DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

April 14, 2003

CONSENT DECREE NOTIFICATION

Marsha Johnson Evans
President and Chief Executive Officer
American National Red Cross
430 17th Street, N.W.
Washington, D.C. 20006

Re: United States v. American National Red Cross, Civil Action No. 93 0949 (JGP)

Dear Ms. Evans:

A team of Food and Drug Administration (FDA) investigators inspected the American National Red Cross (ARC), Biomedical Headquarters (BHQ), located at 1616 Fort Myer Drive, Arlington, Virginia, from April 2002 through December 2002. During that inspection, the FDA investigators observed numerous deviations from FDA law, regulations, and the Consent Decree of Permanent Injunction (Decree) entered May 12, 1993. Pursuant to Paragraph VI.A. of the Decree, FDA is notifying ARC of its determination that ARC has violated the law. Corrective action by ARC is necessary. This is the thirteenth letter issued by FDA to ARC, pursuant to Paragraph VI.A. of the Decree. Numerous violative conditions cited in this letter have also been cited in other such letters issued by FDA to ARC.

At the conclusion of the inspection, the investigators issued a Form FDA 483, Inspectional Observations (FDA 483). The observations include, but are not limited to, the following:

HOTLINE RECORDS:

1. ARC failed to thoroughly investigate employee allegations of serious deviations from the law and to correct and prevent recurrences of such deviations. For example employees reported:

   a. that records were created to document work that was not actually performed;

   b. blood components were labeled with results of a test that was not actually performed;

   c. supervisors instructed records to be falsified;

   d. training records were falsified;

e. Blood Donation Records (BDR) were altered to allow acceptance of an unsuitable donor;

f. employees were reprimanded for deferring too many donors; and

g. inappropriate handling of donor adverse reactions, such as failure to discontinue phlebotomy of two donors who had "passed out."

In August 2000, ARC informed FDA that it had implemented an employee hotline program to "reinforce the ARC policy which requires all staff to report any potential violative activities, and to further ensure all staff understands their role in ensuring patient and donor safety and the need to follow legal requirements and ARC standards." ARC promised to thoroughly investigate each hotline report. However, ARC established no written procedures for correcting confirmed deviations from the law and ARC's procedures. The quality assurance /quality control unit was not informed of all reported problems to determine whether they bear on product quality and donor safety. ARC also failed to maintain an adequate record of each hotline report and the conclusion and follow up for each investigation.

[21 CFR 211.22, 21 CFR 211.198, Decree Paragraph III.B.1.; FDA 483 observations 1, 2, 3, 4, 5, 89, 90, 93, 94]

INADEQUATE INVESTIGATION OF SUSPECTED POST TRANSFUSION HEPATITIS CASES:

2. ARC failed to thoroughly investigate suspected transfusion transmitted disease cases, including one fatality. Additionally, ARC's procedures are inadequate in that they do not require a thorough investigation of reports of suspected transfusion transmitted diseases. For example,

a. In November 2001, a post transfusion fatality was reported to an ARC Blood Service Region (region). Viral marker test records and associated quality control records were not reviewed. Donors of the transfused blood products were not contacted for additional testing and health history verification. Additionally, ARC failed to determine the disposition of other blood components manufactured from the two suspected donations and failed to determine whether other recipients experienced post transfusion infections.

b. ARC's procedure for investigating suspected post-transfusion hepatitis (SPTHEP) cases limits investigation of such reports to only those cases involving transfusion of components from 10 or fewer donors, unless ARC is contacted by a local government health department or becomes involved in

litigation and receives approval by BHQ to perform the investigation. FDA investigators found that, during the period January 1, 2000 through June 30, 2002, 134 SPTHEP cases were reported to, but not investigated, by ARC.

[21 CFR 606.170(a), Decree Paragraph III.B.14; FDA 483 observations 6, 7, 8, 9]

INVENTORY MANAGEMENT:

3. ARC failed to establish procedures that include a system by which the distribution of each unit of blood or blood component can be readily determined to facilitate recall, if necessary, and to investigate and correct continuing inventory management deviations. For example,

a. During the period April 1, 2000 through August 12, 2002, ARC could not determine the final disposition of (lost)1062 blood products, including at least six products with positive viral marker tests.

b. ARC procedures fail to require regions to investigate and prevent recurrence of lost blood products unless their individual monthly rate of loss is equal to or greater than the upper control limit, established by ARC, or unless a region has a three consecutive month upward trend for rate of loss.

c. In November 1998, ARC was first notified by a region of the inability to fully track the disposition of plasma products. As recently as September 2, 2002, another region reported that 52 units of plasma could not be located for recall or market withdrawal. As of September 23, 2002, ARC had not fully corrected this problem.

d. ARC failed to investigate and correct continuing deviations that involve shipment of blood products physically, but not electronically. When ARC ships blood products physically, but not electronically, there is no record of distribution to facilitate recall, if necessary. During the period, July 1, 2001 through June 30, 2002, 233 such deviations were reported to BHQ by regions.

e. ARC failed to ensure that inventory management procedures are adequate and are being followed in each region. BHQ did not assess deviations associated with inventory reconciliation of quarantine locations until this inspection.

f. ARC failed to establish an adequate procedure to control storage of frozen red blood cells. For example, results of an April 2001 BHQ audit of a region revealed problems with controlling storage and quarantine of frozen red blood cells. ARC has not implemented a system to maintain control of inventory of its rare frozen red blood cells.

[21 CFR 606.165, 21 CFR 211.22, Decree Paragraphs III.B.1., III.B.12., III.B.13.; FDA 483 observations 10, 13, 14, 15, 17, 19, 25, 26, 27, 28, 30]

4. ARC failed to establish an adequate procedure to prevent reissue of unsuitable blood products that have been returned, recalled, or market withdrawn. FDA observed that between November 2000 and April 2002, ARC reissued 16 unsuitable products.

[21 CFR 606.100(b), 21 CFR 606.100(b)(12), 21 CFR 211.204, 21 CFR 211.22, Decree Paragraphs III.B.1., X.; FDA observation 20]

5. ARC failed to correct and prevent deviations that resulted in release and/or distribution of unsuitable blood products. For example,

a. Between January 2001 and June 2002, ARC identified 1850 blood products that were unsuitable due to blood collection quality control errors.

b. In January 2002, ARC documented a systemic problem related to release and/or distribution of blood products that had been identified by ARC as unsuitable during review of quality control records, during review of BDRs, during review by regional Material Review Boards, or through post donation information received from donors. ARC records state that its corrective action for this systemic problem would be considered effective if, based on data collected six months post-implementation, release of unsuitable blood products was decreased by only 50%.

c. Biological Product Deviation Reports for the period December 20, 2001 through June 1, 2002 show continuing deviations involving distribution of unsuitable blood products collected from donors who were not eligible to donate. For example,

i. Blood products collected from approximately 58 donors were collected and distributed, although the donors reported to ARC's health historians that they had traveled in malarial areas.

ii. Blood products from 16 donors were collected and distributed, although the donors reported to ARC's health historians that they were taking medication that caused them to be ineligible to donate blood for transfusion.

iii. Blood products from 48 donors were collected and distributed, although the donors reported to ARC's health historians information that caused them to be ineligible to donate blood for transfusion, such as a history of hepatitis and residence in certain European countries.

[21 CFR 211.22, 21 CFR 211.100(b), 21 CFR 640.3(a), Decree Paragraphs III.B.1., X.; FDA 483 observations 21, 22, 23, 24]

FDA first notified ARC of similar deviations pertaining to inventory management in the October 20, 1999 VI.A. letter issued following the inspection of ARC's Southern Region. Additionally, FDA investigators observed these same types of inventory management deviations during the February-April 2000 inspection of BHQ. More recently, inventory management deviations were brought to ARC's attention in the October 19, 2001 VI.A. letter FDA issued following the inspection of ARC's Salt Lake City facility and in the July 31, 2002 VI.A. letter FDA issued following the inspection of the ARC's Greater Chesapeake and Potomac Region.

LABELING:

6. ARC failed to establish and implement procedures to ensure that blood products are labeled correctly. ARC also failed to investigate and correct deviations involving mislabeled blood products. For example,

a. Between April and July 2001, regions reported 29 deviations relating to release of blood products labeled with incorrect CMV test results. BHQ did not assess those deviations and implemented no corrective action.

b. On June 12, 2002, a region incorrectly labeled and subsequently distributed three blood products as CMV negative.

c. On July 9, 2002, another region incorrectly labeled and subsequently distributed one blood product as CMV negative.

[21 CFR 211.22, 21 CFR 211.130, 21 CFR 606.122(h), Decree Paragraphs III.B.1.,X.; FDA observations 31, 32, 37, 38]

7. ARC failed to establish and implement adequate labeling procedures, including safeguards to prevent labeling mix-ups and to correct deviations, such as discrepant blood types caused by test tube mix-ups, different BDRs associated with the same whole blood number, and different whole blood numbers on primary and satellite bags.

[21 CFR 211.22, 21 CFR 606.100(b)(16), 21 CFR 606.120(b)(3), 21 CFR 606.160(c), Consent Decree Paragraph III.B.1; FDA 483 observations 95, 96, 101, 102]

FDA investigators observed similar deficiencies, involving CMV labeling and labeling mix-ups, during the February-April 2000 inspection of BHQ.

NATIONAL DONOR DEFERRAL REGISTRY and DONOR FILE CHECK:

8. ARC failed to establish and implement an adequate procedure to ensure maintenance of a record from which unsuitable donors may be identified so that products from such donors will not be distributed. For example,

a. Two National Biomedical Computer System (NBCS) queries run in May 2000 found more than 3,000 unsuitable donors who were not included in the National Donor Deferral Registry (NDDR). A query run in March 2001 found 39 donors who had not been screened against the NDDR.

b. On February 27, 2001, BHQ failed to enter three deferred donors into the March 2001 Donor Deferral Registry (DDR) cycle, resulting in those donors not appearing in the NDDR until April 2001.

c. On May 3, 2001, BHQ failed to compare the NDDR and each regional copy of the NDDR, in accordance with ARC's procedures, resulting in 30 discrepant records in the March 2001 DDR cycle.

d. ARC's procedure failed to describe the complete donor file check process that must be performed by regions in order to identify any donations accepted from donors who should have been deferred, but whose names had not been properly placed in the NDDR.

e. ARC procedures fail to include a time frame for completion of donor file check processes, resulting in delay of recall of unsuitable blood products. BHQ allowed the regions up to one year to complete donor file check for two

lists of donors. The results of that donor file check included three donors who were not properly placed in the NDDR and who had donated after having been determined to be unsuitable.

f. Effective March 28, 2002, ARC procedures state that certain categories of donors may be omitted from the monthly donor file check process. Those categories include donors who are at high risk for HIV, hepatitis, and CJD.

[21 CFR 606.100(b), 21 CFR 606.160(e), 21 CFR 211.22, Decree Paragraphs III.B.1., III.B.12., III.B.13.e.; FDA 483 observations 40, 42, 43, 44, 48, 49, 50, 51, 53]

FDA investigators also noted similar deficiencies relating to the NDDR and donor file check process during the February-April 2000 inspection of BHQ.

AUTOASSERTION [redacted] SYPHILIS & OTHER COMPUTER SOFTWARE DEFICIENCIES:

9. ARC failed to maintain a record of unsuitable donors so that products from such individuals will not be distributed. For example,

a. On January 31, 2002, a NBCS query determined that 11 donations did not have the correct [redacted] deferral code for syphilis.

b. NBCS queries run on July 26, 2001 and in February 2002 determined that approximately 1,500 donor records with positive test results for HIV did not have the appropriate deferral code.

c. An undated NBCS query identified 796 records without a deferral code for unacceptable health history.

[21 CFR 606.160(e), Decree Paragraphs III.B.1, III.B.12., III.B.13.e.; FDA 483 observations 58, 106, 107, 119]

10. ARC failed to maintain or review records of investigations of software problems. For example,

a. Records do not identify the individual who reviewed the results of a query run on NBCS records on July 26, 2001 to identify donor records without the appropriate deferral code for HIV positive test results.

b. Records do not identify the individual who reviewed the results of an NBCS query run on [redacted] records on August 3, 2001 to identify donors without an appropriate deferral code.

c. NBCS queries run to identify donor records without the appropriate deferral code for Nucleic Acid Test (NAT) positive test results were not maintained, and records did not document the identity of the individual reviewing the results.

[21 CFR 606.160(a)(1), 21 CFR 211.22, Decree Paragraph III.B.1; FDA 483 observations 106, 110, 115]

11. ARC failed to investigate computer software deficiencies or to implement effective corrective action. For example,

a. Although a query identified approximately 1500 donor records without the appropriate deferral code for NAT positive test results, there is no record of investigation of the donor records, including deferral or identification of subsequent donations that may have been unsuitable.

b. ARC did not investigate to determine why [redacted] software was released for use by the regions without the correct assertion table.

[21 CFR 211.22, Decree Paragraph III.B.1.; FDA 483 observations 106, 113, 117]

12. ARC failed to maintain or follow procedures. For example,

a. ARC repeatedly failed to follow a work-around to resolve the problem of deferral code omissions, when the blood type was [redacted] (no type determined).

b. ARC failed to follow its own procedures requiring the resolution within specific time frames of donor records that have a deferral code, indicating incomplete, discrepant, or the absence of infectious disease marker test results.

[21 CFR 606.100 (b), 21 CFR 211.100(b), Decree Paragraph III.B.1.; FDA-483 observations 111, 113, 179]

FDA investigators observed deficiencies relating to the deferral code for syphilis during the February-April 2000 inspection of BHQ.

DONOR HOLD

13. ARC failed to adequately investigate and promptly correct a problem with releasing donors from a computer hold in the proper sequence during the registration data entry process which resulted in failure to screen each donor against the regional DDR or NDDR. For example,

a. Written procedures issued on June 15, 2000, as part of a corrective action, were not followed by all regions. FDA investigators discovered that employees were not consistently following the new procedure during inspections of two ARC regions conducted in January-March 2001.

b. A June 2001 query of NBCS performed to determine whether employees had released donor holds in the correct sequence revealed approximately 30 deviations from a third procedure issued in April 2001 as part of the corrective action. A July 2001 query of NBCS revealed 26 incidents of employee failure to follow the procedure.

c. In July 2001, ARC released a new NBCS software version to correct the donor hold sequence problem. However, on November 14, 2001, ARC modified another new software version and inadvertently caused the system to issue an erroneous message indicating no potential matches in NBCS for donors being screened against the NDDR, instead of flagging all donors who had potential matches in the NDDR. BHQ fixed the software problem in all regions on January 2, 2002, developed a query for all regions to detect donors who were NDDR matches, but failed to review the results of the queries until April 16, 2002.

[21 CFR 211.22, 21 CFR 606.160(e), Decree Paragraph III.B.1.; FDA 483 observations 61, 62, 63, 64, 65, 66, 67, 68]

FDA investigators noted similar deficiencies pertaining to the donor hold process during the February-April 2000 inspection of BHQ.

PICK PAN

14. ARC failed to implement adequate corrective action to ensure that correct donors are selected from a computer screen pick pan during the donor registration process. Selection of the wrong donor results in association of a whole blood number with the wrong donor record in NBCS, inability to trace blood products in the event of a recall or

lookback investigation, and inability to prevent release of blood products from a donor who has been previously determined to be unsuitable. For example,

a. Effective June 2000, ARC's implemented corrective action to prevent incorrect donor selection by data entry personnel. BHQ ended the monthly monitoring requirement in April 2002, although regional reports showed continuing deviations.

b. ARC failed to perform a retrospective review of donor records in NBCS to determine whether all donors were properly selected from the pick pan during the registration process.

[21 CFR 211.22, 21 CFR 606.160(b)(1)(vii), 21 CFR 606.160(c), 21 CFR 606.165(a), Decree Paragraphs III.B.1., III.B.12., III.B.13.e.; FDA 483 observations 72, 73]

FDA investigators observed similar deficiencies relating to the selection of the incorrect donor from the computer screen pick pan during donor registration, in the February-April 2000 inspection of BHQ.

DUPLICATE DONOR RECORDS

15. ARC failed to resolve all duplicate donor records, which can result in donations being associated with the wrong donor record and potential release of blood products collected from unsuitable donors. ARC also failed to report unresolved duplicate donor records to FDA. For example,

a. ARC performed a retrospective review of records and found that two regions had reported to FDA unresolved duplicate donor records in November 2000 and April 2001. BHQ failed to determine the reason for the deviations and to identify a preventive action.

b. In February 2002, ARC reported to FDA that one region had unresolved duplicate donor records. BHQ's investigation failed to determine whether any other regions had unresolved duplicate donor records.

[21 CFR 211.22, 21 CFR 606.160(e), Consent Decree Paragraphs III.B.8., III.B.9; FDA 483 observation 74]

FDA investigators observed similar deficiencies involving unresolved duplicate donor records during the February-April 2000 inspection of BHQ.

MISSING/INCORRECT INFORMATION ON BLOOD DONATION RECORDS

16. ARC failed to implement adequate corrective action to ensure that procedures for determining donor suitability during the donor screening process are followed. For example,

a. An audit conducted by ARC in November 2001 found 29 BDRs in one region that had missing or incomplete answers to health history questions. Forty-four blood components were recalled as a result of the deviations. The audit found that these 29 deviations were not discovered during ARC's required review process.

b. Biological Product Deviations reported to FDA for the period December 30, 2001 through June 1, 2002, show 35 instances of released blood products collected from donors who had not completed their BDRs. The errors were not discovered during ARC's required review process.

[21 CFR 211.22, 21 CFR 640.3(a), 21 CFR 211.100(b), Decree Paragraphs III.B.1., X.; FDA 483 observations 75, 76, 77]

FDA notified ARC of similar deficiencies in the October 19, 2001 VI.A. letter issued following the inspection of ARC's Salt Lake City facility, and in the July 31, 2002 VI.A. letter issued following the inspection of ARC's Greater Chesapeake and Potomac Region.

RED BLOOD CELL MANUFACTURING

17. ARC failed to ensure that leukoreduced red blood cells (RBC) were manufactured in accordance with its procedures and with blood bag manufacturer instructions, and failed to implement adequate corrective action after detecting RBC manufacturing deviations. For example,

a. ARC recalled over 5,000 RBC components after discovering in July 2001 that, since April 1998, regions were not manufacturing RBCs within eight hours of collection, when the components had been held at room temperature.

b. BHQ's corrective action plan required only a 90% reduction of deviations in RBC manufacturing. The corrective action plan also required an effectiveness check by June 2002, but BHQ failed to perform that check. Additionally, BHQ failed to determine whether manufacturing employees received adequate training in the procedures and blood bag manufacturer instructions applicable to RBC manufacturing.

c. BHQ identified an NBCS software modification to prevent such RBC manufacturing deviations in July 2001 and an NBCS software modification to detect RBCs created outside of time limits in January 2002. Neither modification has been included in an NBCS release.

[21 CFR 211.22, 21 CFR 211.100(b), 21 CFR 606.65(e), Decree Paragraph III.B.1.; FDA 483 observations 82, 85, 86, 87, 88]

RELEASE OF INCOMPLETE TEST RESULTS

18. ARC failed to thoroughly investigate and to adequately correct deviations related to electronic transfer of incomplete viral marker test results. For example, blood samples that had initial reactive results for hepatitis B surface antigen (HBsAg) were not retested in duplicate, as required. Although the tests were incomplete, ARC's software allowed negative test results for those samples to be transferred to customers for whom ARC performs viral marker testing. For example,

a. BHQ did not perform a review of all electronically transferred test results, did not document a rationale for failing to do so, and did not determine whether any unsuitable blood products were released as a result.

b. BHQ's corrective action included issuing written instructions for review of test results, when multiple National Testing Laboratories (hereafter, NTL) have responsibility for testing. However, those instructions were inadequate, in that critical parameters were omitted, such as specifying the NTL responsible for reviewing and releasing test results when more than one NTL performs testing.

c. Records of BHQ's investigation do not address the failure to follow ARC's change control procedure and the adequacy of that procedure.

[21 CFR 211.22, Decree Paragraph III.B.1.; FDA 483 observations 178, 179, 180]

TRAINING:

19. ARC failed to ensure that personnel responsible for the collection, processing, compatibility testing, storage, or distribution of blood or blood components have adequate training to assure competent performance of their assigned functions. For example,

a. ARC provided no training for individuals responsible for receiving, prioritizing, and evaluating hotline reports. Additionally, ARC provided no training for individuals responsible for directing hotline report investigations, evaluating those investigations, and evaluating the final resolution of hotline reports.

b. ARC has no formal training program to ensure that employees responsible for performing donor file checks have a thorough understanding of the procedures.

c. BHQ did not require employee training in a new donor hold procedure implemented as a corrective action for donor hold deviations. BHQ's investigation of the failure by personnel to follow that procedure did not determine whether employee training was adequate.

d. ARC failed to determine whether employees received adequate training in the procedures for manufacture of red blood cells and the blood bag manufacturer's instructions applicable to red blood cell manufacture.

[21 CFR 606.20(b), Decree Paragraph III.C.; FDA 483 observation 49, 62, 64, 65, 87, 92]

During the inspection of BHQ, FDA investigators had difficulty obtaining records. For example, ARC management stated that FDA's request for access to ARC's regional deviations relating to the donor file check process should not be covered during the inspection of BHQ. Additionally, FDA investigators requested access to hotline records in August 2002, but all records were not provided until November 2002. FDA is very concerned about the delayed access to these records, and therefore, reminds ARC that FDA has authority under 21 U.S.C. 374 to inspect ARC blood establishment facilities. Such inspections shall, according to the law, extend to all things therein, including records, files, and papers. Additionally, paragraph IX of the Decree states that ARC shall permit duly authorized FDA representatives to make inspections to evaluate ARC's compliance with the Decree as FDA deems necessary.

This list is not intended to be an all-inclusive list of deficiencies at your establishment.

Although this letter focuses on observations made during the April—December 2002 inspection of BHQ, FDA expects that all corrective actions taken in response to this letter will also be implemented at other ARC regions and facilities, as necessary. FDA expects

ARC to promptly take steps necessary to fully comply with the law, ARC's standard operating procedures, and the Decree.

Paragraph VI.B. of the Decree requires that ARC respond to this notification within ten business days. As with other correspondence submitted pursuant to the Decree, the response should be sent to Lee Bowers, District Director, Baltimore District Office, 6000 Metro Drive, Suite 101, Baltimore, Maryland 21215, with a copy to Jesse Goodman, M.D., Director, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852.

Sincerely,

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for Regulatory Affairs

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