DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
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September 13, 2013

ADVERSE DETERMINATION LETTER

BY ELECTRONIC & CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. J. Chris Hrouda
Executive Vice President
Biomedical Services
American National Red Cross
2025 E Street, N.W.
Washington, D.C. 20006

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

Dear Mr. Hrouda:

From February 4 through March 1, 2013, United States Food and Drug Administration (FDA) investigators inspected American National Red Cross (ARC) Blood Services, Donor Management Center (Tulsa DMC facility), 2448 East 81st Street, Suite 2700, Tulsa, Oklahoma, and observed significant violations of the law, regulations, and the Amended Consent Decree of Permanent Injunction (Decree), entered on April 15, 2003[1]. At the conclusion of the inspection, the investigators issued a Form FDA 483, Inspectional Observations (FDA 483) on March 1, 2013, and an amended FDA 483 on March 28, 2013. The amended FDA 483 is attached (Attachment A). FDA is now, pursuant to Paragraph VIII of the Decree, notifying ARC of its determination that ARC has violated the Federal Food, Drug, and Cosmetic Act (the Act), FDA regulations, and the Decree, specifically Section 501(a)(2)(B) of the Act [21 U.S.C. § 351(a)(2)(B)], Title 21, Code of Federal Regulations (CFR) § 606, and Paragraphs IV.A and IV.B of the Decree. The violations include, but are not limited to, the following:

[1] FDA conducted the inspection of the Tulsa DMC facility in conjunction with inspections of three other ARC facilities where related objectionable conditions were also observed, specifically ARC's Heart of America Region, 405 W. John H. Gwynn Jr. Avenue, Peoria, IL 61005 [7/10/2012 – 8/10/2012]; Southern California Region, 100 Red Cross Circle, Pomona, CA 91768 [7/10/2012 – 8/22/2012]; and the Donor and Client Support Center, 417 North Eighth Street, Philadelphia, PA 19123-3508 [9/5/2012 – 10/26/2012]. Copies of the FDA 483s issued at the conclusion of those inspections are included as Attachments B, C, and D, respectively.

GMP VIOLATIONS

Duplicate Donor Records[2]

1. Failure to have records available from which unsuitable donors may be identified so that products from such individuals will not be distributed **[21 CFR § 606.160(e)]**, and failure to maintain records that relate the donor with the unit number of each previous donation from that donor **[21 CFR § 606.160(b)(1)(vii)]**.

   Specifically, in preparation for the merger of ARC's National Donor Deferral Register (NDDR) and ARC's 36 regional National Biomedical Computer System (NBCS) databases into one national database known as eProgesa/BioArch Release 2.0 (hereafter, referred to as eProgesa)[3], ARC established three projects known as DMC 1, DMC 2, and DMC 3. The DMC 1 project was established in April 2006 primarily to resolve potential duplicate donor records without deferral assertions[4]; it was not established to resolve higher risk inter-regional duplicate donor records with deferral assertions recorded in a regional NBCS database or the NDDR[5]. The DMC 2 project, which was established in March 2010, was designed to resolve such records and to manage potentially unsuitable blood products, as appropriate. The DMC 3 project, which was established in July 2012, was designed to work concurrently with the DMC 2 project to resolve duplicate donor records other than those with inter-regional deferral assertions and refer those with assertions to the DMC 2. ARC delayed identification, investigation, and/or resolution of the potential duplicate donor records that presented the most risk of distribution of unsuitable blood products, specifically those involving donors who were indefinitely deferred in one of the regional NBCS databases and those involving donors who are permanently deferred in the NDDR. **[FDA 483 Observations 1 and 2.B]** For example,

   a. ARC paused the BioArch project from April 2008 through March 2010 to re-evaluate the implementation of eProgesa. During these two years, the DMC project did not investigate the thousands of already identified inter-regional duplicate donor records with known deferral assertions. Because duplicate donor records with deferral assertions present a potential for the release of unsuitable blood products, it is imperative that such records be promptly investigated and resolved. Each day these

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[2] Decree paragraph III.B.33 defines duplicate donor records as "multiple donor records for the same donor which, because of inconsistent or duplicated information, may result in release for distribution of *unsuitable blood components*."

[3] BioArch is a project which ARC is implementing in three stages: (1) BioArch Release 1 (R1), which upgraded the collections software solution and replaced collections equipment in the field; (2) BioArch Release 2 (R2), which replaced the NDDR and the regional NBCS databases with eProgesa; and (3) (b) (4) which has not been released.

[4] A deferral assertion is a code applied to a donor's record in ARC's computer system to ensure that the donor is identified as ineligible to donate blood products. Although ARC uses different terms to categorize deferrals such as indefinite and permanent, all deferrals entered into the NDDR are considered permanent.

[5] Inter-regional duplicate donor records are created when a donor donates in more than one region and has donation records in each of those regions. The NDDR contains records for all donors with specific categories of deferral assertions, such as Class X and surveillance class S assertion 99. In contrast, many other categories of donors who are deferred are only added to the NBCS database in the region where they are deemed ineligible to donate blood products. Whereas donor records with deferral assertions in the NDDR can be identified as deferred by all regions and thus distribution of unsuitable blood products from such donors can be prevented in the event of an inter-regional duplicate donor record, donors with a deferral in one of ARC's 36 regional NBCS databases are not included in the NDDR and cannot be identified by other regions as ineligible to donate blood products in the event of a duplicate donor record.

records are not resolved, the likelihood that unsuitable blood products being released for distribution increases.

b. ARC did not conduct the DMC projects in such a manner that placed a priority on identifying potentially unsuitable donors who were deferred in one region but subsequently donated in other regions. For instance, although ARC had the data needed to identify inter-regional duplicate donor records with NDDR Class X deferral assertions since April 2006, it did not design queries to identify such records and/or assign those cases to DMC 2 until November 2012, thereby significantly delaying the identification and investigation of unsuitable donors and the appropriate management of any unsuitable blood products. Instead, ARC prioritized DMC tasks on the basis of its internal implementation plans for eProgesa.

DECREE VIOLATIONS

Managerial Control and Duplicate Donor Records

2. Failure to comply with Decree paragraph IV.A which requires ARC to "take steps necessary to ensure continuous compliance with this Order, *the law*, and *ARC SOPs*, including but not limited to *BSDs*, *BSLs*, local operating procedures, and any other written instructions used by *ARC* in connection with the collection, manufacture, processing, packing, holding, or distribution of *blood* and *blood components*"; and failure to comply with Decree paragraph IV.B.6.b which requires that within 30 days of learning that a region failed to adequately investigate and completely correct duplicate donor records, ARC shall, "either (i) ensure that all such inadequately investigated or uncorrected records for the *region* have been reviewed and corrected, that all applicable *ARC SOPs* have been complied with, that all *unsuitable blood or blood components* have been identified and quarantined or retrieved…; or (ii) if such actions cannot be completed within the 30 *day* period, submit to FDA a written explanation for failure to meet that time-frame and implement a plan that establishes specific time-frames to complete each of the foregoing steps."

   Specifically, in a June 20, 2008[6] letter to FDA, ARC stated that "[u]pon discovery of a donation from a donor who was deferred at one region and subsequently donated at another region, the donor has been entered into the National Donor Deferral Registry until donation eligibility has been clarified." However, FDA's review of ARC records found that the DMC projects had not and still does not follow this procedure. **[FDA 483 Observations 2.A and 5]** For example:

   a. During the DMC 1 project, ARC identified thousands of inter-regional duplicate donor records with deferral assertions, but did not place those donors into the NDDR pending investigation of their suitability to donate blood products. It was not until the DMC 2 project began in March 2010 that ARC actively began investigating those cases.

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[6] In its June 20, 2008 letter, ARC responded to concerns raised by FDA during a May 24, 2007, meeting between FDA and ARC pertaining to ARC's project to merge donor information in preparation for the implementation of the eProgesa computer system.

b. DMC 2 does not apply NDDR Class X deferral assertions to inter-regional duplicate donor records with deferral assertions in one region at the time they are identified, so that such donors will be recognized as ineligible to donate by other regions pending investigation of their suitability. Instead, DMC 2 applies the NDDR Class X deferral assertion only after the inter-regional duplicate donor records have been investigated and determined to be true duplicate records. Because the investigation process may take several months, ARC's failure to apply the NDDR Class X deferral assertion at the time the donor is identified may result in the distribution of unsuitable blood products if the donor is later confirmed to have true duplicate records with indefinite deferral assertions.

This list is not intended to be an all-inclusive list of deficiencies at your facilities. FDA has reviewed ARC's March 22, 2013, April 30, 2013, and June 28, 2013, responses to the Tulsa DMC FDA 483 and will verify promised corrective actions and evaluate their effectiveness during future inspections of ARC facilities.

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ORDERS

Paragraph VIII of the Decree provides that "[i]n the event that FDA determines, based upon inspection...review of *ARC* records, or other information that comes to FDA's attention...that *ARC* is not following any *SOP* that may affect donor safety or the *purity* or labeling of *blood* or any *blood component*...; has violated *the law*; has failed to fully comply with any time frame, term, or provision of this Order...; then FDA may order *ARC* to come into compliance with *the law, ARC SOPs*, or this Order, assess penalties, and/or take any step that FDA deems necessary to bring *ARC* into compliance with *the law, ARC SOPs*, or this Order."

For the reasons stated above, FDA has determined that ARC did not comply with the law, ARC's SOPs, and the Decree. Therefore, FDA orders ARC to take the following actions:

1. Within 30 days of receipt of this letter and thereafter on a monthly basis, report to FDA, in writing, the status of ARC's progress towards investigating all inter-regional duplicate donor records. Such monthly reports shall continue until such time as FDA notifies ARC that the reports are no longer required. Each report should include the following:

    a. The number of cases that have been resolved between March 1, 2013 and the date of ARC's initial report under this Order. For all reports after the initial report, the report should include the number of cases resolved since the prior report, specifically identifying the number of cases involving inter-regional duplicate donor records with assertions;

    b. The number of cases pending and the number of cases in-process, specifically identifying for each the number of cases involving inter-regional duplicate donor records with assertions;

c. The number of unsuitable blood products that were retrieved from subsequent donations each month;

2. Within 30 days of receipt of this letter, provide FDA ARC's written schedule for identifying and updating the population of inter-regional duplicate donors that require investigation by the DMC project.

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For the reasons stated above, FDA has determined that ARC did not comply with the law, ARC SOPs, and the Decree. Although FDA regards the violations discussed in this letter to be significant and could have assessed penalties as in previous Adverse Determination Letters issued to the ARC under paragraph IX of the Decree, we are notifying you of the violations that we found so that you can take appropriate action to address them and comply with the orders set forth above. If FDA determines that ARC is not complying with the above stated orders, FDA will reevaluate assessing penalties or consider an alternate or additional regulatory measure.

As provided in Paragraph IX of the Decree, if ARC agrees with this adverse determination, it must within 20 days of receipt of this letter, notify FDA of its agreement. If ARC disagrees with FDA's adverse determination, it must respond in writing within 20 days of receipt of this letter, explaining its reasons for disagreeing with FDA's determination. Your response must be submitted to me at the Food and Drug Administration, Baltimore District Office, 6000 Metro Drive, Suite 101, Baltimore, Maryland 21215, with a copy to Karen Midthun, M.D., Director, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200N, Rockville, Maryland 20852.

Sincerely yours,

Evelyn Bonnin
Director, Baltimore District

Enclosures

cc: Gail McGovern
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