DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of Inspector General

Memorandum

Date MAY 31 1995

From June Gibbs Brown
Inspector General

Subject Reporting Process for Blood Establishments to Notify the Food and Drug Administration of Errors and Accidents Affecting Blood (A-03-93-00352)

To Philip R. Lee, M.D.
Assistant Secretary for Health

The attached final report provides you with the results of our review of the process in which blood establishments notify the Food and Drug Administration (FDA) of errors and accidents that may affect the safety, purity, or potency of their blood and blood products. The FDA is responsible for the oversight of blood establishments, but the establishments are primarily responsible for the safety of their products.

According to FDA, the blood industry's compliance with standards and safeguards accounts for the relatively few accidents of the severity to warrant a blood recall. In Fiscal Year (FY) 1994, there were 427 blood recalls involving 8,529 units of blood, or about 3/100ths of 1 percent of the 26 million units collected nationally that year. The FDA confirmed that the vast majority of these recalls related to technical violations, and represented remote risks to the public.

Blood establishments engaging in interstate shipment of their blood products must be licensed by FDA and are required to submit to FDA reports of errors and accidents. Unlicensed establishments (i.e., those with only intrastate activity) have been asked by FDA to voluntarily submit these reports. The FDA's error and accident reporting process is a valuable management tool, enabling the agency to evaluate and monitor the blood establishment's actions taken in response to the errors and accidents detected. In FY 1992, FDA received 10,456 error and accident reports from blood establishments. While the vast majority of these reports did not involve situations that resulted in blood recalls or the release of contaminated blood, FDA recognizes the value of these reports and plans to expand their use as an "early warning" device for field offices and the blood industry.

Our review disclosed that FDA generally processed error and accident reports in accordance with established procedures. We identified two conditions, however, which could hamper the successful implementation of FDA's plan to expand the use of the error and accident reports. Specifically, we found that: (1) licensed blood establishments continued, even after being reminded by FDA in 1991, to submit error and accident reports long after detecting the errors and accidents; and (2) there was no assurance that unlicensed establishments were submitting reports. We further found that FDA was not

using error and accident reports to identify blood establishments that were submitting the reports untimely, or to regularly provide field staff and blood establishments with trend analysis of the types of errors and accidents reported.

We are making specific recommendations that the Commissioner of Food and Drugs: (1) expedite the development and issuance of revisions to the Federal regulation on error and accident reporting (21 Code of Federal Regulations (C.F.R.) 600.14(a)) to be more specific concerning the time frame in which error and accident reports are required to be submitted; (2) expedite the development and issuance of a regulation to require unlicensed blood establishments to submit error and accident reports; and (3) expand the Center for Biologics Evaluation and Research's (CBER) use of existing information in its current error and accident data base to identify blood establishments that regularly fail to submit error and accident reports in a timely manner, and provide additional trend analysis reports to FDA field offices and blood establishments.

In responding to our draft audit report, the Public Health Service (PHS) agreed with our recommendations. The PHS' comments are presented as an Appendix to this report.

We would appreciate your views and the status of any further action taken or contemplated on our recommendations within the next 60 days. If you have questions, please call me or have your staff contact Joseph E. Vengrin, Acting Assistant Inspector General for Public Health Service Audits, at (202)619-1157. Copies of this report are being sent to other interested Department of Health and Human Services officials.

To facilitate identification, please refer to Common Identification Number A-03-93-00352 in all correspondence relating to this report.

Attachment

cc:
David A. Kessler, M.D.
Commissioner of Food and Drugs

Anthony L. Itteilag
Deputy Assistant Secretary
for Health Management Operations
Public Health Service

Department of Health and Human Services

OFFICE OF INSPECTOR GENERAL

REPORTING PROCESS FOR BLOOD ESTABLISHMENTS TO NOTIFY THE FOOD AND DRUG ADMINISTRATION OF ERRORS AND ACCIDENTS AFFECTING BLOOD

JUNE GIBBS BROWN
Inspector General

MAY 1995
A-03-93-00352

EXECUTIVE SUMMARY

BACKGROUND

The Public Health Service (PHS) Act (Title 42 United States Code (U.S.C.) 262) and the Federal Food, Drug and Cosmetic Act (Title 21 U.S.C. 331) place the responsibility for the oversight of blood establishments[1] with the Food and Drug Administration (FDA). According to the Commissioner of Food and Drugs, an agency goal is to ensure that the Nation's blood supply is as safe as possible.

The FDA has oversight responsibility for blood establishments. Blood establishments, however, are responsible for the safety of their own blood products.

The FDA registers all blood establishments, and licenses those establishments that engage in interstate shipment of their blood products. Registered blood establishments that do not ship interstate are not licensed by FDA but fall under State licensing procedures. While FDA provides guidance to all blood establishments to help them comply with industry standards and safeguards, the establishments, both licensed and unlicensed, are responsible for ensuring the safety of their blood products by complying with established good manufacturing practices standards and implementing all safeguards over blood and blood products.

According to FDA, compliance with industry standards and safeguards accounts for the relatively few accidents of the severity to warrant a blood recall. In Fiscal Year (FY) 1994, there were 427 blood recalls involving 8,529 units of blood, or about 3/100ths of 1 percent of the 26 million units collected nationally that year. The FDA confirmed that the vast majority of these recalls related to technical violations, and represented remote risks to the public.

In September 1993, FDA proposed a plan to improve its oversight of the blood industry. A component of this plan focuses on the blood industry's self-reporting of errors and accidents that may affect the safety, purity, or potency of blood and blood products. The FDA's regulations require reporting of errors and accidents by licensed blood establishments, and FDA recommends reporting by unlicensed establishments. In FY 1992, FDA's Center for Biologics Evaluation and Research (CBER), Office of Compliance, received 10,456 error and accident reports from blood establishments. While the vast majority of these error and accident reports did not involve situations that resulted in blood recalls or the release of

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[1] A blood establishment is a place of business under one management at one general physical location. The term includes human blood and plasma donor centers, blood banks, transfusion services, other blood product manufacturers, and independent laboratories that engage in quality control and testing for registered blood product establishments.

contaminated blood, FDA envisions that the reports can be used to identify trends and develop appropriate "early warning" guidance to the field offices and the blood industry.

OBJECTIVES

The primary objective of our review was to assess the reporting process for blood establishments to notify FDA of errors and accidents that may affect the safety, purity, or potency of blood and blood products. Specifically, we determined whether: (1) blood establishments reported errors and accidents in a timely manner, or at all; (2) FDA processed the error and accident reports submitted by blood establishments in accordance with its procedures; and (3) FDA maximized the use of the information currently available in the error and accident reports.

SUMMARY OF FINDINGS

Our review showed that FDA's error and accident reporting process is a valuable management tool, enabling the agency to evaluate and monitor the blood establishments' actions taken in response to the errors and accidents detected. The reports also have the potential to provide FDA with an overview of the problems that are being detected throughout the blood industry. We determined that FDA processed error and accident reports in accordance with established procedures. We intend to follow up and report separately on the actions taken by the blood establishments and FDA with regard to 17 errors and/or accidents in our sample which, because of their severity and possible health consequences, warranted evaluation for a recall classification.

The error and accident reporting process provides valuable intelligence to FDA relative to the Nation's blood supply in addition to that gathered during routine inspections. To enhance the usefulness of the error and accident reporting process, all registered blood establishments, including those not licensed by FDA, need to report errors and accidents more timely.

We identified two conditions, however, that could hamper the successful implementation of FDA's plan to expand the usefulness of error and accident reports: (1) error and accident reports were not being submitted timely by the blood establishments; and (2) there was no assurance that unlicensed blood establishments were voluntarily submitting the reports. We also found that FDA was not using the error and accident reports to identify blood establishments that were submitting the reports untimely, or to regularly provide field staff and blood establishments with trend analysis of the types of errors and accidents reported.

Without timely and complete reporting by blood establishments on the number and types of errors and accidents that are detected, FDA may be hampered in its efforts to evaluate and monitor the blood industry. It must be noted, however, that delays in reporting by licensed

blood establishments and/or failure to voluntarily report by unlicensed establishments should not cause corresponding delays in initiating action aimed at correcting the specific problems being reported. All blood establishments are required to investigate and correct all errors and accidents detected, independent of the reporting process. While we did not evaluate the timeliness or appropriateness of the blood establishments' actions, we noted that all of the 163 error and accident reports in our sample contained information showing that some action was taken. According to FDA, the actions reportedly taken by the blood establishments were appropriate.

RECOMMENDATIONS

We, therefore, recommend that the Commissioner of Food and Drugs:

1. expedite the development and issuance of revisions to the Federal regulation on error and accident reporting (21 Code of Federal Regulations (C.F.R.) 600.14(a)) to be more specific concerning the time frame in which error and accident reports are required to be submitted;

2. expedite the development and issuance of a regulation to require unlicensed blood establishments to submit error and accident reports; and

3. expand CBER's use of existing information in its current error and accident data base to identify blood establishments that regularly fail to submit error and accident reports in a timely manner, and provide additional trend analysis reports to FDA field offices and blood establishments.

In its April 28, 1995 response to our draft audit report, PHS agreed with our recommendations, and indicated that FDA was taking action to implement them.

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INTRODUCTION

BACKGROUND

The PHS Act (Title 42 U.S.C. 262) and the Federal Food, Drug and Cosmetic Act (Title 21 U.S.C. 331) place the responsibility for the oversight of blood establishments with FDA. The FDA has the authority to register all blood establishments, and to license those establishments that ship blood and blood products interstate. Registered blood establishments that are not licensed by FDA (these unlicensed establishments do not engage in interstate shipments of blood products) fall under State licensing procedures. Although FDA is required by law to inspect both licensed and unlicensed blood establishments every 2 years, it has been performing most inspections on an annual basis because of public concern over the safety of the Nation's blood supply. The FDA has several regulatory options available to it, ranging from warning letters to product seizures, to protect the blood supply. These enforcement options apply to all registered blood establishments.

Over the past decade, and in particular since the emergence of the Acquired Immune Deficiency Syndrome (AIDS) epidemic, ensuring the safety of the blood supply has become more complex than before. While FDA provides guidance to blood establishments to help them comply with industry standards and safeguards, blood establishments including unlicensed establishments, are responsible for ensuring the safety of their blood products. To meet this responsibility, blood establishments are to comply with established good manufacturing practices standards, which are defined as those standards that would be generally acceptable in a particular industry and would result in the manufacturing of products which would meet standards of the Federal Food, Drug and Cosmetic Act. They are also required to fully implement all safeguards over blood and blood products including:

- eliminating high risk donors by encouraging them to exclude themselves, and by evaluating their behavioral and medical history as a basis for deferral;
- updating a list of unsuitable donors and checking the donors' names against this list to prevent use of their blood;
- testing the blood for such blood-borne agents as HIV, hepatitis, and syphilis;
- quarantining all donated blood until tests and other control procedures established its safety; and
- investigating all incidents, auditing their systems, and correcting all deficiencies.

Error and Accident Reports

According to FDA, compliance with industry standards and safeguards accounts for the relatively few accidents of the severity to warrant a blood

recall. In FY 1994, there were 427 blood recalls involving 8,529 units of blood, or about 3/100ths of 1 percent of the 26 million units collected nationally that year. The FDA confirmed that the vast majority of these recalls related to technical violations, and represented remote risks to the public. When an error or accident occurs that may affect the safety, purity, or potency of blood, licensed blood establishments are required to self-report the incident to FDA. Unlicensed establishments are not required to self-report, but have been requested to do so on a voluntary basis. The FDA has provided guidance to the blood establishments as to what constitutes a reportable error or accident. The reportable incidents include, but are not limited to, the following:

- release of units repeatedly reactive to tests indicating hepatitis or HIV;
- release of units in which testing was performed incorrectly or misinterpreted;
- release of units from donors who are, or should have been, permanently or temporarily deferred due to medical history or a history of repeatedly reactive viral test results for hepatitis or HIV;
- release of units prior to completion of all tests or that are incorrectly labeled, e.g., incorrect expiration date;
- release of microbially contaminated blood components when the contamination is attributed to an error in manufacturing; and
- incorrect identification of samples used in compatibility testing, errors in compatibility testing which result in the wrong unit being released for transfusion, issuing the wrong unit for transfusion, or wrong cell infusion.

The error and accident report identifies the blood establishment, the donor, the blood product, and the final disposition of the blood product. It contains appropriate dates such as date the incident occurred, date it was discovered, date of the report, and type of error or accident involved. There are three basic types of incidents: (1) labeling error or accident--testing correctly performed, but incorrect label applied to product; (2) testing error or accident--test either incorrectly performed or misinterpreted, or product released inadvertently before tests completed; and (3) manufacturing/control procedure error or accident. The report also lists contributing factors causing the error or accident, and the actions taken by the blood establishment.

The error and accident reports are to be submitted to CBER's Office of Compliance, which is responsible for analyzing the reports. If the report clearly does not require further evaluation of the severity of the incident, it is sent to the appropriate district office for follow up at the next inspection. The FDA's Office of Regulatory Affairs (ORA) is responsible for the coordination of all field office activities. The field offices, under the direction of ORA, are responsible for conducting all routine blood establishment inspections.

If an error and accident report indicates that further evaluation of the severity of the incident is warranted, the report is forwarded to Case Management within the Office of Compliance. This group evaluates the error or accident being reported and, based on the severity of the incident, may recommend that it be classified as a blood recall. Of the 10,456 error and accident reports submitted by blood establishments to FDA in FY 1992, 791 (7.6 percent) were referred to Case Management to be evaluated for a recall classification.

A recall is a blood establishment's voluntary removal or correction of a marketed blood product that violates laws administered by FDA. The FDA cannot issue a product recall but can request that a firm do so. The FDA recognizes that a voluntary recall is generally more appropriate and affords better protection for consumers than seizure, which is a FDA option when a firm refuses to undertake a recall. In the case of blood, blood establishments are responsible for voluntarily initiating recalls to protect the public health from any defective products. They are also responsible for developing a recall strategy and determining whether the recall is progressing satisfactorily. Blood recalls differ from other product recalls because blood, having a short shelf life, is often used before it can be retrieved. If the blood cannot be retrieved, the blood establishment is responsible for identifying all recipients of the blood subject to the recall so that they can take extra steps to guard their health and avoid infecting others.

The FDA is responsible for classifying the blood establishment's recall according to the health hazard presented by the incident, and conducting its own audit checks to assess whether the establishment has notified all affected parties and taken appropriate action. The FDA will publish all recall actions in its weekly Enforcement Report regardless of when the recall was made.

Since blood establishments are required to investigate all errors and accidents, including those that are eventually classified as blood recalls, the corrective action relative to the specific incident being reported is generally completed by the blood establishment before the recall is classified by FDA.

FDA's Plan for Error and Accident Reports

In September 1993, FDA proposed a plan to establish a blood quality assurance initiative aimed at ensuring the safety of the Nation's blood supply, and upgrading the operational quality of the blood industry.

The goals of this plan are for FDA to: strengthen its capability to identify blood center operational deficiencies; provide appropriate guidance to the blood industry; educate and assist blood centers in conforming to this guidance; provide more timely decisions on licensing applications and amendments; and carry out inspections that will assess the progress of the industry in bringing its operations to a higher standard.

One component of this plan focuses on the blood industry's self-reporting of errors and accidents that may affect the safety, purity, or potency of blood and blood products. The FDA envisions that the error and accident reports submitted by blood establishments can be used to identify trends and develop appropriate "early warning" guidance to the field offices and the blood industry. Another component of this plan is the consolidation of FDA's multiple automated systems into a single relational data base designed to facilitate the exchange of information between field and headquarters staff, and permit FDA to identify trends and problems in early stages of development and issue guidance to blood establishments to prevent errors and accidents.

OBJECTIVES, SCOPE AND METHODOLOGY

Objectives

The primary objective of our review was to assess the reporting process in which blood establishments notify FDA of errors and accidents that may affect the safety, purity, or potency of blood and blood products. Specifically, we determined whether:

- blood establishments reported errors and accidents in a timely manner, or at all;
- FDA processed the error and accident reports submitted by blood establishments in accordance with its procedures; and
- FDA maximized the use of the information currently available in the reports.

Scope and Methodology

Our review was performed in accordance with generally accepted government auditing standards. To understand FDA's role in processing error and accident reports, we reviewed pertinent laws, regulations, and FDA policies and procedures. We also reviewed statistics and reports provided by FDA regarding the blood industry. In addition, we discussed blood safety-related issues and management information system functions with cognizant officials of CBER. To obtain information about FDA's anticipated use of error and accident reports, we reviewed its plan for strengthening its role with respect to the blood industry.

To determine if FDA followed its policies and procedures, and to gauge the timeliness of the reporting, we randomly selected for review 163 of the approximately 5,000 error and accident reports received by CBER during the first half of FY 1993. The sample selected was not a statistically valid random sample because the objective of the review did not require the use of statistical projections. For each selected error and accident report, we identified the blood establishment; the timeliness of submission; and the type of error or accident which may have affected the safety, purity, or potency of blood and blood products.

While we did not evaluate the timeliness or appropriateness of the blood establishments' actions, we noted that all of the 163 error and accident reports in our sample contained information showing that some action was taken. According to FDA, the actions reportedly taken by the blood establishments were appropriate. We intend to follow up and report separately on the actions taken by the blood establishments and FDA relative to 17 of the reports that warranted an evaluation for a blood recall classification.

In May 1993, in the United States District Court for the District of Columbia, a major licensed blood establishment operating at multiple locations nationwide entered into a consent decree under which the blood establishment agreed to take specific steps relative to its management controls, quality assurance/quality control program, and employee training. One of the issues addressed in the consent decree was the timeliness of reporting errors and accidents. Effective 60 days from entry of the decree, the individual locations were to complete their reviews of errors and accident reports within 30 days and submit the reports to their national headquarters. Within 20 days of receipt, the national headquarters was required to forward to FDA all error and accident reports involving the release for distribution of any unsuitable blood product.

Because the decree became effective after we had selected for review our sample of 163 error and accident reports, we did not determine whether the licensee was complying with the stipulated time frame, or the effect of the decree on the overall timeliness of error and accident reports. We intend to follow up on this issue at a later date.

Our review was performed primarily at CBER's Office of Compliance, located in Rockville, Maryland. Our review did not include a visit to any FDA district office or a review of the district office files.

RESULTS OF REVIEW

According to FDA, compliance with industry standards and safeguards accounts for the relatively few accidents of the severity to warrant a blood recall. In FY 1994, there were 427 blood recalls involving 8,529 units of blood, or about 3/100ths of 1 percent of the 26 million units collected nationally that year. The FDA confirmed that the vast majority of these recalls related to technical violations, and represented remote risks to the public. When errors and accidents occur that may affect the safety, purity, or potency of blood and blood products, FDA has a reporting process that licensed blood establishments are required to follow and unlicensed establishments are requested to follow. Using this reporting process, blood establishments submitted 10,456 error and accident reports to FDA in FY 1992.

According to FDA statistics, errors and accidents warranting a blood recall because of significant risk to the public rarely occur. When errors or accidents that may affect the safety, purity or potency of blood are detected, all blood establishments are required to take immediate corrective action. Licensed establishments are also required to report the incidents to FDA. The usefulness of the reporting process could be enhanced by requiring all blood establishments to report errors and accidents more timely.

Our review of FDA's error and accident reporting process shows that it is a valuable management tool, enabling the agency to evaluate and monitor the blood establishments' actions taken in response to the errors and accidents detected. The reporting process also has the potential to provide FDA with an overview of the problems that are being detected throughout the blood industry. We determined that FDA generally processed error and accident reports in accordance with established procedures. Of the 163 error and accident reports that we reviewed, CBER identified 17 reports (10.4 percent) that warranted a recall evaluation due to the severity of the incidents reported and possible health consequences. These 17 reports were forwarded to Case Management as required, and the remaining 146 reports were sent to the appropriate district office for follow-up during the next inspection. We intend to follow up and report separately on the actions taken by the blood establishments and FDA with regard to the 17 reports to ensure that all appropriate steps were taken to protect the public.

The FDA recognizes the value of the error and accident reports and plans to expand their use as an "early warning" device for field offices and the blood industry. We identified two conditions, however, which could hamper the successful implementation of this plan: (1) error and accident reports were not being submitted timely by the blood establishments; and (2) there was no assurance that unlicensed blood establishments were voluntarily

submitting the reports.[2] We also found that FDA was not using the error and accident reports to identify blood establishments that were submitting the reports untimely, or to regularly provide field staff and blood establishments with trend analysis of the types of errors and accidents reported.

Untimely reporting or failure to report errors and accidents by blood establishments hampers FDA's intelligence gathering efforts. It should not affect the timeliness of corrective actions, however, because all blood establishments are required to investigate errors and accidents and take appropriate corrective actions independent of the reporting process.

Aside from affecting FDA's plans for expanded use of error and accident reports, lack of timely and complete reporting by blood establishments also limits FDA's ability to accurately assess the number and types of errors and accidents that are being detected throughout the blood industry. It must be pointed out, however, that delays in reporting by licensed blood establishments and/or failure to voluntarily report by unlicensed establishments should not cause corresponding delays in initiating action aimed at correcting the specific problems being reported. All blood establishments are required to investigate and correct all errors and accidents detected, independent of the reporting process.

While we did not evaluate the timeliness or appropriateness of the blood establishments' actions, we noted that all of the 163 error and accident reports in our sample contained information showing that some action was taken. According to FDA, the actions reportedly taken by the blood establishments were appropriate.

Timeliness of Reporting

Although licensed blood establishments are required to report errors and accidents "promptly" to FDA, and unlicensed establishments are requested to do so, we found that blood establishments were not always submitting the error and accident reports timely after detecting the incidents. We believe that blood establishments, in light of the lack of specificity concerning the submission of the error and accident reports, are taking a most liberal interpretation of the time frame in which they are to report incidents affecting blood and blood products.

Regulation 21 CFR 600.14(a) states that:

> "...the Director, Office of Compliance, Center for Biologics Evaluation and Research shall be notified promptly of errors or accidents in the manufacture of products that may affect the safety, purity, or potency of any product."

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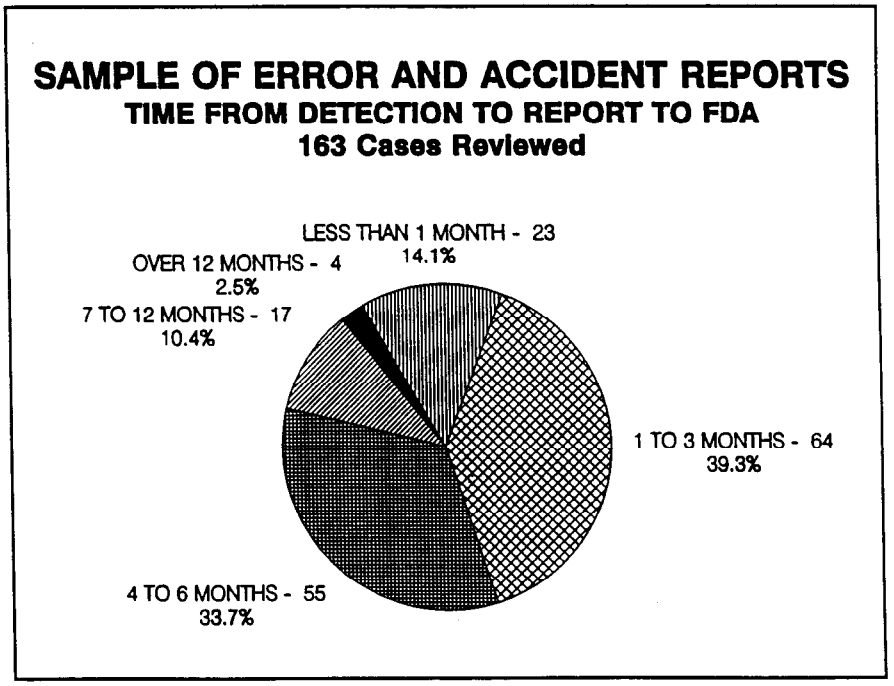
[2] It should be noted that FDA has another means of assessing the operations of blood establishments other than error and accident reports. Both licensed and unlicensed establishments are subjected to periodic FDA inspections to ensure they are following good manufacturing practices standards.

The regulation does not, however, define the term "promptly" or indicate the length of time in which the licensed blood establishment is expected to submit its error and accident report to CBER.

By memorandum dated March 20, 1991, entitled, "Responsibilities of Blood Establishments Related to Errors & Accidents in the Manufacture of Blood & Blood Components," CBER alerted blood establishments to the problem of untimely reporting of errors and accidents, and reminded them of the circumstances which warrant a report. To determine if blood establishments were reporting errors and accidents in a timely manner after receipt of this alert, we randomly selected and reviewed 163 error and accident reports submitted to FDA during the first 6 months of FY 1993.

The time between the date the error or accident was detected and the date it was reported to FDA ranged from less than 1 month to over 1 year, with an average of a little over 4 months. In our opinion, such a reporting time lapse after detection is not "prompt." As shown in the following chart, only about 14 percent of the error and accident reports reviewed were submitted by the blood establishment within 1 month after the detection of the incident, while 13 percent were reported 6 months or more after detection.



When the reports are not submitted timely, as shown in the table above, FDA is not in a position to evaluate and monitor the actions taken by the establishments to correct the deficiencies detected. As previously stated, however, the timeliness of the actions should not be affected by untimely reporting.

Reporting by Unlicensed Establishments

Although FDA has requested all unlicensed blood establishments to voluntarily submit error and accident reports, our analysis indicates that such establishments may not always be submitting the reports. If FDA is to more effectively evaluate and monitor the blood industry--as outlined in its plan--it should have reports from the full spectrum of establishments.

There are about 2,900 registered blood establishments regulated by FDA. About one-fourth of these registered blood establishments are licensed by FDA, and are required to submit error and accident reports involving blood and blood products. The remaining 75 percent of the registered blood establishments do not ship blood or blood products interstate and, therefore, are unlicensed. These establishments are not required to submit these reports to FDA except for cases involving fatalities. According to FDA, unlicensed establishments account for about one-tenth of the blood collected in this country. In its March 20, 1991 memorandum to all blood establishments, CBER requested that all unlicensed establishments voluntarily submit the error and accident reports. Regardless of whether an establishment is licensed, all of them are required to meet the same safety standards, and all are periodically inspected by FDA.

According to FDA, between October 1, 1991 and September 30, 1992, CBER's Division of Inspections and Surveillance received 10,456 reports of errors and accidents. Of these, 10,308 reports (99 percent) were submitted by licensed blood establishments. Only 148 reports (about 1 percent), were submitted by unlicensed blood establishments. We found a similar split between the licensed and unlicensed establishments for the error and accident reports reviewed in our sample. Of the 163 error and accident reports in our sample, only 2 were from unlicensed establishments. We believe these statistics may be indicative of nonreporting, rather than unlicensed establishments having less problems than their licensed counterparts.

The CBER did not have a process to readily identify unlicensed blood establishments that did not voluntarily submit error and accident reports. Therefore, CBER was not in a position to determine whether lack of submission was widespread among the unlicensed establishments. The FDA can, however, determine the extent of nonreporting by unlicensed blood establishments through its inspection process. The 21 C.F.R. 606.160(b)(7)(iii) requires that all blood establishments, both licensed and unlicensed, maintain records relating to errors and accidents. The FDA inspectors are required to determine, among other things, if errors or accidents affecting products were detected since the last inspection. If an error or accident occurred, the inspectors are to indicate on the inspection report whether CBER was notified as soon as possible.

This information on CBER notification, if captured from the inspection reports, would enable FDA to identify specific unlicensed blood establishments that did not voluntarily submit error and accident reports. Using this information, FDA could also determine the extent of

nonreporting. The FDA could then focus attention on those blood establishments that repeatedly failed to submit the error or accident reports.

Management Information

We believe that CBER can make better use of the information on error and accident reports while it awaits the development and implementation of an integrated management information system that is included in FDA's proposed plan. The plan is to convert CBER's management information systems from "antiquated and incompatible information systems" to a "single relational data base" which will facilitate the exchange of information between field and headquarter staff. Such an integrated system will also permit CBER to monitor blood establishment performance, identify trends and problems in early stages of development, and issue guidance to prevent errors and accidents.

The FDA currently uses the error and accident reports to identify incidents that warrant an evaluation for a recall classification, and to alert its district offices of problems that warrant a follow-up during the next inspection. Data contained in error and accident reports are entered into a data base maintained by the Biological Product Inspections Branch, Division of Inspections and Surveillance. At the end of each quarter, a summary report is prepared showing, among other things, the number of reports received, the number identified as potential recalls, a breakdown of when the error or accident occurred versus when the reports were received, and a chart illustrating the distribution of the types of errors. A summary report for the year is also prepared containing basically the same type of information. The reports are forwarded to the Director, Division of Inspections and Surveillance, who informed us that the reports are used primarily for training purposes.

We believe the reports are a useful training device for inspectors. We also believe, however, they could be equally useful to all inspectors as the reports do provide an analysis of the errors and accidents that are found nationally by both type of incident and type of establishment; that is, licensed blood establishment, unlicensed blood establishment, plasma centers, and so on. Furthermore, the data base itself could be used to identify blood establishments that do not submit their reports timely. To do this, FDA would have to compare the date that the error or accident was detected (not when it occurred) to the date that the report was received.

We also believe the information could be useful to the blood establishments. We noted that CBER had in the past forwarded this information to the blood establishments, but had not done so recently. By memorandum of March 20, 1991, entitled, "Deficiencies Relating to the Manufacturing of Blood and Blood Components," CBER alerted all blood establishments to the types of deficiencies relating to the release of unsuitable blood and blood products. The deficiencies reported came in part from CBER's analysis of error and accident reports. The CBER stated that the information "will be beneficial to blood establishments and provide information that may be useful in performing self audits." We agree with CBER's

assessment of the usefulness of this information, and believe the practice of providing it to the blood establishments should be continued.

CONCLUSIONS AND RECOMMENDATIONS

Our review showed that FDA's error and accident reporting process is a valuable management tool, and that FDA was processing the error and accident reports submitted by the blood establishments in accordance with established procedures. These reports enable FDA to evaluate and monitor the blood establishments' actions taken in response to the errors and accidents detected. The reports also have the potential to provide FDA with an overview of the problems that are being detected throughout the blood industry.

The FDA recognizes the value of self-reporting by blood establishments and, as part of its plan to improve its oversight function, intends to maximize the usefulness of error and accident reports. The FDA plans to use these reports to identify problem areas and trends and to develop appropriate "early warning" guidance to FDA field offices and the blood industry.

For this plan to be fully successful, however, all error and accident reports, regardless of whether their source is a licensed or unlicensed blood establishment, should be received timely. Without timely and complete reporting by blood establishments on the number and types of errors and accidents that are detected, FDA may be limited in its efforts to evaluate and monitor the blood industry. We also believe that FDA should make better use of the information currently available to determine the scope of voluntary nonreporting by unlicensed establishments, and to provide information on error and accident trends to both its field offices and the blood industry.

We, therefore, recommend that the Commissioner of Food and Drugs:

1. expedite the development and issuance of revisions to the Federal regulation on error and accident reporting (21 C.F.R. 600.14(a)) to be more specific concerning the time frame in which error and accident reports are required to be submitted;

2. expedite the development and issuance of a regulation to require unlicensed blood establishments to submit error and accident reports; and

3. expand CBER's use of existing information in its current error and accident data base to identify blood establishments that regularly fail to submit error and accident reports in a timely manner, and provide additional trend analysis reports to FDA field offices and blood establishments.

PHS COMMENTS AND OIG RESPONSE

On April 28, 1995, PHS responded to our January 31, 1995 draft report. In agreeing with our recommendations, PHS stated that in FY 1994, $1.4 million was reprogrammed to improve CBER's information management system and to make other systems improvements. It stated that many of the ideas discussed in the report were already being worked on by FDA prior to the report's issuance and asked that this be reflected in the presentation of our recommendations. The PHS also made some general and technical comments relative to the language in our draft report.

We have made changes to this report that we believe adequately address PHS' general and technical comments. We are encouraged that FDA has taken action to implement our recommendations for improving the reporting of errors and accidents by all blood establishments.

APPENDIX

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

MEMORANDUM

Rockville MD 20857

APR 28 1995

Date:

From: Assistant Secretary for Health

Subject: Office of Inspector General (OIG) Draft Report "Reporting Process for Blood Establishments to Notify the Food and Drug Administration (FDA) of Errors and Accidents Affecting Blood," A-03-93-00352

To: Inspector General, OS

Attached are the Public Health Service's comments on the subject report. We concur with the report's recommendations. Our comments delineate the actions taken or planned to implement these recommendations.

Philip R. Lee, M.D.

Attachment

PUBLIC HEALTH SERVICE (PHS) COMMENTS ON THE OFFICE OF INSPECTOR GENERAL (OIG) DRAFT REPORT "REPORTING PROCESS FOR BLOOD ESTABLISHMENTS TO NOTIFY THE FOOD AND DRUG ADMINISTRATION OF ERRORS AND ACCIDENTS AFFECTING BLOOD," A-03-93-00352

General Comments

The objective of OIG's review was to assess the reporting process by which blood establishments notify the Food and Drug Administration (FDA) of errors and accidents that affect the safety, purity, or potency of blood and blood products. The OIG found that FDA's error and accident reporting process is a valuable management tool for evaluating and monitoring the actions taken by blood establishments in response to errors and accidents detected. They also determined that FDA processed error and accident reports in accordance with established procedures. However, they identified two conditions which could hamper FDA's plan to expand the usefulness of error and accident reports: (1) blood establishments were not always making timely submissions of error and accident reports; and (2) there was no assurance that unlicensed establishments were voluntarily submitting the reports.

Based on these findings, the OIG concludes that all error and accident reports should be received by the FDA in a timely manner, and that FDA should make better use of the information currently available to determine the scope of nonreporting and to provide information on error and accident trends. The OIG's recommendations stem from these conclusions. We concur with these recommendations and are taking actions to implement them.

The report makes references to an FDA proposal to establish a blood safety initiative. As the report notes, several aspects of this proposal could relate to the objective of the OIG review. For example, one component of the proposal focussed on the blood industry's self-reporting of errors and accidents; another concerned improvements in automated systems.

Though not transformed into a broad FDA initiative, certain aspects of this proposal are currently being pursued by FDA. In Fiscal Year 1994, $1.4 million dollars were reprogrammed to FDA's Center for Biologics Evaluation and Research (CBER) to fund information management and other systems improvements such as those envisioned in the proposal. These funds are now part of CBER's base and are available to assist in priority undertakings. In addition to these "systems" improvements, the regulatory and procedural changes described in the PHS response to the OIG recommendations will increase the timeliness and usefulness of error and accident reporting.

Finally, many of the ideas surfaced in this report were already being translated into action in CBER prior to the initiation of the OIG's audit. Accordingly, we believe that the OIG should consider revising its recommendations to reflect more fully CBER's ongoing efforts. Our suggested revisions are provided in the PHS comments following each of the OIG recommendations.

OIG Recommendation

We recommend that the Commissioner of Food and Drugs:

1. Revise the Federal regulation on error and accident reporting (21 CFR 600.14(a)) to be more specific concerning the time frame in which error and accident reports are required to be submitted.

PHS Comment

We concur. The CBER is pursuing proposed revisions to the rules at Title 21 CFR § 600.14, "Reporting of Errors." These revisions would be specific as to the time frame in which error and accident reports are to be submitted.

Based on the current time frames for both Departmental and Office of Management and Budget clearances for regulations, the proposals should be cleared by FDA by November 1995 and published by February 1996.

In as much as FDA commenced these activities before the OIG initiated its review, we suggest that the OIG consider revising this recommendation to read:

> "Expedite the development and issuance of a regulation to revise the Federal regulation on error and accident reporting (21 CFR § 600.14 (a)) to be more specific concerning the time frame in which error and accident reports are required to be submitted."

OIG Recommendation

2. Take the necessary regulatory action to require unlicensed blood establishments to submit error and accident reports.

PHS Comment

We concur. The CBER is developing a new regulatory proposal to revise Title 21 CFR § 600.14, "Reporting of Errors," to require unlicensed establishments to submit error and accident reports. As noted above, we expect that the proposals will be

cleared by FDA by November 1995 and published by February 1996.

In the interim, the CBER will revise inspectional guidance so that field staff (1) review any reports of errors and accidents during inspections of unlicensed establishments and (2) encourage voluntary reporting. The CBER will also prepare letters to the industry providing feedback on certain aspects of error and accident reporting.

For the reason indicated above, we suggest that the OIG consider revising this recommendation to read:

> "Expedite the development and issuance of a regulation to require unlicensed blood establishments to submit error and accident reports."

OIG Recommendation

3. Require CBER to use existing information in its current error and accident data base to identify blood establishments that regularly submit error and accident reports untimely, and provide trend analysis reports to the FDA field offices and blood establishments.

PHS Comment

We concur. The CBER is currently using its existing data base and information management systems to identify establishments which do not make timely reports of errors and accidents. Since "timely" is not yet defined in FDA regulation, this process is somewhat difficult. However, in situations where it is defined (e.g., when specified in establishments' standard operating procedures) the CBER does perform evaluations of conformity with procedures.

The CBER currently provides trend reports to ORA headquarters for dissemination to the field. Starting April 30, 1995, the CBER plans to send trend reports directly to FDA Regional and District Directors.

As indicated above, we suggest that the OIG consider revising this recommendation to read:

> "Expand CBER's use of existing information in its current error and accident data base to identify blood establishments that regularly fail to submit error and accident reports in a timely manner, and provide additional trend analysis to the FDA field offices and blood establishments."

Technical Comments

We would like to clarify several statements in the report which relate to technical issues:

First, we note that the report states (page i and others) that intrastate blood banks are unlicensed by FDA, but fall under State licensing procedures. We believe it would be useful to emphasize that although intrastate blood banks are unlicensed, they nevertheless are subject to FDA's good manufacturing practice standards.

In addition, we believe that the report should clearly state that inspectional and enforcement activities are similar for both licensed and registered establishments.