# Memorandum

Date APR 12 1996

From June Gibbs Brown
Inspector General

Subject Review of the Food and Drug Administration's Processing of 17 Error and Accident Reports Involving Blood (A-03-95-00350)

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

The attached final audit report provides you with the results of our review of the processing of 17 error and accident reports involving blood which had been identified by the Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) as requiring further evaluation on whether to be classified and reported as a blood recall. We identified the 17 reports in a prior review, which concluded that the reporting process used by blood establishments to notify CBER of error and accidents is a valuable management tool.

The objective of this review was to determine if FDA followed its internal procedures regarding the 17 error and accident reports it had identified as requiring further evaluation for a blood recall classification. Our review disclosed that FDA processed 12 of the 17 error and accident reports in accordance with established procedures. Five of the 17 reports were not processed in accordance with established procedures. Although errors in processing the five error and accident reports caused delays in classifying the blood recalls and publishing them in the FDA Enforcement Report, FDA does not believe the public was placed at additional risk. Classification and publication of a blood recall generally take place long after the error or accident occurs.

We recommend that FDA improve its tracking system to ensure that all error and accident reports warranting further evaluation for blood recall classification are tracked until final resolution. We also recommend that FDA complete the recall classification and publication of the five error and accident reports identified in the report as not being processed in accordance with established procedures.

In responding to our draft audit report, FDA agreed with our recommendations. The FDA's comments are presented as Appendix B 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 any questions, please call me or have your staff contact Joseph J. Green, Assistant Inspector General for Public Health Service Audits, at (301) 443-3582.

To facilitate identification, please refer to Common Identification Number A-03-95-00350 in all correspondence related to this report.

Attachment

Department of Health and Human Services

# OFFICE OF INSPECTOR GENERAL

# REVIEW OF THE FOOD AND DRUG ADMINISTRATION'S PROCESSING OF 17 ERROR AND ACCIDENT REPORTS INVOLVING BLOOD


JUNE GIBBS BROWN
Inspector General

APRIL 1996
A-03-95-00350

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Subject Review of the Food and Drug Administration's Processing of 17 Error and Accident Reports Involving Blood (A-03-95-00350)

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

This final report provides you with the results of an Office of Inspector General (OIG) review of the processing of 17 error and accident reports involving blood which had been identified by the Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) as requiring further evaluation on whether to be classified and reported as a blood recall.

## OBJECTIVE

The objective of our review was to determine if FDA followed its internal procedures regarding the 17 error and accident reports it had identified as requiring further evaluation for a blood recall classification. In a prior review,[1] we concluded that the reporting process used by blood establishments to notify CBER of errors and accidents that may affect the safety, purity, or potency of blood is a valuable management tool; but that certain improvements were needed. We also concluded that, based on our review of a sample of 163 error and accident reports, CBER generally processed the reports in accordance with established procedures. We pointed out, however, that we were continuing our review of 17 of the 163 error and accident reports that were identified by CBER as warranting further evaluation for a recall classification.

For the purposes of this report, a recall is a blood establishment's voluntary removal or correction of a marketed blood product that violates laws administered by FDA and for which FDA would initiate regulatory action. Blood recalls differ from other product recalls because blood, having a short shelf life, is sometimes used before it can be retrieved. Since blood establishments are required to investigate all errors and accidents, including those that are eventually classified as 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. An FDA official informed us that the blood recall

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[1] Office of Inspector General. Review of the Reporting Process for Blood Establishments to Notify the Food and Drug Administration of Errors and Accidents Affecting Blood. A-03-93-00352 May 31, 1995.

classification is important because its publication in the FDA Enforcement Report[2] acts as an incentive for blood establishments to prevent serious errors and accidents from recurring.

## SUMMARY OF FINDINGS

Our review disclosed that FDA processed, in accordance with established procedures, 12 of the 17 error and accident reports that CBER had identified as warranting further evaluation for a recall classification. Five of the 17 error and accident reports were not processed in accordance with established procedures in that:

- two reports, including one that CBER had not forwarded to the FDA field office, were not followed up on at the blood establishments to ensure that corrective action was taken and to evaluate the appropriateness of a blood recall classification; and

- three reports, although followed up on at the blood establishments by FDA field offices, were not returned to CBER along with a recommendation for recall so that the recall classification could be processed.

Officials at CBER reviewed the files associated with the five error and accident reports, and told us that had the reports been processed in accordance with established procedures, each would have been classified as a blood recall and published in the FDA Enforcement Report. The FDA is taking the required action to complete the processing of the five error and accident reports and classify them as blood recalls.

Although errors in processing the five error and accident reports caused delays in classifying the blood recalls and publishing them in the FDA Enforcement Report, FDA does not believe the public was placed at additional risk. Classification and publication of a blood recall generally take place long after the error or accident occurs and is reported by a blood establishment. In the five error and accident reports that we identified as not being processed correctly, the blood establishments acted shortly after detecting the error or accident. Four of the blood shipments were either destroyed or appropriately relabeled prior to transfusion into a patient. One shipment, mislabeled with an incorrect expiration date (dated earlier than the correct expiration date), was transfused before the blood establishment detected the error. In this instance, however, the transfusion occurred before the correct expiration date of the blood. As part of our prior review, FDA reviewed the documentation at our request, and concluded that the blood establishments took adequate action on each error or accident prior to submitting the reports to CBER.

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[2] The FDA Enforcement Report is a weekly publication which contains a descriptive listing of each new recall according to its classification. The report is distributed to the press, throughout FDA, other Federal Government agencies, and consumers.

## RECOMMENDATIONS

Our review was limited to 17 error and accident reports selected in a prior review. Because of this limited number, we cannot reach overall conclusions as to the effectiveness of FDA's controls over blood recall classifications. We believe, however, that the processing errors associated with the five error and accident reports, which were not processed in accordance with established procedures, could have been detected had FDA tracked the reports until final resolution.

We, therefore, recommend that FDA:

1. improve its tracking system to ensure that all error and accident reports warranting further evaluation for blood recall classification are tracked until final resolution, such as a blood recall classification; and

2. complete the recall classification and publication of the five error and accident reports identified in this report as not being processed in accordance with established procedures.

In its March 5, 1996 comments to our draft report, FDA indicates agreement with our recommendations.

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## BACKGROUND

The Public Health Service Act (Title 42 of the 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[3] with FDA. The FDA has the authority to register all blood establishments, and to license those establishments that ship blood and blood products interstate. While FDA provides guidance to blood establishments to help them comply with regulations, industry standards and safeguards, blood establishments are primarily responsible for ensuring the safety of their blood products.

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[3] As used in this report, a blood establishment is a place of business under one management and 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. The FDA establishment licenses may cover multiple locations.

**Processing Error and Accident Reports**

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 CBER. Unlicensed establishments currently are not required to self-report, but FDA is taking action to require mandatory reporting for such establishments. The error and accident report identifies, among other things, the blood establishment, the unit, the blood product, the nature of the error or accident, and the final disposition of the blood product. The report also lists contributing factors causing the error or accident and the actions taken by the blood establishment.

Within CBER, the Division of Inspection and Surveillance (DIS) is responsible for receiving and analyzing error and accident reports. If a report clearly does not require further evaluation of the severity of the incident, DIS sends the report to the appropriate FDA field office for follow-up at the next inspection of the blood establishment. The FDA's Office of Regulatory Affairs (ORA) is responsible for coordinating all of the field office's activities.

If DIS concludes that an error and accident report warrants further evaluation for a blood recall classification, it prepares an Alert to Possible Recall document (hereafter referred to as Alert document), and forwards it and the error and accident report to the Division of Case Management (DCM),[4] also within CBER. Among the numerous potential recall situations contained in Attachment F of FDA's Standard Operating Procedure for Processing Error and Accident Reports are: (1) a blood donor had intimate contact with a person who is HIV positive; (2) a blood donor had exposure to hepatitis; and (3) a blood product label contained an incorrect product expiration date (dating period extended). The Alert document summarizes much of the information on the error and accident report, and records the date the field office was alerted to a recall and the recall initiation date. Of the 10,456 error and accident reports submitted by blood establishments to DIS in Fiscal Year (FY) 1992, 791 (7.6 percent) were referred to DCM to be evaluated for possible recall consideration.

A recall is a blood establishment's voluntary removal or correction of a marketed blood product that violates laws administered by FDA and for which FDA would initiate regulatory action. The Code of Federal Regulations (C.F.R.) (21 C.F.R. Part 7 Subpart C) allows FDA to request a firm to initiate a recall when it determines that a product is distributed that presents a risk of illness or injury; the firm has not initiated a recall; and the action is necessary to protect the public health and welfare. The FDA recognizes that a voluntary recall is generally more appropriate and affords better protection for consumers than seizure, which is an FDA option when a firm refuses to undertake a recall.

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[4] Subsequent to our review, FDA reorganized CBER. The recall function was transferred to DIS for all recalls and error and accident reports. The DCM no longer receives error and accident reports.

Blood recalls differ from other product recalls because blood, having a short shelf life, is sometimes used before it can be retrieved. Since blood establishments are required to investigate all errors and accidents, including those that are eventually classified as 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. An FDA official informed us that the blood recall classification is important because its publication in the FDA Enforcement Report acts as an incentive for blood establishments to prevent serious errors and accidents from recurring.

According to FDA, compliance with regulations accounts for the relatively few errors and accidents which warrant a blood recall classification. In FY 1994, there were 427 blood recall classifications involving 8,529 units, or about 3/100ths of 1 percent of the 26 million units of whole blood, blood components, and source plasma 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.

## OBJECTIVE, SCOPE, AND METHODOLOGY

The objective of this review was to follow up on the actions taken by FDA on 17 error and accident reports identified in our prior review as warranting further evaluation for a blood recall classification. In our prior review of the reporting process used by blood establishments to notify FDA of errors and accidents, we concluded that the reporting process is a valuable management tool, but recommended certain improvements. We also concluded that FDA generally processed correctly the 163 error and accident reports that we had selected for review, but pointed out that we were continuing our review of 17 error and accident reports determined by CBER as warranting further evaluation for possible recall classification.

As part of our review of the 17 error and accident reports, we tracked the reports through CBER's DIS and DCM to the appropriate FDA field offices and back to DCM. Specifically, we determined if:

- the DIS forwarded the Alert document and error and accident report to CBER's DCM for evaluation of a blood recall classification;
- the DCM evaluated the error and accident report and forwarded it and the Alert document to the appropriate FDA field office to determine the need for a blood recall classification;
- the FDA field offices followed up on the error and accident report at the blood establishment, and, when appropriate, submitted a recall recommendation to DCM; and

- the DCM evaluated the recall recommendation, made a blood recall classification, and the FDA's Press Relations Staff published it in the FDA Enforcement Report.

We reviewed documentation maintained by DIS and DCM. We also obtained from the appropriate FDA field offices files on the 17 error and accident reports included in our review. The files document the field offices' actions taken on these reports. We determined whether the required actions were taken, not whether the actions taken were effective or scientifically sound.

Our review was performed in accordance with generally accepted government auditing standards; however, the scope of our review was limited to the 17 error and accident reports identified in our prior review. Therefore, we cannot make any overall conclusions about FDA's controls over error and accident reports identified as warranting an evaluation for recall, or the overall impact of any weakness on the blood recall classification process.

Our review was performed at FDA offices in Rockville, Maryland, during May through August 1995. We extended our review to give FDA an opportunity to take actions on the five error and accident reports that we identified as not being processed in accordance with established procedures. Our review did not include a visit to any FDA field office.

## RESULTS OF REVIEW

### FIVE ERROR AND ACCIDENTS REPORTS WERE NOT PROCESSED IN ACCORDANCE WITH ESTABLISHED PROCEDURES

Our review of the 17 error and accident reports identified by DIS as warranting further evaluation for a blood recall classification disclosed that 12 of the reports had been processed in accordance with FDA's established procedures. Six of the 12 reports resulted in a blood recall classification. The remaining six reports were determined to be lesser violations not warranting a recall classification. Most of these resulted in a market withdrawal[5].

The FDA did not process 5 of the 17 error and accident reports in accordance with established procedures. As shown in the following table, neither CBER (one report) nor the FDA field offices (four reports) took all of the required actions to fully evaluate the five error and accident reports to determine the need for a blood recall classification.

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[5] A market withdrawal is a firm's removal or correction of a distributed product which involves a minor violation for which FDA would not initiate legal action, or which involves no violation at all, such as a normal stock rotation.

| REQUIRED ACTIONS NOT TAKEN | | | | |
|---|---|---|---|---|
| Error and Accident Reports | CBER | | Field Offices | |
| | Report Received by DCM | Report Forwarded to Field Office | On-Site Review | Returned Report With Recall Recommendation |
| 1 | No Record | NO | N/A | N/A |
| 2 | Yes | Yes | NONE | NO |
| 3 | Yes | Yes | Yes | NO |
| 4 | Yes | Yes | Yes | NO |
| 5 | Yes | Yes | Yes | NO |
| Total Errors | One | One | Two | Five |

The FDA field offices did not follow up on two of the five error and accident reports at the blood establishments, and did not complete recall recommendations on the five reports. The FDA reviewed the five error and accident reports at our request and agreed that blood recall classifications were warranted in each case. The FDA is taking the necessary action to classify each report.

As a result of not processing the five error and accident reports correctly, FDA was not in a position to classify them as blood recalls and publish them in the FDA Enforcement Report. Although there has been a delay in classifying the five blood recalls, FDA does not believe that the delays placed additional risk on the general public. The blood recall process is generally an after-the-fact process, and blood establishments in these five instances responded shortly after detecting the errors or accidents. Although we cannot reach overall conclusions as to the effectiveness of FDA's controls over error and accident reports identified as warranting further evaluation for potential recall classification, we believe these five instances of non-compliance with FDA procedures could have been detected had FDA had a more effective tracking system for these reports.

**Processing Blood Recall Classifications**

The DCM evaluates the error and accident report received from DIS and, if it concurs with DIS' conclusion that further evaluation for a blood recall classification is warranted, forwards the Alert document and the report to the appropriate FDA field office with instructions to follow up at the blood establishment either immediately, or during the next scheduled on-site inspection of the blood establishment. The follow-up review is to determine the adequacy of corrective actions taken by the blood establishment, and to gather information to be used in evaluating the appropriateness of a blood recall classification.

After the field office follows up on the error and accident report at the blood establishment, it prepares a recall recommendation when it determines that a blood recall

classification is warranted, and forwards the recommendation to DCM. The recall recommendation includes such information as the reason for the recall, the distribution pattern of the blood subject to the recall, the blood establishment's recall strategy, and the field office's audit program.

The DCM is then required to review the field office's recall recommendation; complete a health hazard evaluation; and, if warranted, classify the blood recall. The three blood recall classifications are:

- Class I - A situation in which there is a strong likelihood that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.

- Class II - A situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

- Class III - A situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences.

Once the recall classification is completed, FDA publishes the recall actions in the FDA Enforcement Report. The procedures for processing an error and accident report and classifying a blood recall are found in FDA's Regulatory Procedures Manual, standard operating procedures, and other guidance documents.

**Follow-Up Reviews Not Conducted**

The FDA field offices did not conduct the required follow-up review of two error and accident reports at the blood establishments. These follow-up reviews are needed to ensure that the blood establishments took corrective action on the error or accident reported, and to develop the information needed to make a recall recommendation. Our review of FDA documentation associated with the two reports disclosed that one error and accident report was misplaced between CBER's DIS and DCM. According to the available documentation, DIS evaluated the report (Appendix A--Case 1) and prepared an Alert document, both of which were forwarded to DCM on October 27, 1992. The DCM, however, had no record of ever receiving the Alert document or the error and accident report. As a result, the report was not forwarded to the field office for follow-up review, and no recall recommendation was made.

The second error and accident report (Appendix A--Case 2) was received by DIS and forwarded to DCM on January 25, 1993. The DCM determined that the field office should follow up on the error and accident report during the next inspection of the blood establishment and forwarded this instruction to the field office on January 28, 1993. The field office conducted the inspection of the blood establishment beginning on April 18,

1994, but there was no documentation to show that the error and accident report was followed up on or that a recall recommendation was sent to DCM.

**Follow-Up Reviews Made But Recall Recommendations Not Sent to DCM**

The FDA field office conducted follow-up reviews of three error and accident reports at the blood establishments as required, but did not forward their recall recommendations to DCM for concurrence and classification. We found evidence in the field office establishment inspection file that the three error and accident reports were reviewed during the inspections of the blood establishments. The field office developed a recall recommendation for one of the error and accident reports (Appendix A--Case 3), but did not send it to DCM for recall classification. There were no recall recommendations developed for the other two error and accident reports (Appendix A--Cases 4 and 5).

**Errors and Accidents Should Have Been Classified as Recalls**

The FDA officials who reviewed the documentation for the five error and accident reports agreed that the field offices should have submitted recall recommendations and that the errors or accidents being reported should have been classified as blood recalls. After we brought this matter to their attention, FDA initiated immediate actions to classify the five error and accident reports. Two were classified as Class II recalls, two were classified as Class III recalls, and all four recall classifications were published in the FDA Enforcement Report as of August 31, 1995. The remaining error and accident report is under review with an anticipated classification as a Class III blood recall.

**Incorrect Processing Caused Delays But Did Not Increase Health Risk**

Failure to correctly process the five error and accident reports caused delays in classifying the blood recalls. The FDA required an average of about 31 months from receipt of the error and accident reports to classify and publish the four blood recalls that have been completed. This compares to about 10 months needed to classify the 6 recalls that were processed in accordance with FDA procedures.

Although the recall classifications and publications were delayed in 5 of the 17 error and accident reports that we reviewed, corrective actions taken by the blood establishments after detecting the errors were not. For four of the five reports, the error or accident was corrected prior to the blood being transfused into a patient. In these cases, the blood was destroyed; or, in the case of mislabeled blood, returned to the blood establishment where it was relabeled and reissued.

The one exception (Appendix A--Case 5) involved six units with an incorrect expiration date on the label. The label showed the expiration date to be September 10, 1993, when the correct date was August 10, 1993. Three units of blood were returned to the blood

establishment, relabeled with the correct expiration date, and reissued. The remaining three units of blood were transfused before the blood establishment detected the error on August 14, 1992, but long before the correct expiration date of August 10, 1993. According to CBER staff, which reviewed the case file, it is unlikely that the use of or exposure to the mislabeled blood could cause any adverse health consequences since the blood was used prior to the expiration date.

**Better Tracking System Could Have Detected Errors**

Four of the five errors in processing the error and accident reports resulted from the field offices not complying with requirements to: (1) conduct follow-up reviews of the reports at the blood establishments; and (2) forward recall recommendations to DCM when appropriate. We believe these errors, as well as the other error involving a missing error and accident report within CBER, could have been detected had FDA had a better means of tracking error and accident reports identified for recall consideration.

We noted that CBER did have a computer system for error and accident reports. The system was not used, however, to track error and accident reports within CBER or responses from the field offices to DCM's Alert documents and accompanying error and accident reports. We also noted that DCM maintained a manual file of error and accident reports that are sent to the field offices. We were informed that the file is periodically reviewed for those reports outstanding for over 1 year. However, the four error and accident reports that we identified as being sent from DCM to the field offices were outstanding (forwarded to an FDA field office and not returned) over 2 years and remained unclassified by DCM personnel.

We believe that a system is needed to track all error and accident reports identified by DIS as warranting further evaluation for blood recall classification. To implement a more effective tracking system, field offices would likely have to respond to all Alert documents received and not just those where they conclude that a recall recommendation is warranted.

## CONCLUSIONS AND RECOMMENDATIONS

Our review of the 17 error and accident reports identified in our prior review as requiring an evaluation for possible recall classification disclosed that 5 reports were not processed in accordance with established procedures. Failure to properly process the five reports resulted in FDA being unable to classify and publish five blood recalls, but did not increase the public health risk.

Because of the limited number of error and accident reports reviewed, we cannot reach an overall conclusion as to the adequacy of FDA's controls over the processing of error and accident reports identified as requiring an evaluation for a blood recall classification. It is

clear, however, that CBER's tracking system did not identify the five error or accident reports that were not expeditiously processed.

We, therefore, recommend that FDA:

1. improve its tracking system to ensure that all error and accident reports warranting further evaluation for blood recall classification are tracked until final resolution, such as a blood recall classification; and

2. complete the recall classification and publication of the five error and accident reports identified in this report as not being processed in accordance with established procedures.

## FDA COMMENTS AND OIG RESPONSE

By memorandum dated March 5, 1996, FDA responded to our draft report. The FDA agreed with our recommendations stating that a tracking system has been instituted for error and accident reports, and that four of the five reports have been closed. The CBER is following the remaining case so that it can be closed as soon as possible. The FDA also made some general and technical comments relative to the language in our draft report, which have been addressed in this report.

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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 any questions, please call me or have your staff contact Joseph J. Green, Assistant Inspector General for Public Health Service Audits, at (301) 443-3582.

To facilitate identification, please refer to Common Identification Number A-03-95-00350 in all correspondence related to this report.

Appendices

# APPENDICES

# ERROR AND ACCIDENT REPORTS NOT PROCESSED CORRECTLY

## CASE 1

Blood Establishment Error

On June 4, 1992, one unit of liquid plasma was shipped to a consignee who immediately determined that the blood was mislabeled (it was labeled fresh frozen plasma). The consignee returned the blood unit to the blood establishment on the same date. The mislabeled blood was not transfused into a patient.

The blood establishment relabeled the unit liquid plasma correctly and reissued it.

FDA Recall Classification Process

The DIS received the error and accident report on October 9, 1992, and reportedly forwarded it and the Alert document to DCM on October 27, 1992, for possible recall classification. However, DCM had no record of receiving this report. As a result, DCM could not evaluate the error and accident report, and forward it to the appropriate FDA field office for further evaluation of a blood recall classification.

The DCM indicated that had it received the error and accident report, it would have concluded that an evaluation for possible recall classification was warranted.

FDA Corrective Action

The FDA is in the process of taking corrective action. The DCM received the Alert document and the error and accident report and forwarded it to the appropriate field office where it is currently under review. As of August 28, 1995, the field office has not submitted a recall recommendation to DCM. The FDA anticipated a recommendation for a Class III recall (classification will be at least 35 months after receipt of the error and accident report).

## CASE 2

Blood Establishment Error

On November 9 and 10, 1992, the blood establishment shipped two units of contaminated red blood cells to one consignee. On November 11, the blood establishment detected the contamination--the blood was stored at room temperature for 18 to 20 hours--and notified the consignee. The consignee was contacted and returned the two blood units. The contaminated blood was not transfused into a patient.

The blood establishment destroyed the two units of contaminated blood returned by the consignee, and two other units recovered from the establishment's stock.

FDA Recall Classification Process

The DIS received the error and accident report on December 28, 1992, and forwarded it and the Alert document to DCM on January 25, 1993. On January 28, 1993, DCM sent the Alert document and the error and accident report to the FDA field office, instructing it to follow up during the next scheduled inspection of the blood establishment.

The field office conducted the inspection from April 18, 1994, through May 13, 1994. According to the field office establishment inspection file, the error and accident report was not evaluated during the inspection. As a result, the field office could not develop the recall recommendation for submission to DCM.

FDA Corrective Action

The FDA has taken corrective action. The field office developed the recall recommendation and submitted it to DCM for recall concurrence and classification on May 18, 1995. The FDA classified it as a Class II recall on June 23, 1995, and published the recall in the FDA Enforcement Report on June 28, 1995, about 30 months after receiving the error and accident report.

## CASE 3

Blood Establishment Error

On October 26, 1992, the blood establishment shipped one unit of contaminated source plasma to one consignee. On the same day, the blood establishment detected that the blood was anti-Hepatitis C Virus reactive and immediately notified the consignee before delivery. The consignee destroyed the unit upon receipt of the contaminated unit. The contaminated blood was not transfused into a patient.

FDA Recall Classification Process

The establishment prepared the error and accident report on February 12, 1993, as a result of a field office establishment inspection performed February 8 and 9, 1993. The DIS received the error and accident report on March 3, 1993, and forwarded it and the Alert document to DCM on March 16, 1993. On March 19, 1993, DCM forwarded the Alert document and the error and accident report to the appropriate field office, instructing it to follow up during the next scheduled inspection of the blood establishment.

According to the field office's file, the office had developed documentation to justify a recall recommendation, but could not locate the documentation in the case files and did not send the recommendation to DCM.

FDA Corrective Action

The FDA has taken corrective action. The field office developed the recall recommendation and submitted it to DCM for recall concurrence and classification on June 9, 1995. The DCM classified it as a Class II recall on July 31, 1995, and published the recall in the FDA Enforcement Report on August 9, 1995, about 30 months after receiving the error and accident report.

## CASE 4

Blood Establishment Error

On December 12, 1991, a blood establishment collected three units of whole blood. The units were shipped to two consignees between December 13 and December 20, 1991. On December 20, the blood establishment discovered that the units were mislabeled with a incorrect expiration date. The blood establishment informed the consignees of the error and the consignees returned the units. The mislabeled blood was not transfused into a patient.

The blood establishment relabeled the three units with the correct expiration date and reissued them.

FDA Recall Classification Process

The DIS received the error and accident report on November 6, 1992, and forwarded it and the Alert document to DCM on November 12, 1992. On November 17, 1992, DCM sent the Alert document and the error and accident report to the FDA field office, instructing it to follow-up during the next scheduled inspection of the blood establishment.

The field office conducted the inspection from January 21, 1993, through February 8, 1993. According to the field office establishment inspection file, the error and accident report was evaluated during this inspection. The field office, however, did not develop the recall recommendation and send it to DCM.

FDA Corrective Action

The FDA has taken corrective action. The field office developed the recall recommendation and submitted it to DCM for recall concurrence and classification on June 8, 1995. The FDA classified it as a Class III recall on July 24, 1995, and published the recall in the FDA Enforcement Report on August 2, 1995, about 33 months after receiving the error and accident report.

## CASE 5

Blood Establishment Error

On August 13, 1992, the blood establishment shipped six units of fresh frozen plasma to two consignees. On August 14, one consignee detected that the expiration date on the label was listed as September 10, 1993, instead of August 10, 1993. The consignee notified the blood establishment who immediately informed both consignees to return the six units.

Three units were returned on August 14, 1992, relabeled with the correct expiration date and reissued. The remaining three units were transfused on August 13, 1992, which is within the correct expiration date. The CBER staff stated that it is unlikely that use of or exposure to the recalled product could cause any adverse health consequences.

FDA Recall Classification Process

The DIS received the error and accident report on October 19, 1992, and forwarded it and the Alert document to DCM on November 4, 1992. On November 6, 1992, DCM sent the Alert document and the error and accident report to the FDA field office, instructing it to follow up during the next scheduled inspection of the blood establishment.

The field office conducted the inspection from March 11-25, 1994. According to the field office inspection report, the error and accident report was evaluated during the inspection. The field office, however, did not develop the recall recommendation and send it to DCM.

FDA Corrective Action

The FDA has taken corrective action. The field office developed the recall recommendation and submitted it to DCM for recall concurrence and classification on February 4, 1995. The FDA classified it as a Class III recall on May 12, 1995, and published the recall in the FDA Enforcement Report on June 21, 1995, about 33 months after receiving the error and accident report.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

# Memorandum

Date MAR - 5 1996

From Deputy Commissioner for Management and Systems (Acting)

Subject Food and Drug Administration's (FDA) Comments on the Office of Inspector General's (OIG) Draft Report, "Review of the FDA's Processing of 17 Error and Accident Reports Involving Blood"

To Deputy Inspector General for Audit Services

We reviewed the referenced draft report and prepared the attached comments.

The FDA's Center for Biological Evaluation and Research agrees with your report's recommendations and is beginning to implement them.

If your staff has any questions, please have them contact Jim Dillon on (301) 443-6392.

Robert J. Byrd

Attachment

# COMMENTS OF THE FOOD AND DRUG ADMINISTRATION (FDA) ON THE OFFICE OF INSPECTOR GENERAL (OIG) DRAFT REPORT, "REVIEW OF THE FOOD AND DRUG ADMINISTRATION'S PROCESSING OF 17 ERROR AND ACCIDENT REPORTS INVOLVING BLOOD," A-03-95-00350, JANUARY 23, 1996

## General Comments

We appreciate the opportunity to review and comment on the referenced OIG draft report.

The FDA's Center for Biologics Evaluation and Research (CBER) generally agrees with the OIG draft report's findings and recommendations and notes that steps have already been taken to carry out the recommendations.

We believe that the OIG recommendations should be directed to the Agency level instead of CBER since many functions related to the error and accident program are done by the Office of Regulatory Affairs (ORA).

## OIG Recommendation

We recommend that CBER improve its tracking system to ensure that all error and accident reports warranting further evaluation for blood recall classification are tracked until final resolution, such as a blood recall classification.

## FDA Comment

FDA concurs. CBER has instituted a tracking system for those Error and Accident (E&A) reports that are forwarded to ORA field offices for follow-up. This tracking system will assist both CBER and ORA in determining whether those E&A reports should be assessed for possible recall consideration. At this time, CBER coordinates this tracking system, but plans call for ORA headquarters and field offices to use the system as well.

We also note that in April 1995, CBER reorganized its Office of Compliance. The Division of Inspection and Surveillance was given responsibility for all recalls and error and accident reports. The change has eliminated the referral procedure mentioned in the draft OIG report.

As stated in our general comments, we believe the recommendation should be redirected to the Agency level to incorporate the other components involved in the E&A program.

OIG Recommendation

We recommend that CBER complete the recall classification and publication of the five error and accident reports identified in this report as not being processed in accordance with established procedures.

FDA Comment

FDA concurs. CBER reported that four of the five E&A reports identified as not being processed according to established procedures have been closed. CBER is following the remaining case so it can be closed as soon as possible.

As stated in our general comments, we believe the recommendation should be redirected to the Agency level to incorporate the other components involved in the E&A program.

Technical Comments

Cover Memorandum, second paragraph and Page 1, second paragraph

The report states that its objective was to determine if FDA took all the "required actions." It might be clearer to state that the objective was to determine if FDA followed its internal procedures.

Cover Memorandum, third paragraph, Page 3, second paragraph, Page 7, second paragraph, Page 10, paragraph accompanying caption, "Better Tracking System Could Have Detected Errors," and Page 11, recommendations

Where the report suggests actions, CBER should be replaced by FDA, since many of the functions related to the E & A program are performed by ORA components.

Page 1, third paragraph, first line

We note that the report defines a recall as an establishment's "voluntary" removal or correction. The definition as used is correct. Because there are also mandatory recalls (see 42 U.S.C. § 262 (d) (2)), an introductory phrase, such as "for purposes of this report," would be helpful.

Page 1, third paragraph, first sentence and Page 4, third paragraph, first sentence

To clarify the sentence, please add the phrase after the word, "FDA," "and for which FDA would initiate regulatory action."

We also note that this section as well as others in the report should be clarified to insure a reader understands that a recall is only classified as such when a product is violative, and would be subject to regulatory action. Other steps taken to remove products from commerce are considered "market withdrawals."

Page 2, "Summary of Findings," third paragraph, eighth line

Please insert the following "i.e., extended," after the word, "incorrect," to improve the accuracy of the sentence.

Page 3, "Background," first paragraph, third sentence

The word, "regulations," should be inserted into the sentence, "While FDA provides guidance....comply with regulations, industry standards, and safeguards..."

Page 3, "Background," second paragraph, third sentence

The entire sentence needs to be rewritten to clarify the items identified in an error and accident report. The rewritten sentence would be as follows with changes in italics:

"The error and accident report identifies *among other things* the blood establishment, the *unit*, the blood product, *the nature of the error or accident*, and the final disposition of the blood product."

Page 3, footnote

We would like to clarify the definition for a blood establishment. We suggest the following be used as preface to the text, "As used in this report, a blood establishment...." After the word, "establishment," in the second sentence, please add the following sentence, "FDA establishment licenses may cover multiple locations."

Please note many blood establishments have more than one general physical location. For example, the Red Cross is a licensed establishment with over 50 different blood centers throughout the United States.

Page 4, second paragraph, first sentence

We suggest that a note be inserted after the sentence indicating that the recall function was transferred to Division of Inspections and Surveillance (DIS), and the E &A reports are no longer sent to the Division of Case Management to be sent to the field.

Page 4, second paragraph, second sentence, item 2

Insert words, "and extended date," after the word, "date," to clarify the sentence.

Page 4, second paragraph, fourth sentence

Delete the last word of the sentence, "classification," and replace with word, "consideration."

Page 4, last paragraph, first sentence

We suggest the sentence be rewritten as the following: "According to FDA, compliance with regulations accounts for the relatively few errors and accidents which warrant a blood recall classification."

Page 5, "Objective, Scope, and Methodology," second paragraph, first sentence

We suggest that a footnote should be asterisked after the acronym, "DCM." The footnote would read, "CBER's Office of Compliance reorganization has eliminated the referral procedure. All recalls and E &A reports are processed in the Division of Inspections and Surveillance.

Page 5, second paragraph, second sentence, fourth bullet

Insert the word, "Agency," after the word, "and," to clarify the fact that another agency component publishes the FDA Enforcement Report.

Page 6, "Results of Review," first paragraph, last sentence

The last sentence should be revised to reflect the deletion of the term, "reverse notification." The revised sentence would read as follows, "Most of these resulted in a market withdrawal."

In addition, the footnote defining a "reverse notification" should be deleted. The reason for this revision is that the term, "reverse notification" is not a definition found in the Code of Federal Regulations and the reference used is not accurate from the standpoint of CBER's operating procedures.

Page 7, Paragraph accompanying caption, "Processing Blood Recall Classifications," second sentence

The phrase, "gathering information to be used in evaluating," should be inserted after the second time the word, "to," is used. The revised sentence would read as, "The follow-up review is to determine the adequacy of corrective actions taken by blood establishment, and to gather information to be used in evaluating the appropriateness of a blood recall classification."

Page 8, third paragraph, second sentence

We note that some of the documents that guide FDA recall policy that are referenced in the report (other than the Regulatory Procedures Manual) are not accurately identified. The terms used in the report, (for example, "General Guidance Document") are not generally recognized.

Page 10, first paragraph accompanying caption, "Better Tracking System Could Have Detected Errors, last sentence

To clarify the sentence, please insert phrase, "identified for recall consideration," after the word, "reports."

Page 10, second paragraph accompanying caption, "Better Tracking System Could Have Detected Errors, last sentence

To clarify the sentence, please replace the word, "undetected," with the word, "unclassified."

Page 10, "Conclusions and Recommendations, second paragraph, last sentence

To clarify the sentence, please replace the words, "classified correctly," with the words, "expeditiously processed."