Errors & accidents in manufacturing (3/20/91)

DATE : March 20, 1991

TO : All Registered Blood Establishments

SUBJECT: Responsibilities of Blood Establishments Related to Errors & Accidents in the Manufacture of Blood & Blood Components

FROM: Acting Director
Center for Biologics Evaluation & Research

During the past two years, there has been a significant increase in the number of product recalls initiated by blood establishments. A large percentage of these recalls were directly attributed to errors or accidents in manufacturing resulting in the release of unsuitable blood and blood components. Many of these errors or accidents were not reported to the Center for Biologics Evaluation and Research (CBER), and frequently reports were not submitted in a timely manner. For these reasons, we are reminding licensed blood establishments of the reporting requirement of 21 CFR 600.14 that CBER shall be notified promptly of errors or accidents in the manufacture of products that may affect the safety, purity, or potency of the biological product.

This memorandum also requests that unlicensed, registered blood establishments and transfusion services voluntarily report to CBER those errors or accidents in the manufacture of blood and blood components that may affect the quality of blood and blood components, i.e., units that are not suitable for transfusion or for further manufacturing use. In addition, this memorandum reminds blood collection and transfusion facilities of requirements in 21 CFR, Part 606 relating to investigations and recordkeeping associated with errors and accidents.

Examples of reportable errors or accidents in manufacturing which may affect product quality include, but are not limited to, the release of: (1) units repeatably reactive to viral marker testing; (2) units from donors for whom test results were improperly interpreted due to testing errors related to improper use of equipment or failure to strictly follow the reagent manufacturer's directions for use; (3) units from donors who are (or should have been) either temporarily or permanently deferred due to medical history or a history of repeatably reactive results to viral marker tests; 4) units prior to completion of all tests; (5) incorrectly labeled blood components [e.g., ABO, expiration date]; and (6) microbially contaminated blood components when the contamination is attributed to an error in manufacturing.

Blood collection or transfusion facilities may receive complaints and/or adverse reaction reports that include information relating

to cases of hepatitis or evidence of HIV infection associated with transfusion of blood or a blood component. Records of such reports must be maintained and investigations conducted as required by 21 CFR 606.160 and 606.170(a), and notification to CBER is required under 21 CFR 600.14 if the investigation reveals that the release of the implicated unit(s) was the result of an error or accident in manufacturing.

We request that all directors and appropriate personnel of blood collection and transfusion facilities promptly review procedures to determine that written standard operating procedures include provisions for recording errors and accidents as required by 21 CFR 606.160(b)(7)(iii). These standard operating procedures should supplement procedures which have been established to comply with the requirement of 21 CFR 606.100(c) that: (1) manufacturing (including testing) records must be reviewed before release or distribution of final products, (2) any unexplained discrepancy or failure to meet any product specifications shall be thoroughly investigated, and (3) follow-up actions and conclusions shall be recorded. The Food & Drug Administration (FDA) will continue to review and evaluate these procedures and related records during scheduled inspections.

Notification to CBER under 21 CFR 600.14 is necessary when the error or accident is associated with making a finished unit available for distribution whether or not actual shipment has occurred. If an error is detected during product manufacturing or processing and prior to the finished unit being made available for release, notification is not necessary. However, a thorough investigation and documentation of corrective action is required by 21 CFR 606.100(c) and 606.160. The notification requirement under 21 CFR 600.14 is separate from the requirement of 21 CFR 606.170(b) for reporting to CBER fatalities associated with blood collection or transfusion.

Product quality and labeling errors discovered in transfusion facilities and relating to blood and blood components received from outside sources should be referred to the manufacturer. The manufacturer of the unit should then notify CBER concerning these types of errors. However, errors in manufacture which occur in transfusion facilities, such as incorrect identification of samples used in compatibility testing, errors in compatibility testing which result in the wrong unit being released for transfusion, or issuing the wrong unit for transfusion, should be reported to CBER directly by the transfusion facility.

The release and distribution of unsuitable blood and blood components requires prompt action to identify all affected components and to advise all consignees as to the appropriate action for correction or disposition of the distributed product. Each situation relating to the distribution of unsuitable blood and blood components should be evaluated within the context of Title 21, Code of Federal Regulations, Part 7.40 - Recalls (Including Product Corrections) - Guidelines on Policy,

Procedures, and Industry Responsibilities. In the event that a field correction or product recall is initiated by a blood establishment, CBER and the local FDA district office should be advised.

Notification of errors or accidents pursuant to 21 CFR 600.14 should be forwarded to:

Food & Drug Administration
Center for Biologics Evaluation & Research
Division of Inspections & Surveillance (HFB-120)
8800 Rockville Pike
Bethesda, Maryland 20892

In order to facilitate the Food & Drug Administration's review and evaluation, the attached outline may be used as a guide for the type of information that should be reported.

Telephone contact with the CBER/Division of Inspections & Surveillance can be made at: (301) 295-8191.

Gerald V. Quinnan, Jr., M.D.