BY THE U.S. GENERAL ACCOUNTING OFFICE

Report To The Secretary Of Health And Human Services

FDA Can Further Improve Its Adverse Drug Reaction Reporting System

The Food and Drug Administration has improved the use of its adverse drug reaction reporting system since GAO reported on it in 1974. Medical officers are more familiar with the system and are using it more. However, improvements can still be made.

Many adverse reaction reports do not get to the Division maintaining the system and many others require a long time to get into the system. Some of the missing or late reports involved serious reactions which were not discussed in the drug labeling. Reporting by nonmanufacturer sources, such as hospitals or physicians, could also be increased.

GAO recommends actions to resolve these and other problems.

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MARCH 8, 1982

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UNITED STATES GENERAL ACCOUNTING OFFICE
WASHINGTON, D.C. 20548

HUMAN RESOURCES
DIVISION

B-206458

The Honorable Richard S. Schweiker
The Secretary of Health and
Human Services

Dear Mr. Secretary:

This report discusses our review of the Food and Drug Administration's adverse drug reaction reporting system. The report contains recommendations to you for further improving the use of the system and for improving the completeness and timeliness of data entering the system.

As you know, section 236 of the Legislative Reorganization Act of 1970 requires the head of a Federal agency to submit a written statement on actions taken on our recommendations to the Senate Committee on Governmental Affairs and the House Committee on Government Operations not later than 60 days after the date of the report and to the House and Senate Committees on Appropriations with the agency's first request for appropriations made more than 60 days after the date of the report.

We are sending copies of this report to the cognizant Senate and House Committees and Subcommittees and to the Director, Office of Management and Budget.

We would appreciate being advised of your views and any action you plan to take regarding the matters discussed in this report.

Sincerely yours,

Gregory J. Ahart
Director

GENERAL ACCOUNTING OFFICE
REPORT TO THE SECRETARY OF
HEALTH AND HUMAN SERVICES

FDA CAN FURTHER IMPROVE ITS ADVERSE DRUG REACTION REPORTING SYSTEM

D I G E S T

The Food and Drug Administration (FDA) maintains a system to collect, identify, and retain information on adverse reactions to drugs. FDA's Division of Drug Experience is responsible for maintaining the system; the Office of New Drug Evaluation, in turn, is responsible for taking any necessary regulatory action, such as requiring the revision of the labeling or withdrawing the drug from the market. (See p. 1.)

In a March 1974 report, GAO noted that the reporting system was underused as a tool to regulate marketed drugs. At that time some of the medical officers did not know the system existed, followup on incomplete reports was inadequate, information needed to regulate drugs was not always sent to the medical divisions, and improvements were needed in the collection of adverse reaction data. (See p. 4.)

GAO made this review because a comprehensive survey of FDA's monitoring of prescription drugs showed that many of the problems found in 1974 still exist. In addition, postmarketing surveillance of drugs, which includes adverse reaction reporting, has been of considerable congressional interest because of its recommended use as a vehicle to expedite approval of new drugs. (See p. 4.)

USE OF THE ADVERSE DRUG REACTION REPORTING SYSTEM HAS INCREASED BUT IMPROVEMENTS CAN STILL BE MADE

Medical officers are making more use of the adverse drug reaction reporting system than they did in 1974. Eighty percent of the 40 medical officers GAO interviewed have used the system at least once and 25 percent of these use it on a regular basis. This is a significant increase over what GAO found in 1974. Many medical officers said the system is useful and is

improving. Some attribute this to the efforts of the staff in the Division of Drug Experience. (See p. 8.)

The Division of Drug Experience has offered seminars and workshops on the capabilities and limitations of the reporting system. Despite this training, some medical officers indicated that they were unaware of what the system could do. The Division needs to increase training efforts, and the Office of New Drug Evaluation needs to act to increase medical officer attendance at these sessions. (See p. 10.)

DELAYS AND MISSING REPORTS HAMPER ADVERSE DRUG REACTION SYSTEM'S ABILITY TO IDENTIFY POTENTIALLY SERIOUS REACTIONS

For 21 drugs, GAO reviewed 2,182 individual adverse reaction reports submitted by manufacturers and found that only 957 reports (44 percent) had been entered into the system at the time of GAO's review and only 1,270 (58 percent) of the reports had ever reached the Division of Drug Experience. (See p. 13.)

GAO also found that reports that were received by the Division took nearly 5 months, on the average, from the time they were received by FDA, to be entered into the computerized system. (See p. 16.)

As a result, the system failed to identify some potentially serious adverse reactions. For one drug, GAO found two cases of aplastic anemia, which in many cases is fatal, and four cases of hypoglycemia, which may result in coma and death, that did not come to the Division's attention. For some of the other drugs, GAO identified reports of adverse reactions such as sudden death and cardiorespiratory, kidney, and liver failure that failed to reach the Division of Drug Experience.

In the above cases, regulatory action may or may not have been warranted. That judgment must be left to FDA. However, FDA needs all the information available if it is to make timely determinations on the need for regulatory action. (See p. 17.)

As a result of GAO's findings and a survey conducted by the Bureau of Drugs, the procedures for routing adverse reaction reports submitted by manufacturers were revised. This should allow more reports to reach the Division of Drug Experience sooner.

This change, however, may not result in more reports getting into the system. Current staff in the Division is unable to process and evaluate its present workload as evidenced by a backlog of over 7,000 reports during GAO's review. Because of the current budget situation, additional staff and resources may not become available and FDA should explore alternative methods of evaluating and entering reports into the system. (See p. 18.)

INCREASED EFFORTS ARE NEEDED TO IMPROVE REPORTING OF ADVERSE REACTIONS

Between 1970 and 1980 the Division of Drug Experience entered over 115,000 reports into the adverse drug reaction reporting system. By far the largest number of reports during this period were received from manufacturers, who are required to report. (See ch. 4.)

The Division has done little in recent years to encourage reporting of adverse reactions from sources other than manufacturers. The number of reports from private and federally operated hospitals has decreased dramatically since 1970.

The Division has reevaluated its data needs and plans to try to increase nonmanufacturer reporting. Although this is a good starting point, GAO believes that better dialog with major medical associations, such as the American Medical Association and the American Hospital Association, would be useful. In addition, greater efforts are needed to encourage reporting from Federal hospitals.

GAO explored alternative methods of increasing adverse reaction reporting. These methods have been effective in other types of programs and merit consideration by the Division. (See ch. 4.)

RECOMMENDATIONS TO THE SECRETARY OF HEALTH AND HUMAN SERVICES

The Secretary should require the Commissioner of FDA to:

--Require medical officers to attend seminars and workshops sponsored by the Division of Drug Experience intended to train them on the capabilities of the adverse drug reaction system. (See p. 11.)

--Instruct the Division of Drug Experience to solicit feedback from medical officers in the Office of New Drug Evaluation as to how the system could be improved to better meet their needs and implement those proposals which are cost effective and could increase medical officers' use of the system. (See p. 11.)

--Explore alternative methods for evaluating and processing nonserious, known reactions to drugs. Consideration should be given to not entering into the system some of the common known reactions which add little or nothing to the knowledge of marketed drugs. (See p. 19.)

--Explore alternative methods, such as a toll-free or collect-call service, to increase the quantity and quality of reports from non-manufacturer sources. (See p. 27.)

In addition, the Secretary should:

--Encourage other Federal agencies operating hospitals to develop an adverse drug reaction reporting system. (See p. 27.)

--Direct administrators of hospitals within the Department of Health and Human Services to cooperate with the Division of Drug Experience by establishing and using reporting systems in their hospitals. (See p. 27.)

VIEWS OF FDA OFFICIALS

The Commissioner of FDA generally agreed with the recommendations and pointed out actions FDA is taking or plans to take.

Contents

ABBREVIATIONS

AMA	American Medical Association
FDA	Food and Drug Administration
GAO	General Accounting Office
USP	United States Pharmacopeia

CHAPTER 1

INTRODUCTION

Each year millions of Americans use prescription drugs. In addition to positive therapeutic effects, drugs may cause undesirable side effects or adverse reactions. These can be as minor as a headache or an upset stomach or as serious as death.

The Food and Drug Administration (FDA) is responsible, under the Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 301 et seq.), for ensuring that drugs used in interstate commerce are safe and effective. FDA carries out these responsibilities by monitoring new drugs throughout all stages of development and use--including testing the drugs on human subjects, commonly known as clinical tests. During these limited tests many of the adverse reactions which may be attributed to each drug are discovered. In some instances, however, adverse reactions to new drugs are only discovered through widespread use of the drug. As a result, FDA continuously collects and analyzes data on adverse reactions to new drugs so it can be in a position to notify physicians and the public of previously unknown adverse effects.

ADVERSE DRUG REACTION REPORTING SYSTEM

FDA developed an adverse drug reaction reporting system in 1960 to collect, identify, and retain information on adverse reactions to drugs. Since 1965 data reported have been entered into a computerized data base.

The Division of Drug Experience within FDA's Bureau of Drugs is responsible for maintaining the system. Essentially these responsibilities include developing sources of adverse reaction reports; collecting, analyzing, and storing that information; and, in the case of serious reactions, forwarding that information to the six medical divisions in the Office of New Drug Evaluation. The Office, in turn, is responsible for taking regulatory action, which may include limiting the use of the drug, requesting changes to the approved labeling, or removing the drug from the market.

As adverse reaction reports are received, medical evaluators in the Division analyze the information and determine (1) how probable it is that the specific drug or drugs indicated in the report caused the reaction, (2) how serious the reaction is, and (3) whether the reaction is included in the drug's approved labeling.

The criteria used by the Division in categorizing the cause and effect relationship of the adverse reaction and the drug are as follows:

"Highly probable" - A highly probable causal relationship between a drug and an event exists when the reaction follows within a reasonable time after the administration of the drug, follows a known response pattern to the suspected drug, and is confirmed by improvement when the drug is stopped and reappearance of the reaction when the drug is readministered.

"Probable" - A probable causal relationship exists when the reaction follows a known response pattern to the drug and is confirmed by improvement when the drug is stopped but cannot be reasonably explained by the known characteristics of the condition being treated.

"Possible" - A possible relationship exists when the reaction follows within a reasonable time after the administration of the drug, follows a known response pattern to the suspected drug but could have been caused by the condition being treated or by other drugs.

"Remote" - A remote relationship exists when there is no reasonable temporal relationship between the reaction and the administration of the drug.

In addition to determining a cause and effect relationship, the Division of Drug Experience must also determine if the reaction is serious or nonserious. The Division defines a serious reaction as an event that meets one or more of the following criteria: (1) is potentially life-threatening, (2) is permanently disabling, (3) requires hospitalization for treatment, (4) requires drug or other extensive therapy for treatment, or (5) takes longer than 15 days for recovery to occur.

When a report of a serious, previously unreported reaction is received, the Division is required to forward the information to the responsible medical officer in the Office of New Drug Evaluation. This information can then be used by the medical officer in evaluating the need for possible regulatory action.

The adverse drug reaction reporting system is only a portion of FDA's total postmarketing surveillance program. In addition to compiling and analyzing adverse reactions reported by drug manufacturers, physicians, hospitals, and other health professionals, the program includes:

--A literature search of 140 English language medical journals, the results of which are published monthly in a publication called "Current Drug Experience Literature."

--Funding of several registries (collections of adverse reactions affecting a particular body organ or body system), such as the Hepatic Registry, reactions affecting the liver, and the Ophthalmology Registry, reactions affecting the eyes. The data from these registries are not included in the adverse reaction data base but are accessible by the Division of Drug Experience.

--Receipt of adverse reaction information from the World Health Organization and foreign country drug regulatory agencies as well as information from other Federal agencies, such as the National Institutes of Health, the Drug Enforcement Administration, and the Centers for Disease Control.

--Collection of drug experience information on patients in a clinical or hospital setting through intensive drug monitoring studies funded by FDA. These studies have provided some firm incidence rates for acute adverse reactions due to drugs commonly used in a hospital setting and allow FDA to explore potentially drug-related disorders which would not usually be detected in spontaneous reporting systems.

--Funding of a contract to explore the use of Medicaid data in postmarketing surveillance. Data on 1.2 million patients from two States will be used to identify possible adverse reactions to drugs and to corroborate data generated by the adverse drug reaction reporting system.

FDA disseminates information on new, serious, or unexpected drug reactions to the medical community by responding to requests for information from physicians or hospitals or through such publications as the "ADR [Adverse Drug Reaction] Highlights" and articles in the "FDA Drug Bulletin," which is circulated to over 300,000 health professionals.

Postmarketing surveillance of drugs has been of considerable congressional interest because of its recommended use as a vehicle to expedite approval of new drugs. For example, the Subcommittee on Science, Research and Technology, House Committee on Science and Technology, recommended in a November 1980 report on FDA's process for approving new drugs that greater use be made of postmarketing surveillance. It believed that improved postmarketing surveillance would allay fears regarding the safety of new drugs.

PREVIOUS GAO REVIEW

In a March 1974 report to the Congress, 1/ we noted that the adverse drug reaction reporting system was underutilized as a tool to regulate marketed drugs. At that time we found that: (1) some of the medical officers in the medical divisions did not know the system existed, (2) followup on incomplete reports was inadequate, (3) information needed by the medical divisions to regulate drugs was not always sent to them, and (4) improvements were needed in the collection of adverse reaction data.

We recommended that the Commissioner of FDA (1) ensure that the medical officers in the regulatory divisions (medical divisions in the Office of New Drug Evaluation) are made aware of the information available to them in the reporting system and that they use the system, (2) take more aggressive action to develop sources of adverse reaction reporting and to improve communication with private hospitals, (3) require the monitoring unit (now the Division of Drug Experience) to obtain followup information on incomplete reports, (4) centralize all information on adverse drug reactions, and (5) require the monitoring unit to comply with established procedures for notifying the regulatory divisions of all serious reactions.

FDA concurred with most of our recommendations and took steps to correct the communication problems between the monitoring unit and the regulatory divisions. However, as discussed in the following chapters of this report, many of the problems discussed in our 1974 report still exist.

OBJECTIVES, SCOPE, AND METHODOLOGY

We performed this review because our comprehensive survey of FDA's monitoring of prescription drugs showed that some of the problems we identified in our 1974 report still existed. Our objectives in this review were to determine: (1) the extent to which adverse reaction reports received by the medical divisions were in turn received by the Division of Drug Experience and entered into the adverse reaction data base, (2) the extent to which the medical divisions were using adverse reaction data to monitor and regulate prescription drugs, (3) the current efforts employed by the Division of Drug Experience to improve the quantity and quality of adverse drug reaction reports, and (4) the usefulness of grants and contracts to generate adverse drug reaction data.

1/"Assessment of the Food and Drug Administration's Handling of Reports on Adverse Reactions From the Use of Drugs" (B-164031(2)).

We interviewed 40 medical officers in the Office of New Drug Evaluation. Nineteen either were responsible for the drugs selected in our review or were suggested by Office personnel, and the other 21 were selected from a list of all medical officers within the Office. Our selections included the directors of five 1/ of the six medical divisions and included medical officers from all six divisions. We also spoke with the Director of the Division of Drug Experience and evaluators in that Division. The purpose of these interviews was to determine their impressions of the adverse drug reaction system, its uses, limitations, and ways in which it could be improved.

In addition, we reviewed files for contracts and grants to collect adverse drug reaction data. We reviewed pertinent regulations, reports, and other documents at FDA headquarters in Rockville, Maryland. We also visited five hospitals, four in the Washington-Baltimore area, and one in New York City, to discuss their adverse drug reaction reporting systems, their interface with FDA, and possible methods of improving hospital reporting.

We contacted officials of the American Medical Association (AMA) and the Joint Commission on the Accreditation of Hospitals to discuss barriers to reporting and methods to improve reporting from private physicians and hospitals and to determine what, if any, action they had taken to encourage reporting of adverse reactions.

We also spoke with United States Pharmacopeia (USP) officials concerning the feasibility of using a toll-free telephone service as a method to improve the quantity and quality of reports from nonmanufacturer sources. USP operates a drug product reporting system under a contract with FDA. We also spoke with an official in another FDA Bureau that employs a collect-call telephone service designed to assist small manufacturers in registering and applying for approval of their products with FDA, and interpreting FDA regulations.

To determine if all manufacturers' reports were getting to the Division of Drug Experience and into the computerized system, we selected 21 drugs. We selected two to five drugs from each of FDA's six review divisions which were approved between 1975 and 1978 and, to the extent possible, represented new molecular entities or new salts with at least modest therapeutic gain. The 21 drugs we selected did not constitute a statistical sample, but we have no reason to believe that our observations were not

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1/The other division director was not available for interview when we were performing the audit work.

representative of what we would have found had we selected a different sample. We selected the 1975-78 time frame to allow sufficient time for marketing experience so that manufacturers would have submitted periodic reports to FDA.

For 19 of the 21 drugs selected for review, we extracted identifying information from each individual adverse reaction report submitted by manufacturers from the date each drug was approved through September 1980. Because of the large number of reports submitted on the other two drugs, we selected a sample of reports submitted. These drugs are identified in the table on page 15 as drugs "A" and "H." The adverse reaction reports we reviewed included both those manufacturers submit on a regularly scheduled basis and those they are required to submit within 15 days of the date they are notified of the reaction.

We requested computer printouts which contained all the reports that had been entered into the system for each of the selected drugs. By matching the Division of Drug Experience data with the data we abstracted from individual adverse reaction reports, we identified the reports that had been entered into the system. To ensure that we had identified all the reports in the system, we asked the Division staff to review the results.

In addition, we scanned over 7,500 individual adverse drug reaction reports in the Division which represented the backlog of reports awaiting input during our review. This was done to determine which reports in the backlog applied to the 21 drugs included in our review. We also reviewed reports that had arrived in the Division but had not yet been evaluated.

We selected a random sample of the reports identified as already in the system to determine how long it took manufacturers' reports to get from the Office of New Drug Evaluation to the Division of Drug Experience and, from that point, how long it took to input the data into the automated data base. For the purpose of this review, we believed that a 25-percent sample of the reports identified as in the system would be sufficient. The selection was made using a random start and selecting every fourth report thereafter from a list of all reports determined to be in the system.

The Division supplied us with an alphabetical list of all suspected adverse reactions that had been reported on each drug. We compared these lists with the most current approved labeling for each drug to determine which adverse reactions were not included in the manufacturers' labeling and what action, if any, should have been taken by either the Division or the Office.

Finally, to determine what impact the delays and missing reports had on regulating new drugs, we analyzed the manufacturers' reports that were sent to the Office but had not been received by the Division. We compared the reactions reported with those already in the approved labeling for each drug to determine if regulatory action should have been taken but was not.

We provided FDA with a statement of facts which included our findings and suggestions for program improvement. FDA's comments have been incorporated, as appropriate, into this report.

This review was performed in accordance with GAO's current "Standards for Audit of Governmental Organizations, Programs, Activities, and Functions."

CHAPTER 2

USE OF THE ADVERSE DRUG REACTION REPORTING SYSTEM HAS INCREASED BUT IMPROVEMENTS CAN STILL BE MADE

Medical officers are making more use of the adverse drug reaction reporting system than they did in 1974. Eighty percent of the medical officials we interviewed had requested data from the system at least once, and 25 percent of these use the system on a regular basis. This is a significant improvement over what we found in 1974. However, additional improvements can be made.

Despite workshops held by the Division, some medical officers are apparently unaware of the capabilities and limitations of the system. Greater efforts are needed to ensure that all medical officers attend the workshops.

The Division needs to increase medical officer confidence in the system. As discussed in chapter 3, this requires improving the timeliness with which reports get into the system and assuring, to the extent possible, that all new reports and reports of serious reactions get into the system. Consideration should also be given to implementing suggestions made by the medical officers for improving the system (see p. 9).

MEDICAL OFFICERS ARE USING THE ADVERSE DRUG REACTION SYSTEM MORE

The medical officers in the Office of New Drug Evaluation have increased significantly their use of the adverse drug reaction system since our previous review. At that time less than half of the medical officers interviewed used the system. Currently, 80 percent of the medical officers we interviewed have used the system at least once, and 25 percent of these use it regularly. Of the other medical officers, most had not had an occasion to use the system but planned to use it in the future.

As discussed on page 5, we interviewed 40 medical officers. We asked them (1) how much use they made of the system, (2) how timely the information received from the Division of Drug Experience was, and (3) how useful the information was as a regulatory tool.

Two division directors told us that, in their present positions, they do not get much opportunity to use the system. Two directors encourage their staff to use it. One division director believes the system is a very important asset. He told us that on one recent occasion, information supplied by the Division of

Drug Experience resulted in FDA's removing a drug from the market. According to this director, if it had not been for the system his division might not have become aware of these serious reactions until much later. Some of the reports had come from private physicians and had been sent directly to the Division of Drug Experience.

Several medical officers told us the system was useful. One said that it was useful in spotting trends early. Another said that it saved her time. A third medical officer stated that the information from the system was useful as supporting data. Another medical officer told us that he liked the adverse reaction system because all the data are in one place and requesting information is preferable to searching through the literature in the library. Several commented that they use the system as a source for backup information.

Several medical officers said that the Division of Drug Experience sends them information on their drugs without their having to request it. According to one medical officer, the Division staff keep in close contact with his medical division and are able to anticipate its needs.

One medical officer said that he was satisfied with the system. He told us that the data are incomplete, but this is a result of incomplete reports and not the system itself. A few medical officers told us that the system has improved, and they are now able to rely on data more than they could in the past. They attribute the improvement to both good staff and an interested division director.

USE OF ADVERSE DRUG REACTION SYSTEM CAN BE FURTHER INCREASED

As part of our discussion with the 40 medical officers, we asked them what changes could be made to improve the system to better meet their needs.

By far, the most common response we received was that information on all reports received to date on a drug be sent to them periodically rather than only upon request. Medical officers in two of the six divisions told us that their counterparts in the Division of Drug Experience do this already and believe the information is received on a more timely basis and is much more useful to them.

A number of medical officers suggested that reports not be routed through the Indexing and Abstracting Service because they were getting lost (as discussed in ch. 3, this change has been made). Others suggested that the Division strive to improve the accuracy of its printouts, or include its opinion on the causality

of the reactions. Still others would like to have reports on adverse reactions which occurred during clinical trials included in the system.

We discussed these suggestions with the Director of the Division of Drug Experience, who believes all are feasible and desirable. The Director, however, has some reservations concerning causality assessments. She told us that the information is in the system, but there are many ways of assessing causality, none of which is commonly accepted. Because of the medical-legal problems that may occur based on any assessment, she would prefer to give the medical officers the data that the Division used to make its determination and allow the medical officers to reach their own conclusion. She stated that the Division would also like to have reports in the system on adverse reactions which occurred during clinical trials but cannot accomplish this within currently limited staff and resource levels.

We received suggested changes from the medical officers interviewed concerning the format and quantity of the information received from the Division. The suggestions indicate that the medical officers are not fully aware of the capabilities of the system--what the system can and cannot do for them. Our own experience with the system throughout the review showed that data requests can be specifically tailored to suit the needs of the requestor.

The Division has conducted workshops and seminars on the system's capabilities. The purpose of these seminars is to tell the ultimate users of the system, the medical officers, what the system can and cannot do, what information is or is not retained, and how they should go about getting the information they need.

One of the medical officers we spoke with attended one such seminar. She told us that it was very useful and answered many of her questions regarding the system's capabilities and limitations. She also told us that few medical officers attended this seminar. The Director of the Division of Drug Experience also told us that attendance at seminars has been poor and believed that better attendance at future seminars would help facilitate use of the system.

Use of the system can be further increased by improving the accuracy and timeliness of the data base (as discussed in ch. 3), which should give the medical officers more confidence in the system.

CONCLUSIONS

Knowledge of the adverse reaction reporting system among the medical officers in the Office of New Drug Evaluation and use of the system has increased significantly since we last

reported on it in 1974. Medical officers, however, still lack confidence in the data base.

Many of the medical officers we interviewed suggested additional changes to improve the system to better meet their needs. We believe that FDA should consider the proposals and implement those that are cost effective.

Some medical officers were not fully aware of the capabilities and limitations of the adverse reaction reporting system. The Division has held workshops to explain these matters to the medical officers, but the workshops have been poorly attended. We believe greater support is needed from the Office of New Drug Evaluation to increase medical officer attendance at these sessions.

RECOMMENDATIONS TO THE SECRETARY OF HEALTH AND HUMAN SERVICES

We recommend that the Secretary require the FDA Commissioner to:

--Require medical officers to attend seminars and workshops sponsored by the Division of Drug Experience intended to train them on the capabilities of the adverse drug reaction system.

--Instruct the Division of Drug Experience to solicit feedback from medical officers in the Office of New Drug Evaluation as to how the system could be improved to better meet their needs and implement those proposals which are cost effective and could increase medical officers' use of the system.

VIEWS OF FDA OFFICIALS

The Commissioner of FDA advised us that the Associate Director for New Drug Evaluation will stress to medical officers in the Office of New Drug Evaluation the importance of the adverse drug reaction reporting system and the need to become more aware of the system and its capabilities. He said that the medical officers will be encouraged to attend the seminars sponsored by the Division of Drug Experience.

The Commissioner also agreed that feedback from the medical officers on improvements needed in the system is essential. He said that the Division of Drug Experience has appointed contact persons to work with each of the Office of New Drug Evaluation divisions. This interaction facilitates feedback from the medical officers that is used by the Division. He said that some of the divisions have requested and currently receive periodic reports and consideration will be given to implementing this for all divisions. The

Division also uses the series of seminars and the question and answer period provided in each seminar to solicit feedback and suggestions for system improvements. FDA believes that stressing to medical officers the need to attend these seminars will increase attendance and feedback.

CHAPTER 3

DELAYS AND MISSING REPORTS HAMPER ADVERSE DRUG REACTION SYSTEM'S ABILITY TO IDENTIFY POTENTIALLY SERIOUS REACTIONS

The adverse drug reaction reporting system is not fully meeting its primary objective of providing an early warning or indication of potentially serious problems with marketed drugs. We found, based on a sample of about 2,200 adverse reaction reports submitted by manufacturers, that (1) 42 percent of these reports never reached the Division of Drug Experience, (2) an additional 14 percent had been received but either had not been evaluated or were in a backlog waiting to be entered into the system, and (3) reports that had been entered into the system took an average of 5 months to be entered after they were received by FDA.

Although the change in the routing of reports should significantly increase the number of reports received by the Division and the timeliness of those reports, it will exacerbate another problem--the inability to evaluate and process in a timely manner the reports currently being received.

MANY REPORTS DO NOT GET TO THE DIVISION OF DRUG EXPERIENCE

Many adverse reaction reports submitted by manufacturers never reach the Division and thus are not entered into the system. For the 21 selected drugs, we reviewed 2,182 individual adverse reaction reports and found that only 957 (44 percent) had been entered into the reporting system at the time of our review and only 1,270 (58 percent) of those reviewed had ever reached the Division of Drug Experience. 1/ This resulted in many reports of serious reactions not reaching the Division and in the system failing to signal some potentially serious new reactions, as explained in the section beginning on page 17.

Manufacturers are required to submit two copies of each adverse reaction report they receive to FDA. One copy remains in the medical division responsible for that drug; the duplicate copy is sent to the Division of Drug Experience.

1/This work was performed in March and April of 1981. We considered only those reports that were received by FDA by September 30, 1980. Thus, the reports considered in this review had been with the agency for at least 6 months at the time of our review.

For each of the 21 drugs selected, we reviewed new drug application files from the date of approval of the drug for marketing until September 1980 and extracted data from each adverse drug reaction report. We compared these data with computer printouts supplied by the Division which contained all reports that had been entered into the system at the time of our review. Our method of selecting the 21 drugs is explained on page 5.

For two drugs, we found there were no adverse reaction reports submitted by the manufacturers. For one drug, data we collected were insufficient to match data supplied by the Division of Drug Experience. Thus, for this drug, we were unable to ascertain whether a report in our sample was in the system.

For the 18 other drugs we collected information on 2,182 individual adverse drug reaction reports. Of these reports, we were able to identify 957 (or about 44 percent) that had been entered into the system.

During our review, the Division had a significant backlog of reports of mostly minor known reactions that had already been evaluated and were awaiting input into the system. There were also an undetermined number of reports that had been received by the Division of Drug Experience that were awaiting evaluation. We scanned these reports to determine which were applicable to the 21 drugs selected. We were able to identify an additional 180 (or 8 percent) of our universe of 2,182 reports that had been reviewed by the Division's evaluators and were awaiting entry into the Division's computerized system. We also identified 133 (or 6 percent) reports which were awaiting review by Division evaluators. In total, only 58 percent of our universe of reports had reached the Division of Drug Experience.

The following table shows the results of our review on a drug-by-drug basis.

Reports by Drug Identified as in the System, in the Backlog, or Awaiting Evaluation

Drug	Reports reviewed	Reports in the system	Reports in the backlog	Reports awaiting evaluation	Total reports received (note a)	Percent received (note b)
A	153	98	3	0	101	66.0
B	180	108	13	0	121	67.2
C	149	73	3	0	76	51.0
D	23	5	17	0	22	95.7
E	17	11	0	0	11	64.7
F	73	14	6	0	20	27.4
G	86	30	12	2	44	51.2
H	442	260	38	11	309	69.9
I	118	69	15	0	84	71.2
J	53	8	5	0	13	24.5
K	298	82	39	89	210	70.5
L	98	40	7	18	65	66.3
M	180	108	16	12	136	75.6
N	46	12	0	1	13	28.3
O	41	22	1	0	23	56.1
P	211	14	1	0	15	7.1
Q	11	3	4	0	7	63.6
R	3	0	0	0	0	0
Total	2,182	957	180	133	1,270	
Percent	100.0	43.9	8.3	6.0	58.2	

a/Total of columns 3, 4, and 5.

b/Column 6 divided by column 2.

We have not attempted to project our findings to the entire adverse reaction reporting system. However, we noted that the number of reports entering the system in the last 3 years has decreased significantly over reporting in earlier years. From 1970 through 1977 the Division entered an average of about 12,100 reports a year into the system. From 1978 through 1980 an average of only about 6,400 have been entered. The number of reports from manufacturers entered into the system decreased from 9,911 in 1977 to 5,728 in 1980.

We discussed this with the Director of the Division of Drug Experience, who told us that reporting from manufacturers has remained relatively consistent, and one reason for the decrease is that before 1978 manufacturers' reports were sent directly to the Division and did not go through the Bureau of Drugs' Indexing and Abstracting Service section; therefore, fewer reports were getting lost. She believes, however, that the primary reason for the decrease is the way reports are being handled within the Division. She said that in the past, reports were entered much faster and once the data got into the system they were put to little use. Currently her staff is looking at the data more closely and trying to pick up signals and trends before the data are entered. The price paid for longer review time is fewer reports being entered into the system and a larger backlog of minor reaction reports.

REPORTS TAKE A LONG TIME GETTING INTO THE SYSTEM

Compounding the problem that many reports do not get to the Division of Drug Experience, reports that were received by the Division took nearly 5 months to be entered into the computerized system from the time they were received by FDA. This further impeded the system from meeting its objective as an early warning system.

We took a random sample of 244 of the 957 reports identified as being in the adverse drug reaction system to determine their average time to reach the Division and to be entered into the system. On the average, it took 37 days for reports to get to the Division after arriving in FDA. Forty-four reports (18 percent) took over 50 days to reach the Division, including 6 reports that took over 200 days. The Division took an additional 3.3 months on the average to enter the reports into the system. Of the 244 reports, 17 took at least a year to be entered, including 1 report that took over 2 years. The Division considered all 17 cases to be reports of serious reactions. On the average, the reports of nonserious reactions in our sample were input over 1 month faster than the reports of serious reactions.

DELAYS AND MISSING REPORTS HAMPER EARLY IDENTIFICATION OF POTENTIALLY SERIOUS ADVERSE REACTIONS

Because over 40 percent of the adverse drug reaction reports submitted by manufacturers never reached the Division of Drug Experience and those that did took an average of 5 months to be entered, the system failed to identify some potentially serious adverse reactions and hampered timely regulatory action. One primary function of the adverse drug reaction reporting system is to act as an early warning or signaling system for potentially serious adverse reactions to drugs.

In comparing the adverse reactions in the reports that did not reach the Division of Drug Experience with the manufacturer's labeling for each drug in our sample, we found some potentially serious reactions among those reports. Since the Division was unaware of their existence, it did not have the information needed to determine whether it should alert others to a potential problem.

For one drug we found five cases of anemia, a condition in which the number of red blood cells, or the amount of hemoglobin in the blood, is depressed. Two of the five cases reported were aplastic anemia, a persistent form of anemia, which in many cases is fatal. For the same drug we found four cases of hypoglycemia, an abnormally low blood sugar level, which in severe cases may result in coma and death. The adverse reaction reporting system contained only one case of hypoglycemia, which according to the medical officers we spoke with would generally not trigger an alert or attempt to obtain additional information. For some of the other drugs selected, we found cases of such reactions as sudden death and cardiorespiratory, kidney, and liver failure that failed to come to the attention of the Division.

It should be noted that, in each of the above cases, regulatory action may or may not have been necessary. We made no determination of causality. That judgment should be left to the Division of Drug Experience and the regulatory divisions in the Office of New Drug Evaluation. We are pointing out, however, that poor information flow hampered the system from accomplishing its stated purpose--signaling a potentially serious new reaction.

CHANGE IN ROUTING OF MANUFACTURERS' REPORTS MAY RESULT IN LARGER BACKLOG

Changing the routing of manufacturers' reports so that more reach the Division of Drug Experience may not result in more reports getting into the adverse reaction reporting system. The Division has not been able to evaluate and enter into the system all reports being received. Since additional staff resources

to handle the additional workload are unlikely, consideration should be given to alternative ways to eliminate the present backlog and the potentially much greater backlog if significantly larger numbers of reports are received.

After completing our fieldwork, we advised the Director of the Division of Drug Experience that many reports from manufacturers were not getting into the system and noted that routing reports through the Indexing and Abstracting Service in the Division of Drug Information Resources may be the cause. The Bureau of Drugs conducted a survey and concluded that this was a major cause of reports getting lost or taking a long time to get to the Division of Drug Experience. As a result of our findings and the Bureau of Drugs' survey, in September 1981, the procedures for routing reports were revised, thus permitting the Office of New Drug Evaluation to send manufacturers' reports directly to the Division of Drug Experience. The Bureau of Drugs plans to evaluate the procedural change in March 1982.

This change should allow adverse reaction reports to get to the Division in a more timely manner. In addition, the percentage of reports that arrive at the Division should increase significantly if the drugs included in our review are representative of the entire system.

However, this change may not result in more reports getting into the system because the staff is unable to evaluate and process reports already being received, as indicated by the current backlog of over 7,000 reports awaiting input into the system.

Most of the reports in the backlog are not serious reactions to drugs, and input on these will add little or nothing to the Division's current knowledge of marketed prescription drugs. We discussed these nonserious reactions with the evaluators in the Division. In particular, we asked what value these reports have. Most of the evaluators told us that, insofar as the reports pertain to the system's early warning function, they have no value. They do have some value in showing the full spectrum of reactions that may be attributed to any given drug or class of drugs. Some of the evaluators believe the Division of Drug Experience has an obligation to evaluate and ultimately input these nonserious reports into the system. Some told us they should be entered because they are required to be submitted by the manufacturers, and the Division also has the responsibility to respond to Freedom of Information Act requests from the public.

Although some of these reports have value in that they provide the Division with a good general knowledge of the effects of marketed drugs, we believe the Division should explore alternative methods for entering reports of minor known reactions into the system--or in some cases not entering the reports at all.

One alternative which could be considered would be to not input into the system common, nonserious reports or input nonserious reaction reports as a group and enter only limited information. The original copy of the adverse reaction reports, once the data are entered into the system, is microfilmed and then destroyed. If additional information is needed at some future date, the microfilmed report can be retrieved for review. Entering reports by this means should reduce the time required for review and the time needed to enter reports. This action would allow Division personnel to spend more time reviewing and analyzing the more serious adverse reaction reports.

CONCLUSIONS

The adverse drug reaction system does not contain many of the reports submitted by manufacturers apparently because many were misplaced during routing of these reports through FDA's Bureau of Drugs and because of delays in evaluating and entering them into the computerized system. Not only did many reports not get to the Division, but those that did took over 5 months to be entered into the system after they were received by FDA.

Failure to properly and promptly get the reports to the Division of Drug Experience and enter them into the system can delay the identification of previously unknown adverse reactions.

The changes in routing procedures started in August 1981 should significantly increase the number of reports that reach the Division. Because of this change, we are not making any recommendations concerning reports not getting to the Division of Drug Experience. However, this change could exacerbate another problem--the inability to promptly evaluate and process the reports already being received as evidenced by the 7,000 report backlog. FDA should explore possible alternative methods of evaluating and processing the reports. Because of the current budget situation, additional staff resources may not become available. Therefore, FDA could either not enter some nonserious reports into the system or group these reports and enter a minimum of information.

RECOMMENDATIONS TO THE SECRETARY OF HEALTH AND HUMAN SERVICES

We recommend that the Secretary direct the Commissioner of FDA to explore alternative methods for evaluating and processing nonserious, known reactions to drugs. Consideration should be given to not entering into the system some of the common known reactions which add little or nothing to the knowledge of marketed drugs.

VIEWS OF FDA OFFICIALS

The Commissioner told us that FDA will review its methods for evaluating and processing nonserious and known reactions to drugs and determine the most appropriate and efficient ways of processing these reports. He told us that FDA will complete this review and develop a plan for implementing any changes indicated by April 1982.

CHAPTER 4

INCREASED EFFORTS NEEDED TO IMPROVE REPORTING OF ADVERSE REACTIONS

The Division of Drug Experience has done little in recent years to encourage reporting of adverse reactions from nonmanufacturer sources. The number of reports from private and federally operated hospitals has decreased dramatically since 1970. While the Division needs to increase its efforts to encourage reporting of adverse reactions, it particularly needs to increase reporting of new, serious, rare, or unusual reactions with sufficient information provided to establish causality.

The Division has reevaluated its data needs, and has revised the reporting form accordingly. With these tasks completed, the Division should increase its contacts with nonmanufacturing sources in order to increase the quantity and quality of reports received from physicians and private hospitals. Better dialog with major medical associations, such as AMA and the American Hospital Association, may be helpful. In addition, greater efforts are needed to encourage reporting from Federal hospitals.

We explored alternative methods for increasing the reporting of adverse drug reactions. These methods have been effective in increasing both the number and quality of reports in other types of reporting systems and merit consideration by the Division.

SOURCE OF REPORTS

From 1970 through 1980, the Division entered over 115,000 reports into the adverse drug reaction reporting system. As discussed in chapter 3, the number of reports submitted may be considerably greater because of the large number of reports lost, backlogged, or being evaluated. The reports are received from drug manufacturers (who are required to report by FDA regulations (21 CFR 301.300)), private and Federal hospitals, private physicians, and other health professionals. The Division also receives reports through intensive monitoring and registeries by private organizations under contracts and grants with FDA. By far the largest number of reports during this period were received from manufacturers.

As shown by the following schedule, there has been a significant reduction in the number of reports entered into the system in recent years. This reduction has been caused largely by the missing and backlogged reports (as discussed in ch. 3) and by the discontinuance of contracts with private hospitals to encourage reporting.

Adverse Drug Reaction Reports Received by Source

Source	1970 Number	1970 Percent	1975 Number	1975 Percent	1980 Number	1980 Percent
Manufacturers	9,983	55.6	8,470	79.8	5,728	82.4
Physicians	250	1.4	481	4.5	749	10.8
Private hospitals	6,380	35.5	553	5.2	73	1.0
Federal hospitals	1,176	6.6	275	2.6	89	1.3
Others	159	0.9	836	7.9	312	4.5
	17,948	100.0	10,615	100.0	6,951	100.0

Reports from private hospitals have declined considerably

Although the above schedule shows that private hospitals were the second leading source of reports entered into the system in 1970, the number of reports from private hospitals has declined steadily since then. During the late 1960s and early 1970s, a number of hospitals were under contract with FDA to supply adverse drug reaction reports. The Director, Division of Drug Experience, advised us, however, that many of these reports were of known, nonserious reactions. These contracts were discontinued in 1972. In 1970 and 1971 private hospitals submitted nearly one-third of all reports entered into the system. In 1980, however, only 1 percent of the reports were from private hospitals. Of the more than 15,000 reports submitted by private hospitals during the entire period, over 11,000 were submitted before 1973.

Reports from private physicians have increased slightly

The above table shows that reports from private physicians have increased. From 1976 to 1980 physicians' reports accounted for nearly 15 percent of reports entered into the system. The Director of the Division of Drug Experience believes that this may have resulted from the introduction of a shortened reporting form in late 1974.

Although reports from physicians have increased, the number is minimal considering the estimated 429,000 practicing physicians in the United States and the 1.4 billion new and refill prescriptions dispensed by private pharmacies each year.

Reports from Federal hospitals have declined considerably

Reports from Federal hospitals, which were never a particularly strong source of reports, have generally declined throughout the period. According to the Division, Federal hospitals were encouraged to report in the early 1970s, but since that time there have been no significant efforts to encourage reporting.

EFFORTS NEEDED TO IMPROVE REPORTING

In order to increase the quantity and quality of adverse reaction reports, the Division of Drug Experience needs to do more to encourage reporting from nonmanufacturer sources. The efforts needed include establishing better dialog with major medical associations, such as AMA and the American Hospital Association, making reporting more convenient by establishing toll-free or collect telephone service, and making greater efforts to encourage Federal hospitals to report.

In recent years the Division has made little effort to increase reporting from nonmanufacturer sources. According to the Director, the Division has completed a thorough review of its own data requirements. She told us that it has not made any significant efforts to increase reporting because it would be counterproductive if the Division did not know what kind of information it was looking for. The review of data needs has culminated in the Division revising the adverse drug reaction reporting form, which was approved in April 1981. The Director now believes the Division is in a much better position to move toward increased reporting.

As stated above, reports from nonmanufacturer sources make up a small percentage of reports submitted to FDA each year. In the United States, there are over 429,000 practicing physicians, over 7,000 private hospitals, and about 300 Federal 1/ hospitals. These sources are potentially a significant source of information on adverse drug reactions. The Division, now that it has determined what data it requires, should significantly increase its outreach to these groups.

The Director told us that the Division is planning a number of initiatives aimed at increasing both the quantity and quality of reports from nonmanufacturer sources, including

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1/The Federal hospitals include those operated by the Department of Defense, the Veterans Administration, and the Public Health Service, including those operated by the Indian Health Service.

--printing an article in a prominent medical journal describing the current system, how reports are submitted, and how the information is used;

--initiating a general campaign to encourage hospital reporting (at the present time the Joint Commission on Accreditation of Hospitals requires hospitals to have an adverse reaction reporting system and encourages reporting to FDA); and

--sending letters to individual physicians and/or to medical and pharmacy schools encouraging reporting.

These efforts should help to increase reports from nonmanufacturer sources. The Division, however, needs to pursue these sources vigorously if it is to effect any significant increase in reporting. The Division should consider soliciting the assistance of such organizations as the American Hospital Association, the Joint Commission on Accreditation of Hospitals, and AMA to strongly encourage their constituents to report.

The Division also needs to pursue more active reporting from Federal hospitals. The approximately 300 Federal hospitals have supplied only about 4 percent of reports entered over the last 10 years. A more active liaison with hospitals in the Federal sector could serve to open a potentially significant source of reporting and may serve as an example to improve hospital reporting from all sectors. Interagency agreements to encourage reporting may help in developing this source.

Barriers to reporting

We spoke with AMA officials and visited five hospitals to discuss the barriers to reporting to FDA and how reporting could be improved.

An AMA official told us that adverse reaction data are important to the medical profession especially considering ongoing efforts to speed up drug approval. Until 1970, AMA had its own reporting system. This official stated the time it takes to complete the necessary forms is one reason for poor reporting. Probably the most important reason, however, is that many physicians are reluctant to report because they fear the medical-legal ramifications of submitting adverse reactions to FDA. He believes a system that could assure confidentiality could help overcome this obstacle.

Hospital officials gave us the same reasons. In addition, one official believes some physicians who may discover a rare reaction to a drug would be more prone to publish the case in a medical journal than report it to FDA. Others told us that when

they finally do get reports and submit them to FDA they get little or no feedback. None of the hospitals we visited had ever been contacted by FDA in an attempt to get a reporting system started.

Of the five hospitals we visited, four had reporting programs. Of those four, three programs were almost inactive. The fourth hospital, however, had a well-organized method for reporting adverse reactions and submits a large number of reports to FDA. This hospital's system serves as a good example of how a hospital reporting system can work and could be used as a model by the Division of Drug Experience in assisting other hospitals in organizing a reporting system.

At this hospital the pharmacy is the central collecting point for adverse reactions. If a physician or nurse identifies a possible adverse reaction, they are requested to complete a short form and submit that form to the pharmacy. The name of the patient and the prescribing physician remain confidential. Pharmacy staff does the necessary followup work and completes the adverse reaction report. The hospital has organized a subcommittee on adverse reactions which meets monthly to review adverse reaction reports. The data are retained in the hospital's computerized data base and reports are sent to FDA. Some case reports are also published in a prominent hospital journal. In addition, the hospital occasionally monitors a specific drug or drugs. This effort also results in adverse reaction reports.

Hospital officials told us that the key factors in making their program work are (1) feedback to the hospital staff, (2) hospital administration belief in the program, and (3) enthusiastic encouragement of staff to report adverse reactions.

Other possible ways to increase reporting

During our review we explored other methods of receiving adverse reaction reports which could increase both the quantity and quality of reporting.

We spoke to officials of USP which conducts a drug product problem reporting program under a contract with FDA. To encourage reporting, USP uses a toll-free telephone system. About 6,500 reports are received annually from pharmacies or private citizens concerning such drug product problems as broken or discolored pills. About 45 percent of these reports are received by telephone. While some adverse drug reaction reports are received through this system, its purpose is to collect information on such problems as defective or mispackaged products.

A USP official told us that, after the toll-free system was installed, reporting increased about 35 percent and the quality of the reports improved. The system can receive calls 24 hours a day, 7 days a week. During normal business hours the telephones are staffed by personnel who have experience working with drugs and drug products, and a recording is used the rest of the time. During the day the staff can ask questions of the reporter so that complete information can be obtained. All calls are recorded so that any misunderstandings can be rectified and any followup can be done.

The USP official told us that the reporter is assured that he or she will remain anonymous to FDA and the product manufacturer unless disclosure of his/her name is specifically authorized by the reporter. The official also told us that feedback is very important in his program. People tend to report again if they receive meaningful feedback and get the feeling that something is being done with the information. He stated that this is one area that the Division of Drug Experience can improve significantly. He added that the Division's present feedback mechanism is a good acknowledgment to the reporter that a report was received, but beyond that it is of little use to the reporter.

The USP official also told us that a pilot program in association with a respected medical organization would be feasible and a good starting point for improving adverse drug reaction reporting. He believes FDA could conduct a program of this nature on its own or by contract. He said that, in a sensitive area like adverse drug reactions, reports being collected by a third party may yield better results.

An FDA official responsible for administering the contract told us that he believes the quality of reports has increased significantly since the inception of the toll-free service. He said that after the service was established, reporting increased between 35 and 40 percent.

He also told us the real benefit of the service is that it is a time saver for the reporter. Most reporters are pharmacists, and during a busy day the pharmacist may not have time to find a form, fill it out, and get it in the mail. With the telephone service available, all the pharmacist has to do is pick up the telephone and call in the report. He believes this convenience has had a positive impact on the number of reports received.

We discussed another alternative method with an FDA Bureau that currently employs a collect-call service to assist small manufacturers with such things as applying for FDA approval for their products or interpretation of FDA regulations. This service was established when the Bureau asked its constituents how it could improve service. The Bureau official told us that over the

past 2 years inquiries have nearly doubled. About one-third of the calls are collect, costing about $4 per call. When the service was established, the Bureau had considered a toll-free system but decided that its present method would be more effective.

The Bureau official said the program is extremely cost effective for both the Bureau and the manufacturers. He believes that the Bureau could not respond to an inquiry letter for that little cost.

In addition to the above, we discussed possible alternatives with AMA and the hospitals visited. The officials we spoke with all believed a toll-free or some type of call-in service would be beneficial. AMA officials told us this type of service may overcome the physicians' reluctance to report provided it could maintain the confidentiality of the reporter.

CONCLUSIONS

Manufacturers' reports account for an ever increasing share of adverse reaction reports entered into the reporting system. The Division of Drug Experience has done little, in recent years, to increase reporting from nonmanufacturer sources.

We believe that the initiatives planned by the Division to encourage increased reporting are a good starting point, but that the Division must be aggressive if it is to increase reporting significantly. The Division should solicit the assistance of major medical organizations, such as AMA and the American Hospital Association, to encourage their constituents to report. The Division should do more to encourage Federal hospital reporting.

Finally, we believe that FDA could increase the number of adverse reaction reports from other than manufacturers by establishing a toll-free or collect-call system to receive reports.

RECOMMENDATIONS TO THE SECRETARY OF HEALTH AND HUMAN SERVICES

We recommend that the Secretary:

--Encourage other Federal agencies operating hospitals to develop an adverse drug reaction reporting system.

--Direct administrators of hospitals within the Department of Health and Human Services to cooperate with the Division of Drug Experience by establishing and using reporting systems in their hospitals.

In addition, we recommend that the Secretary direct the Commissioner of FDA to explore alternative methods, such as a toll-free

or collect-call service, to increase the quantity and quality of reports from nonmanufacturer sources.

VIEWS OF FDA OFFICIALS

The Commissioner of FDA stated that FDA will recommend that the Secretary send a letter to administrators of all Department of Health and Human Services hospitals directing them to cooperate with the Division of Drug Experience and to establish adverse reaction reporting systems to the extent their budgets allow. Further, he said that FDA will recommend that the Secretary send a letter to other Federal agencies urging their cooperation in adverse drug reaction reporting.

The Commissioner also stated that FDA has long recognized the possible value of an "800" number; this is specifically being tested in the dermatology registry. A possible problem with a telephone reporting system is that many reporters, because of potential liability, are reluctant to report and give full information, including their name and the patient's name. Persons who are discouraged from reporting for this reason would not be likely to report under an 800 number system. He said that the Bureau of Drugs will evaluate the usefulness and cost of a toll-free telephone service after more experience has been gained in the dermatology registry.

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