priority and work continues on those to resolve issues, other, lower priority documents may actually progress faster because there are fewer issues requiring resolution or the issues involved are more amenable to simple and quick resolution. Reviewers are normally assigned a mixture of high and low priority monographs. We believe this makes the best utilization of their time and facilitates completing the review because they can be working on several different documents simultaneously, thus eliminating potential periods of inactivity while major issues are being resolved in more complex documents. It also keeps the "pipeline" filled with documents which must be published and thus processed by other offices in FDA.

GAO Recommendation

2. —Establish goals for expediting the OTC review and develop a system for measuring progress in completing all monograph documents which measures progress against projected milestones, and which provides feedback to FDA and the Department.

Department Comment

We agree. FDA has established goals for completing the OTC review. Goals for completing specific documents are included in the Merit Pay and SES plans of supervisors and managers at various levels in FDA, and in employee performance plans of the Employee Performance Management System. Progress is measured via regular reviews between employees and supervisors at all levels. Progress toward those goals is being tracked by use of a new system designed to provide management with current information on the status of each document and the amount of time elapsed at each stage of the review. The new report will assist FDA managers in identifying potential problems and resolving them in an expeditious manner. Progress toward meeting the goals is also monitored through regular meetings with the Bureau of Drugs' Director and Deputy Director and personnel in the Division of OTC Drug Evaluation (DODE), through regular staff meetings within DODE, through weekly status reports and through regular meetings of FDA-wide OTC Steering Committee, Chaired by the Deputy Commissioner of FDA.

GAO Recommendation

3. —Develop a mechanism for timely identification and resolution of policy issues by high-level agency officials.

Department Comment

We agree and moreover, believe this recommendation has already been implemented. The Bureau of Drugs has a standing meeting bi-weekly with the Associate Director for Drug Monographs at which technical/policy issues in the OTC review are presented to Bureau management for resolution. The General Counsel (Food and Drug Division) and representatives of other FDA components are also invited to attend these meetings as necessary. Issues that cannot be resolved at the Bureau level or that have major policy implications are discussed and resolved at OTC Drug Steering Committee meetings. In addition, the Deputy Bureau Director has initiated frequent one-on-one meetings with the Director of the Division of Over the Counter Drug Evaluation to provide day-to- day guidance and to identify issues to be brought to Bureau or OTC Steering Committee Meetings for resolution.

GAO Recommendation

4. --Review, and revise where appropriate, procedures for reviewing draft monograph documents to ensure that branch personnel are given necessary supervision and authority to develop the products for which they are responsible.

Department Comment

We concur. FDA is currently reviewing the OTC program to determine what, if any, procedural and policy changes may be appropriate. This review will include an evaluation of the organizational structure and placement of the review division, the skills required to complete the review versus those available within the division, and mechanisms for resolving issues that arise in preparing documents for publication.

GAO Recommendation

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

5. --Determine, based on the anticipated cost and timeliness of possible alternative approaches, if the OTC drug listing files are needed. If the listing is not needed, FDA should propose legislation to amend the Drug Listing Act to eliminate the requirement for reporting. If it is needed, FDA should assess the relative efficiency of updating the entire system in the next few years or updating the system by drug category as monographs are published.

Department Comment

We agree that a complete and accurate listing of OTC drug products would contribute to FDA's ability to determine the extent to which the the OTC market is in compliance with published monographs. As GAO points out, resource constraints and staff turnover has resulted in the OTC Drug Products File not being maintained for the past few years.

APPENDIX II

FDA has explored alternative means of developing and maintaining the OTC drug product listing within budget constraints. A consultant firm under contract evaluated the Drug Listing System and submitted a report and options for maintaining it. We are currently exploring the possibility that an outside contractor may be interested in developing and maintaining the drug product listing as an economic venture and under a system where FDA can have access to information it requires for program purposes, thus substantially reducing or eliminating the cost to FDA. A "Sources Sought Notice" will be published inviting expressions of interest in such a system. If this approach is not feasible, FDA will review and make recommendations on the Drug Listing Act requirement for reporting information on OTC drug products. As a result of the lack of an accurate OTC Drug Listing System, FDA has identified marketed OTC drug products by reviewing catalogues and product files of drug manufacturers and distributors in each district. This system is admittedly slower and less efficient than use of a drug listing file, however it is workable and does permit identification of products subject to the program.

GAO Recommendation

6. --Establish measurable objectives for the OTC enforcement effort and the expected timetables for performing the work.

Department Comment

We agree and consider this recommendation implemented. Once a final monograph or order is published, the Bureau of Drugs has sufficient lead time prior to its effective date to identify the large volume producers (designated as high priority) and determine their compliance status. Regulatory letters, which require a response within 10 days, are sent to those firms whose products do not comply with the monograph and a copy of the letter is sent to the appropriate district office. For these high priority products the Bureau of Drugs' objective, with assistance from the district offices as necessary, is to followup to assure that these cases reach closure as soon as is reasonable. The strategy adopted is for the Bureau of Drugs to act on the large volume products and to leave followup on the other products, which may be greater in number but collectively much less in market value, to the field. A compliance program has already been issued to the field which

establishes this procedure, OTC Drug Monograph Implementation - General Compliance Program, 7361.003. As each final monograph or order is published, a compliance program circular is issued to the field with instructions to identify other products subject to the monograph, issue Regulatory Letters and followup as necessary. Each compliance program circular identifies a national coordinator and each district office has a coordinator who is responsible for assuring that the compliance activities proceed in a timely and efficient manner. A specific timetable is not required for district office followup of lower priority products; moreover, the compliance program for OTC drugs has been revised to include a required quarterly report from each district office on all compliance activities covering compliance program circulars (i.e., antacids and daytime sedatives). Common practice is for each district to act promptly on the highest volume products on its list and to followup on the low priority low volume products on a sampling basis. This is consistent with enforcement strategies for other product classes in order to make efficient use of limited resources. This report also must include negative information such as firms and products out of compliance. The program also directs the field to bring to the Bureau of Drugs' attention any problems it is encountering in implementing the program. Problems and solutions can be discussed in meetings or via conference calls with the FDA's districts to handle important issues promptly. The revision was issued via OTC Drug Study Bulletin No. 13, July 13, 1981 and was incorporated into the OTC Compliance Program on September 1, 1981. We believe this will increase the effectiveness of FDA's monitoring efforts. The OTC drug compliance program and compliance program circulars are continuous. The district offices will conduct routine surveillance as part of their ongoing inspectional efforts and attempt to identify new products as they enter the marketplace.

GAO Recommendation

7. --Maintain for each category of drug product a complete master list of firms manufacturing the drug and a list of products as they are identified for each monograph.

Department Comment

Our current enforcement plans described above identify high priority products, and FDA's routine surveillance efforts identify other out-of-compliance products. Please refer to the response to GAO Recommendation Number 5.

GAO Recommendations

8. —Track the progress made in reviewing and following up on products subject to the monographs.

9. —Highlight, through written reports or regular meetings with district representatives, problems that are encountered in enforcing monographs.

Department Comment

We agree that progress in determining compliance with OTC monographs should be tracked and that mechanisms should exist for identifying and resolving problems quickly. The compliance program described in response to Recommendation Number 6 describes the mechanism for district office reporting on their progress and for bringing problems to management's attention.

FDA has effective mechanisms for the timely identification and resolution of problems. Since 1976 the Bureau of Drugs headquarters staff has utilized OTC Drug Study Bulletins to alert the district offices to potential problem areas in enforcement. The Executive Director of Regional Operations, FDA, maintains a telecommunications system whereby headquarters can communicate with all district offices during a conference call to discuss general problem areas periodically as needed. Also, standard operation procedures require that the districts call headquarters when specific problems are encountered.

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