DEPARTMENT OF HEALTH AND HUMAN SERVICES

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January 13, 2012

ADVERSE DETERMINATION LETTER

BY FACSIMILE AND 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 April through October 2010, United States Food and Drug Administration (FDA) investigators inspected sixteen American National Red Cross (ARC) Blood Services facilities and observed significant violations of the law, regulations, and the Amended Consent Decree of Permanent Injunction, entered on April 15, 2003 (Decree). At the conclusion of each inspection, the investigators issued Forms FDA 483, Inspectional Observations (FDA 483), attached hereto (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, FDA regulations, and the Decree, specifically 21 U.S.C. § 351(a)(2)(B), paragraphs IV.A., IV.B.1, IV.B.10, and XIX of the Decree and Title 21, CFR § 210- 211 and § 600-680.

The 2010 inspections cited herein were conducted at the following ARC facilities on the following dates:

Badger Hawkeye Region, 4860 Sheboygan Avenue, Madison, WI, 4/5-23/10
Great Lakes Region, 1800 East Grand River Avenue, Lansing, MI, 4/5-27/10
Penn Jersey Region, 700 Spring Garden Street, Philadelphia, PA, 5/24/10 - 6/4/10
Connecticut Region, 209 Farmington Avenue, Farmington, CT, 5/4/10 - 6/15/10
Detroit National Testing Laboratory, 100 Eliot Street, Detroit, MI, 5/25/10 - 6/16/10
Indiana-Ohio Region, 1212 East California Road, Ft. Wayne, IN, 7/12-21/10
Southwest Region, 10151 East 11th Street, Tulsa, OK, 7/26/10 - 8/9/10
Appalachian Region, 352 Church Avenue, SW, Roanoke, VA, 8/3-13/10
Heart of America Region, 405 West John H. Gwynn Jr. Avenue, Peoria, IL, 6/21/10 - 8/18/10

Northern California Region, Fixed Collections/Distribution Site, 2731 North First Street, San Jose, CA, 9/7-13/10
Arizona Region, Broadway Fixed Collection Site, 7139 East Broadway Blvd., Tucson, AZ, 9/7-15/10
Northern Ohio Region, 3747 Euclid Avenue, Cleveland, OH, 8/27/10 - 9/23/10
Southern California Region, 100 Red Cross Circle, Pomona, CA, 8/9/10 - 9/24/10
Greater Alleghenies Region, 250 Jari Drive, Johnstown, PA, 9/7-24/10
Southeastern Michigan Region, 100 Mack Avenue, Detroit, MI, 8/24/10 - 9/27/10
Donor and Client Support Center, 700 Spring Garden Street, Philadelphia, PA, 9/2/10 - 10/29/10

The Decree requires ARC to establish and properly implement appropriate quality assurance (QA) and quality control (QC) measures. Proper QA and QC programs by blood establishments include measures to prevent, detect, investigate, evaluate, and correct errors. The goals of these programs include preventing the distribution of unsuitable blood products, and preventing the causes of recurrent problems. The proper implementation of a strong QA program is essential to ensure the safety of the nation's blood supply.

Decree paragraph IV requires ARC to "establish, implement, and continuously maintain adequate methods, facilities, systems, and controls to ensure that *ARC* does not collect, manufacture, process, pack, hold, or distribute any article of drug as defined in 21 U.S.C. § 321(g), including any article of *blood*, *blood component*, or other biological product as defined in 42 U.S.C. § 262, that is adulterated, within the meaning of 21 U.S.C. § 351(a)(2)(B); misbranded, within the meaning of 21 U.S.C. § 352(a) or 42 U.S.C. § 262(b); or otherwise in violation of the *FD&C Act*, the *PHS Act*, and regulations promulgated thereunder, including, but not limited to, 21 C.F.R. Parts 210-211 and Parts 600-680." ARC is also required to "take steps necessary to ensure continuous compliance with this Order, *the law*, and *ARC SOPs*..." and "establish, document, and continuously maintain managerial control over training and quality assurance in all *regions* and *laboratories*." Decree paragraph IV.A.1. & 2. ARC is also required to appoint a director of quality assurance who shall "prepare and submit quarterly quality assurance reports in writing to *ARC senior management* and *ARC Biomedical Services senior management*...that completely and accurately: (i) describe the steps that have been and will be taken, with specific dates for implementation of each step, to establish, implement, and continuously maintain the *QA/QC program*; and (ii) describe all unresolved *potential system (systemic) problems, system (systemic) problems*, and *trends* and their corrective action status; and (iii) assess whether ARC is in compliance with *the law*, *ARC SOPs*, and this Order." Decree paragraph IV.A.2.[1]

Violations observed and/or documented during the 2010 inspections include the items listed below. This is not intended to be an all-inclusive list of violations in ARC facilities.

## ***DECREE VIOLATIONS:***

### ***Decree Violations*: Inadequate Managerial Control**

1. Failure to establish, implement and continuously maintain managerial control over QA in all regions and laboratories as required by paragraph IV.A.2. The development of written procedures and processes that are appropriately managed and implemented are essential components of an effective QA

[1] Decree paragraph III.B.57 defines the QA/QC program as the "written *SOPs* for quality assurance and quality control that *ARC* must establish, implement, and continuously maintain under paragraph IV of this Order to ensure that *blood* and *blood components* are collected, manufactured, processed, packed, held, and distributed by *ARC* in accordance with the *law*, *ARC SOPs*, and this Order, and have the *purity* that they purport or are represented to possess." (The italics in the quotations from the Decree are in the original and indicate that the italicized word is defined in paragraph III of the Decree.)

program. ARC management, however, merged certain QA functions into centralized facilities without ensuring that the new facilities were adequately staffed to perform these functions in a timely or effective manner.

Beginning May 2008, ARC began to consolidate certain donor management activities,[2] which were previously performed in 35 of its 36 regional offices, into the Donor Client Support Center (DCSC). The DCSC is located in two facilities, one in Charlotte, North Carolina, and one in Philadelphia, Pennsylvania. The consolidation began in May 2008 and was completed in March 2010. During the consolidation, multiple internal audits and Problem Management (PM)/QA assessments were performed at the two DCSC facilities.[3] The results of the internal audits and assessments and the subsequent internal investigations indicated that the DCSC was chronically understaffed and lacked the process controls to ensure timely and adequate performance of the donor management functions. In response to the internal audits, the DCSC repeatedly promised corrective actions, some of which had not been completed or were ineffective at the time of the FDA inspection in September and October 2010.

During the consolidation phase, ARC had periodic senior management meetings, Quality and Compliance Oversight Committee (QCOC) meetings, and Board of Governors meetings in which the DCSC consolidation project was discussed.[4] Quarterly and annual QA and training reports were also submitted to ARC's senior management.[5] The meeting minutes indicate that ARC management was aware of the audit findings and the staffing and training deficiencies and that the QCOC was monitoring the situation to determine whether the consolidation should continue as scheduled. Despite the repeated, significant internal audit findings, the consolidation was permitted to continue with only one delay. After the consolidation was completed in March 2010, the meeting minutes indicate that ARC management continued to have concerns about the DCSC performance. The DCSC continued to be understaffed and had a backlog of what ARC reported as being approximately 18,000 donor management cases[6] that had not been process-verified as required in Work Instruction 11.3.028, *Process Verification*, Version 1.1, and Form15.4.frm015, *Donor Reaction and Injury Record*, Version 1.2.

Additional internal records that detail the DCSC's management control deficiencies include the following:

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[2] Activities being performed at the DCSC include donor care and qualification functions, such as answering eligibility questions from the donors; donor deferrals; post donation and call back activities, donor complications and complaints; receipt of test results and entry of the results into the NBCS software; management of follow up testing with the donor; donor reentry/reinstatement; deferral and surveillance management; managing donor requests for test results and blood types; donor notification of reactive test results and donor counseling; and military, state, and health department notifications. DCSC also performs client support services that include the management of blood product retrievals; consignee notification for the release of unsuitable blood components; case investigations for possible transfusion transmitted infections, adverse reactions and bacterial contaminations; lookbacks; and serving as the liaison for regional/divisional medical directors. DCSC's data management functions include the management of the National Donor Deferral Registry and the Donor File Check process. Problem management tasks for the Philadelphia DCSC are performed in Philadelphia as well as in the Charlotte DCSC and includes the detection, investigation, evaluation, correction, and monitoring of all problems, trends, and system problems.

[3] Facility Audits: 10/14-17/08 (Philadelphia), 10/14-16/08 (Charlotte), 3/24-27/09 (Charlotte), 6/2-5/09 (Philadelphia), 12/15/09-1/6/10 (Philadelphia), 10/6-22/09 (Charlotte), 4/20-22/10 (Charlotte), 5/18-21/10 (Charlotte); Problem Management Assessment 4/9/10; Quality Assurance Assessment 4/10.

[4] Management Review Minutes for Collections and Donor Management: 2/10/09, 5/15/09, 8/7/09, 12/8/09, 3/19/10, and 6/8/10; QCOC Meetings: 6/27/08, 5/19/09, 8/27/09, 9/24/09, 10/9/09, 10/22/09, 11/13/09, 12/11/09, 2/25/10, 3/24/10, 4/9/10, 4/22/10, 6/11/10, 6/24/10 and 8/13/10; Board of Governors' Meetings: 4/23/08, 6/6/08, 3/26/09, 5/27/09, 6/18/09, 7/22/09, 8/27/09, 9/23/09, 10/5/10, 12/14/09, 1/27/10, 2/24/10, 3/24/10, 4/20/10, 6/9/10 and 8/25/10

[5] Quarterly QA Reports: April/June 2008, 2008 Annual QA Report October 2007/September 2008, October/December 2008, January/March 2009, April/June 2009, 2009 Annual QA Report October 2008/September 2009, October/December 2009 and January/March 2010; Quarterly Training Reports: April/June 2008, July/September 2008, October/December 2008, January/March 2009, April/June 2009, July/September 2009, October/December 2009 and January/March 2010.

[6] At the time of FDA's inspection of the DCSC, FDA determined that the backlog of donor management cases requiring process review was approximately 15,000 (11,531 in the Charlotte facility and 3,552 in the Philadelphia facility) and approximately 5,200 unreviewed DRIRs (4,949 in the Charlotte facility and 306 in the Philadelphia facility).

a. Two DCSC staffing documents (July and September 2009) state that "the organization is currently operating under the façade that the DCSC is self supportive in its QA and PM functions…Regions routinely provide support in problem closure and quality process review, both of which are major functions…over 50% of all problems are closed by non-DCSC QA staff located in the regions….any time something occurs in the field that strains the regional resources, assistance has to be withdrawn…this can immediately cause the DCSC to become unsustainable and fall into a backlog…another large concern is that every five weeks additional regions continue to transfer to the DCSC. Therefore, the situation is escalating to a point where the field will not be able to support the volume." Despite these staffing concerns, ARC management allowed the consolidation to continue.

b. In April 2010, the Biomedical Headquarters (BHQ)/QCOC meeting minutes indicate that the DCSC had a backlog of approximately 18,000 donor management cases that had not been process-verified as required by ARC's Work Instruction 11.3.028, *Process Verification*, Version 1.1.

c. ARC's report from the April 2010 DCSC problem management audit states that the root cause of the repeat observation pertaining to timely problem management is, "The DCSC Problem Management Department does not have the resources to consistently manage problems in a timely manner."

d. The May 2010 Donor Client Service Specialist (DCSS) staffing report indicates that "without additional staff dedicated to answering eligibility calls, the DCSS position would be understaffed. This understaffing could create a situation of a continually growing backlog, overtime pay required, and a decreased ability to handle natural spikes in incoming work."

e. In July 2010, ARC senior management placed the DCSC on a Compliance Improvement Strategy (CIS) because it was determined to be a "high compliance risk" based on internal audits and FDA 483s received since March 2009. The CIS was not finalized until 9/29/10, after FDA began the Philadelphia DCSC inspection. The final CIS states, "Numbers and proficiency of staff are not adequate to effectively execute assigned tasks and responsibilities in a compliant manner; inadequate supervision and oversight." The CIS further states, "The Back-log Plan will provide the details of how any back-log will be managed and monitored, including defined commitments for reducing the back-log while appropriately managing new cases."

In its 12/15/10 response to the FDA 483, ARC stated, "BHQ did not effectively manage consolidation of the donor management functions into the DCSC. BHQ managed the donor management consolidation using existing mechanisms, including the system Quality and Compliance Oversight Committee (QCOC) and the Field Operations Group (FOG), to provide oversight. However, in retrospect, these mechanisms proved to be inadequate…." The response also states that ARC "now recognizes that the DCSC management reports were insufficient in determining a complete and accurate picture of DCSC performance."

***Decree Violations*: Inadequate QA**

2. Failure to comply with paragraph IV.A.2.a., which requires that the "director of quality assurance shall be responsible for all ARC Biomedical Services quality assurance functions including, but not limited to, ensuring the establishment, implementation, and continuous maintenance of comprehensive *QA/QC programs*…." Specifically, the BHQ and DCSC QA programs were not

adequate to ensure that all regulated donor management operations were being performed effectively at the Philadelphia DCSC. Proper management oversight is essential to effectively implement a QA program; without it, the causes of errors may not be promptly corrected and unsuitable blood products may be released. For example,

a. At the beginning of the September – October 2010 inspection, the DCSC had a backlog of open cases that had not received the required review. Donor Status Change Records, Component Status Change Records, and Component Information Forms are required to have process verification prior to closure of a case per ARC's Work Instruction 11.3.028, *Process Verification*, Version 1.1. A backlog of 3,552 cases, dating as far back as July 2009, existed at the Philadelphia DCSC facility. Additionally, Donor Reaction/Injury Records (DRIRs) require a Medical Director (MD) review and a final quality review. A backlog of 306 open DRIRs, dating as far back as August 2009, existed at the Philadelphia DCSC facility. The backlogs were even larger at the Charlotte DCSC facility -- 11,531 DRIRs requiring process verification and 4,949 DRIRs requiring MD review and/or final quality review.

b. Quality Process Reviews have not been consistently performed by the DCSC QA staff since the Philadelphia DCSC was created in 2008. Quality Process Reviews are required in Directive 02.2.012, *Quality Process Reviews*, Version 2.1, and are to be conducted by the QA staff on an ongoing basis to review the systems and processes being performed by the DCSC operations staff. In addition, these reviews are to "identify process improvement opportunities, possible procedure or compliance violations, and confirmation of processes operating in a state of control." During the inspection of the DCSC, FDA repeatedly requested documentation that Quality Process Reviews had been completed at the DCSC, but no documentation was provided. ARC stated that only some of the reviews were completed through December 2009 and that others were not completed due to loss of QA staff.

c. The Quarterly QA reports, required by paragraph IV.A.2.b. to be submitted in writing by the QA director to ARC senior management and ARC Biomedical Services senior management, did not portray the seriousness of the staffing and proficiency problems occurring in the DCSC and identified by ARC internal audits and other internal assessments. For example, eight Quarterly QA reports were submitted to ARC senior management and ARC Biomedical Services senior management beginning in April 2008 through March 2010. However, it was not until the October-December 2009 report that the "capacity for problem management" and the backlog of open problems were mentioned in the quarterly QA report. In its 12/15/10 response to the FDA 483, ARC acknowledged that the "seriousness of the DCSC issues were not clearly documented in the Red Cross Quarterly Quality Assurance reports until the January – March 2010 report."

d. A QA Assessment of the DCSC was performed in October 2009 and a PM Assessment of the DCSC was performed in November 2009. The reports identified staffing and workload issues due to the continuous consolidation of more regions into the DCSC. One report identified that the QA staff in Philadelphia had no donor management experience; some QA staff members already employed at the DCSC for six months were not fully trained; and staff was "struggling" with a lack of support from QA management. The reports also indicate that there had been inadequate planning and inadequate change control associated with the consolidation of donor management functions from the regions into the DCSC. Despite these conditions, ARC continued with the consolidation until it was completed in March 2010. The QA and PM assessment reports were then issued to ARC senior management in April 2010.

e. In multiple Board of Governors Committee meeting notes, ARC's QA (through the QCOC) stated that it was closely monitoring all corrective actions related to internal DCSC audit

observations and ensuring that staffing levels were adequate to continue merging the regions' donor management functions into the DCSC. FDA reviewed numerous problems opened as a result of the internal audit findings and observed that corrective actions were not developed and/or implemented promptly. However, the merging of regions into the DCSC continued. For example, FDA's review of ARC's internal audits of the DCSC problem management function found the following deviations from the Decree and the Problem Management Standard Operating Procedure (PM SOP)[7]:

i. ARC's October 2008 audit of the Philadelphia and Charlotte DCSC facilities cited untimely problem management. In response, the DCSC opened Exception E-0455175 (Issue I-0017862-FC) (discovered 10/22/08 and closed on 3/31/10) and determined root causes that included inadequate staffing levels, inexperienced staff, inadequate training, and a lack of tracking mechanisms to ensure timely problem management. The corrective action plan included hiring and training additional staff, developing tracking queries for the DCSC, and establishing a group to manage post donation information problems. QA approved the corrective action plan on 2/3/10 and implementation is documented as having been completed on 2/4/10 and 3/23/10. Issue I-0017862-FC states that the effectiveness check would be performed under Exception E-0680169 (Issue I-0017441-FC). ARC took approximately 17 months (from 10/22/08 to 3/23/10) to approve and implement a corrective action to address untimely problem management at the DCSC.

ii. ARC's June 2009 audit of the Philadelphia DCSC facility cited untimely management of problems. The audit report indicated that staff had been hired and that all moderate and major risk problems were being managed in Charlotte because Philadelphia was not fully staffed. It further stated that the DCSC continued to have a backlog of problems. In response, the DCSC opened Exception E-0595168 (Issue I-0015324-FC) (discovered 6/5/09) and determined that root causes included inadequate monitoring processes, lack of staffing proficiency, and a heavy workload. QA approved the corrective action plan on 8/24/09 after two corrective action plan extensions. The corrective action plan was not fully implemented until 2/24/10. The final effectiveness check had not been completed as of 10/11/10, approximately 16 months after discovery of the problem, and the problem remained open.

iii. ARC's January 2010 audit of the Philadelphia DCSC facility cited untimely management of problems. The DCSC response referred to previously developed corrective action plans documented in Issue I-0017862-FC (the corrective action plan for the October 2008 audit) and Issue I-0017441-FC (the corrective action plan for the October 2009 audit). The root cause described in the DCSC response was a lack of resources to consistently manage problems in a timely manner. The corrective action plan included hiring staff, including a problem management manager, and establishing a separate post donation information problem group.

iv. ARC's March 2009 audit of the Charlotte DCSC facility cited untimely management of problems. The auditor reported a backlog of more than 200 minor, moderate, and major risk problems. In response, the DCSC opened Exception E-0551794 (Issue I-0013588-FC) (discovered 3/27/09, closed 5/4/10) and determined that the root causes included inadequate staffing, noting that only two staff members had experience with moderate and major

[7] The two DCSC facilities have overlapping problem management responsibilities; therefore, BHQ audit observations and corrective actions affected both locations. For example, one audit report states that all moderate and major problems were being managed in Charlotte because Philadelphia was not fully staffed. QA management also stated that all post donation information problems are managed by staff in Philadelphia.

risk problems and a lack of oversight by the DCSC. The corrective action plan included training more staff to handle moderate and major risk problems, assigning oversight responsibilities, and tracking the age of problems. QA approved the corrective action plan on 4/29/09. Issue I-0013588-FC documented the corrective action plan as implemented between 4/30/09 and 7/30/09. The sustained effectiveness check was not completed until 4/16/10, more than a year after discovery of the problem. ARC deemed the corrective action plan effective at that time.

v. ARC's October 2009 audit of the Charlotte DCSC facility cited untimely management of problems. The DCSC opened Exception E-0680169 (Issue I-0017441-FC) (discovered 10/23/09, closed 6/1/10) and documented the root causes as lack of an adequate tracking mechanism, problems not always being assigned as they were discovered, and the outsourcing of problem management cases due to staffing levels. The proposed corrective action plan included developing tracking mechanisms and hiring QA and problem management staff by 12/1/09. QA approved the corrective action plan on 11/30/09. One tracking mechanism was implemented on 10/26/09 and a second was implemented on 1/29/10. Staff positions were opened on 1/29/10. The effectiveness check was completed on 5/3/10 and the problem closed 6/1/10, eight months after the problem was discovered.

f. ARC's June 2009 audit of the Philadelphia DCSC facility cited observations pertaining to the DCSC failure to review donor management records in a timely manner. For example,

i. ARC's internal audit report includes the observation that post donation information and donor call back cases were not being process-verified in "a reasonable time period." In response, the DCSC opened Exception E-0595192 (Issue I-0020482-FC) (discovered 6/5/09, still open as of 10/8/10) and determined the DCSC did not consider process verification a priority because there is no deadline, there were competing priorities, and there was a lack of staff proficiency. The DCSC audit response states that they were already aware of the process verification backlog and had developed a plan to address it. The corrective action plan included slowing down the consolidation and changing the work flow. The proposed effectiveness check states that QA would do periodic case reviews to ensure that process verification is timely and that cases are completed. QA approved the corrective action plan on 7/20/10. Only one part of the corrective action plan is documented as having been completed on 8/30/10. The Exception Report states that the corrective action plan was ineffective, but at the time of the FDA inspection, there was no documentation of any follow-up corrective action investigation to address this problem.

ii. ARC's internal audit report includes the observation that the DCSC failed to ensure timely and accurate management of DRIRs. The DCSC opened Exception E-0595184 (Issue I-0011152-NF and Issue I-0020136-FC) (discovered 6/5/09, closed 8/3/10). (The problem was later linked to Exception E-0794874, Issue I-0010881-FC, which addresses the FDA 483 observation issued at the Badger Hawkeye Region on 4/23/10.) The DCSC determined the root cause included lack of staff proficiency and lack of a well defined process. The DCSC response stated that it was aware of the problem and had held workshops and proposed to establish a DRIR group by 8/1/09, and to conduct another workshop. Additionally, the corrective action plan included time studies by a 'lean engineer,' development of a backlog plan, clarifying DRIR time frames, and the hiring of [redacted] staff members to handle donor eligibility calls. QA approved the corrective action plan on 6/2/10. Issue I-0020136-FC indicates the corrective action plan was

not fully implemented until 7/21/10. There was no due date documented for one of the effectiveness checks, which was not completed as of 9/2/10, 15 months after the problem was identified.

***Decree Violations*: Failure to Comply with Reporting Requirements**

3. Paragraph XIX requires ARC to report in writing to FDA any partial or complete suspensions of operations of one or more regions and/or laboratories. On 5/10/10, ARC notified FDA of a complete suspension of operations at a mobile blood drive held in the Connecticut Region on 5/8/10 (Exception E-0802346). The report stated that the collections operations were suspended at 1:30 p.m. due to extreme temperature conditions, two donor reactions, and staff feeling ill. However, during an inspection of the Connecticut Region in May-June 2010, FDA discovered that the 5/10/10 report was inaccurate because the operations had not been suspended and ARC collected 16 blood donations at that drive between 1:30 and 2:59 p.m.

***Decree Violations*: Inadequate National Donor Deferral Register[8]**

4. Decree paragraph IV.B.10 requires ARC to maintain a National Donor Deferral Register (NDDR) that contains an accurate and complete list of all ARC nationally deferred donors from each region. The safety of the blood supply depends on effective screening of donors to identify risk factors for diseases transmissible by blood and blood components, and the deferral of high-risk potential donors. Because of the mobility of the population of potential donors, the effective implementation of a national register of deferred donors is necessary to help ensure that accurate and current deferral information is available to ARC facilities nationwide. During an inspection of the Southern California Region in August-September 2010, FDA's review of records pertaining to permanently deferred donors revealed that ARC has not established an accurate and complete list of all permanently deferred donors, as required at 21 CFR 606.160(e). Information pertaining to permanently deferred donors from each ARC region is sent (b) (4) to the DCSC to be incorporated into the ARC's NDDR. The NDDR was created because the ARC's National Blood Computer System, which services its 36 regional facilities, does not share donor deferral information among regions. The (b) (4) updates to the NDDR are shared with all regions in a table format referred to as an NDDR "pushed table"[9] so that any region can identify permanently deferred donors during the donor registration process, regardless of which region deferred the donor.

ARC NDDR is not adequate because, for example: (1) permanently deferred donors may not be identified during donor registration at the regions because the NDDR "pushed tables" only contain the donor's current information and not the "before images"[10] for donors who previously donated under different names; and (2) permanently deferred donors using hyphenated names may not be identified if attempting to donate using just one part of the hyphenated last name. FDA's record review identified nine permanently deferred donors listed on pushed tables that did not include their previously used last names. The absence of such information prevents ARC from performing an adequate evaluation of its NDDR records in order to prevent the distribution of subsequently donated blood products from donors whose blood should not be accepted for donation. For example,

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[8] 21 CFR § 606.160(e) requires that a record be available from which unsuitable donors may be identified so that products made from the blood of such individuals will not be distributed. ACR refers to this record as the Donor Deferral Register.

[9] "Pushed tables" are the mechanism used to share information on permanently deferred donors among regions. If that information is not shared, regions are unaware when another region has permanently deferred donors.

[10] A "before image" is a historical record of changes made to the donor record in National Biomedical Computer System.

a. A donor with a merged record had a newer identity under the initials (b) (6) and an original identity under the initials (b) (6) However, the NDDR contains the donor's current name only (initials (b) (6))

b. Donors with hyphenated names are assigned multiple soundex codes.[11] For example, the soundex code for Donor (b) (6) who has a hyphenated name, is different for the first part, second part and entire hyphenated name. The three parts of Donor (b) (6) s name were given different soundex codes. Therefore, the NDDR only contains the donor's current information.

***Decree Violations*: Inadequate Problem Management**

5. Paragraph IV.B.1. requires ARC to establish and submit to FDA a PM SOP to detect, investigate, evaluate, correct, and monitor all problems, trends, and systemic problems.[12] The Decree directs that the PM SOP include specific instructions to implement and document problem management requirements at ARC's BHQ as well as at the regional and laboratory facilities.

***Decree Violations*: Problem Management [Management of Suspect Blood Products]**

Failure to promptly implement adequate corrective actions to prevent recurrence of the failure to control suspect[13] blood or blood components. FDA has repeatedly cited ARC for this deviation, in letters issued pursuant to paragraph VI.A. of the original Consent Decree of Permanent Injunction entered on May 12, 1993, and in ADLs issued pursuant to the Decree entered on April 15, 2003. ARC has repeatedly promised to implement and monitor corrective actions, but the corrective actions have not prevented recurrence of the problem.[14] The failures described below are particularly serious because the failure to control suspect products and to correct the causes of errors increases the likelihood that unsuitable blood products will be transfused. For example,

a. The DCSC identified trends related to the improper management of suspect blood products and inventory management, but failed to promptly and thoroughly correct the problems. For example,

i. A trend was identified for Biological Product Deviation (BPD) code QC-96-01-25 (product in wrong physical location, wrong electronic location) in October 2009. The trend was discovered on 11/30/09, and Exception E-0707671 (Issue I-0018721-FC) was created. The problem was closed on 2/18/10. The documented root cause was "Current process flows and functional roles do not meet System 11 requirements as they include hand-offs with steps that should be performed consecutively and immediately." The Issue report states that no formal

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[11] A soundex code is a [redacted] digit code. The soundex algorithm calculates a (b) (4) [redacted]

[12] Paragraph III.B.52 defines "problem" as "any deviation from *the law, ARC SOPs*, or this Order, however discovered, recorded, or reported, including, but not limited to deviations reported in *ARC Clarify reports* (and/or in any other successor or similar deviation-reporting systems and/or reports), *biological product deviation* reports, *internal deviation reports, trends, adverse reaction* reports, *lookback* cases, cases of *suspected transfusion-transmitted disease, potential system (systemic) problems, system (systemic) problems,* supply and *equipment* problem reports, *FDA-483s*, compliance-related FDA correspondence, internal and external audit reports, and *retrievals*." Paragraph III.B.63 defines "system (systemic) problem" as "a *problem* that results from a defect in *ARC* policies, procedures, *equipment,* or supplies and affects either more than one *ARC region* and/or *laboratory,* or warrants corrective action which, when implemented, could affect more than one *ARC region* and/or *laboratory*." Paragraph III.B.64 defines "trend" as "the recurrence or multiple contemporaneous occurrences of the same or similar *problems* in one or more than one *ARC region* and/or *laboratory*."

[13] ARC defines "suspect" blood products as those which "may or may not meet safety, quality, identity, purity, and potency (SQUIPP) requirements and are potentially non-conforming." Directive: Mismanagement of Suspect Products, 11.2.002, version 1.6.

[14] See **Attachment B** for details of compliance history related to failure to control suspect blood or blood components.

corrective action will be taken due to the corrective actions implemented under another problem on 11/18/09 (Exception 0599613/Issue I-0015339-FC) which QA approved on 2/16/10.

ii. A trend was identified for the same BPD code in February 2010. The trend was discovered on 3/24/10, and Exception E-0774042 (Issue I-0019647-FC) was created. As of 10/1/10, the problem was still open. The documented root cause was, "Due to the original design of the Donor and Client Support Center (DCSC) workflow, there is a waiting period from the point when unsuitable components are identified to the time when they are managed or retrieved." The Issue report indicates that QA approved the corrective action plan on 5/27/10, and it was implemented the same day; however, the approved corrective action plan is only a reference to corrective actions related to another problem. The interim effectiveness checks were deemed effective on 7/27/10; however, as of 10/1/10, there was no record that the sustained effectiveness check, which was due 8/26/10, was completed. Additionally, the records related to the other referenced problem indicate that implementation of the corrective action plan was not fully completed until 10/5/10.

iii. A trend was identified for BPD code QC-90-01-05 (failure to adequately manage potentially non-conforming products, product not released) in May 2010. The trend was discovered on 6/30/10, and Exception E-0831104 (Issue I-0011219-NF) was created. The problem was closed on 8/2/10. The root cause was identified as, "The original process flows associated with these gain control and retrieval processes did not provide staff with the experience and responsibility to perform their required functions as a suspect product identifier." The problem was closed without developing a corrective action plan, but instead referenced corrective actions and effectiveness checks addressed under four other Issue reports (Issue I-0020891-FC, Issue I-0016426-FC, Issue I-0019143-FC, and Issue I-0019389-FC). A review of Exception E-0625538 (discovered 7/31/09) and Exception E-0780785 (discovered 3/31/10), which are both associated with Issue I-0019389-FC, found that a corrective action plan extension was approved for both problems on 4/30/10 and an additional corrective action plan extension was requested for Exception E-0625538 on 8/17/09. QA approved the corrective action plan under Issue I-0019389-FC on 5/19/10. One part of the corrective action plan was implemented by 5/31/10, but the other three parts were not implemented until 10/5/10. Both problems remained open as of 10/14/10—one for more than 15 months and one for more than six months.

b. ARC discovered approximately 18 major risk problems coded as QC-90-01-05 (failure to manage potentially non-conforming products, product not released) that occurred at the Philadelphia DCSC facility during calendar year 2010. A review of those problem records found problem management deficiencies. For example,

i. ARC did not conduct an adequate root cause analysis, develop an appropriate corrective action plan, or conduct an effectiveness check for Exception E-0790730 (Issue I-0020041-FC), which was discovered on 4/16/10 and remained open as of 10/7/10. The problem description states that a hold was not applied to an in-date product for a donor with an XW3 assertion.[15] The root cause is described as "Due to the peculiarity of this case, [a supervisor] was puzzled which resulted in unclear guidance to a new staff." The corrective action plan stated that the supervisor "recognizes how to appropriately handle these types of cases so that he can better

[15] An XW3 assertion is ARC's donor indefinite deferral code for donors with a history of hepatitis, bleeding conditions, blood diseases and/or who tested positive for the HIV/AIDS virus by a non-ARC facility.

communicate to staff the appropriate actions that are required." QA approved the corrective action plan on 5/21/10 and Issue I-0020041-FC states the corrective action plan was implemented on 5/21/10; however, a corrective action plan was not listed in the report. The effectiveness check was due on 8/27/10, but as of 10/7/10 had not been completed.

ii. ARC failed to implement a corrective action plan in a timely manner for Exception E-0751845 (Issue I-0019143-FC), which was discovered 2/17/10 and remained open as of 10/7/10. The problem description states that no immediate effort was made to regain physical control of the blood products for a possible DRIR-related infection. The documented root cause was that the staff is feeling overwhelmed and frustrated. The corrective action plan was to develop a process to ensure a more structured management of DRIR cases and to develop a phone schedule. QA approved the corrective action plan on 3/17/10, but it was not implemented until 9/27/10.

iii. ARC failed to implement a corrective action plan and complete an effectiveness check in a timely manner for Exception E-0746476 (Issue I-0018941-FC), which was discovered on 2/5/10 and remained open as of 10/8/10. The problem description states that no hold was applied and the receiving region was not notified to gain physical control of a component imported from another ARC region. The documented root cause was the staff failed to identify the importance of gaining physical and electronic control of the component, "due to her lack of knowledge with the American Red Cross and DCSC." The corrective action plan was that staff will be counseled and will continue to gain experience; and the training department will develop a communication to all staff and will conduct a training refresher. QA approved the corrective action plan on 3/10/10. Implementation of all corrective actions was not completed until 7/27/10, more than five months after discovery. Effectiveness checks due dates were 9/7/10 and 9/9/10, but were not completed as of 10/8/10, more than eight months after discovery of the problem.

6. Failure to promptly, thoroughly, and adequately investigate and correct problems in accordance with the Decree and with ARC's PM SOP. For example,

***Decree Violations*: Problem Management [Donor Reaction/Injury Records (DRIRs)]**

a. During the inspection of the DCSC, FDA observed that ARC identified trends[16] related to DRIRs beginning in June 2009, but failed to promptly and thoroughly correct and prevent recurrence of DRIR documentation problems. For example:

i. On 9/30/09, ARC identified a trend, which occurred in June 2009, related to BPD code BC-40-01-02 (adverse reaction donor: incorrect/missing documentation on Donor Reaction/Injury Reports). Exception E-0664347 was created on 9/30/09. The root cause investigation and corrective action plan development (Issue I-0018632-FC) did not begin until 2/5/10, four months after discovery of the trend problem. An extension of the 30-day corrective action plan development time frame was granted by QA on 2/6/10. The documented justification for the extension was that the original corrective action plan was due on 10/30/09, but the problem was not assigned to a Problem Investigator until 1/12/10. The root cause is documented

[16] "Trend" is defined in note 11 above. The DCSC began trending in accordance with the Decree and with WI 10.3.13, *Trend Identification by Facilities*, in September 2009.

as "staff are hurried and rushing to complete the form and overlook errors and omissions. The DRIR is filled out electronically and it is easy to overlook omissions on the form." The Issue further states that "no additional corrective actions are necessary at this time" and refers to corrective actions implemented on 11/24/09 and 1/31/10 under BHQ system trend Exception E-0603257. The DCSC QA staff approved the proposed corrective action plan on 2/18/10 and closed the trend on 2/24/10, five months after the trend was discovered.

ii. ARC BHQ system trend (referenced in 6.a.i above) was discovered on 6/23/09. Exception report E-0603257 (Issue I-0000334-EFC) was created on 6/23/09 and was closed on 6/29/10. The described problem is incomplete or incorrect documentation of DRIRs. The root causes cited in Issue I-0000334-EFC include: "donor adverse reactions are rare stressful events and staff busy attending to the donor fail to document all required information…;" "staff inattention to detail and lack of focus…; misinterpretation of the Work Instructions; failure to refer to the form instructions; gaps in DRIR instructions; and the format of the DRIR form." The corrective action plan was approved by QA on 12/2/09, approximately five months after discovery of the trend. The corrective action plan included the release of a communication in November 2009 to remind staff of requirements and clarify instructions. The effectiveness check success criterion was (b) (4) improvement. On 6/15/10, ARC used data from 2/1/10 through 4/30/10 to perform the effectiveness check. They deemed the corrective action effective with only a 41% improvement. However, 41% is not sufficient and (b) (4) is clearly inadequate as a goal.

iii. On 5/25/10, a trend was discovered again at the DCSC for BPD code BC-40-01-02 (adverse reaction donor: incorrect/missing documentation on Donor Reaction/Injury Record). The trend occurred in April 2010. Exception E-0811555 (Issue I-0020944-FC) was created and was still open as of 10/1/10. The root causes cited include staff not reviewing their work and "shortage of dedicated DRIR staff." An extension for the corrective action plan development was requested on 6/17/10 and was granted by the DCSC QA the same day. A second extension was requested on 7/13/10 and was granted on 7/14/10. The corrective action plan, which was approved by QA on 9/8/10, included a reminder to affected staff of the DRIR requirements, hiring additional DRIR staff, and providing refresher training to other staff members that perform DRIR tasks. The staff reminder is documented as completed on 9/27/10, four months after discovery of the trend.

***Decree Violations*: Problem Management [DRIRs Failing to Reach the DCSC from the Regions]**

b. On 7/9/10, ARC discovered a problem related to missing DRIRs that were sent by the regions to the DCSC. Exception E-0836426 was created on 7/12/10. As of 10/8/10, ARC had not completed an investigation into the root cause of missing DRIRs and had granted two extensions for the development of a corrective action plan until 11/12/10, four months after initially discovering the problem. A record review was completed in July 2010 for the period 12/1/09 through 6/30/10, and identified 292 donor adverse reaction or injury cases with missing DRIRs. The safety of donors depends on the prompt investigation into the causes of donor injuries and reactions, to correct causes of such injuries where possible, and to implement training for appropriate staff intervention. The mismanagement of records interferes with that process.

***Decree Violations*: Problem Management [Confirmatory Test Results and the Donor Deferral Register]**

c. During the inspection of the DCSC, FDA observed that ARC identified trends related to management of confirmatory infectious disease test results and Donor Deferral Registry (DDR) entry, but failed to promptly and thoroughly investigate, correct, and prevent the problems. For example,

i. On 10/29/09, ARC identified a trend for BPD code DD-30-01-10 (confirmatory results/DDR entry not performed/not timely) that began in September 2009. Exception E-0683307 (Issue I-0017599-FC) was created and was closed on 2/23/10. The root causes were cited as inattention to detail due to staff being new, not understanding, or rushing. The proposed corrective action plan refers to corrective action taken under another problem (Issue I-0016921-FC). QA approved the corrective action plan on 12/18/09 and the Issue report shows the corrective action plan was implemented on 12/18/09. It is described as "Reiterate the need for staff to slow down and pay closer attention to information being entered and to make sure that they go back and review entries prior to moving to the next step." The corrective action plan also required supervisors to observe the involved staff while performing test result entry. The effectiveness check was performed and the corrective action was deemed effective by ARC on 2/19/10. However, the records for Issue I-0016921-FC, which was referenced as the corrective action plan for the trend problem, indicate that it was not fully implemented until 4/27/10 and the effectiveness check was not completed until 6/23/10.

ii. On 10/29/09, ARC identified a trend for BPD code DD-30-01-12 (incorrect/no computer property/assertion applied, no product released) for September 2009. Exception E-0683302 (Issue I-0017306-FC) was created 10/29/09. The root causes included misinterpretation of instructions, staff new to task, staff not aware they could remove assertions, and limited experience with holds. The investigation did not address why staff had been released to perform tasks they did not understand, yet QA approved the corrective action plan on 11/18/09. The Issue report shows that the corrective action plan included the development of a communication document for staff as well as the development and implementation of a new operational team. The problem was closed on 5/11/10. However, because of the inadequacy of the corrective action plan, the DCSC subsequently had a trend recurrence for BPD code DD-30-01-12 in August 2010.

***Decree Violations*: Problem Management [Consignee Notification[17]]**

d. During the inspection of the DCSC, FDA observed that ARC identified trends related to consignee notification, but failed to promptly and thoroughly correct and prevent the problems. Prompt notification to consignees regarding the distribution of unsuitable blood products is essential to preventing such products from being transfused. For example,

i. On 9/30/09, ARC identified a trend for BPD code MI-00-01-19 (48 hour notification to consignee not performed/complete/timely for distributed expired products) in June

[17] Paragraph X.E of the Decree requires ARC to notify consignees and FDA's Baltimore District Office within 48 hours after initially learning that a unit of unsuitable blood or blood component has been distributed. Paragraph X.F. of the Decree requires ARC, within 10 days of initially discovering a problem that may have resulted in the release for distribution of units of unsuitable blood or blood components, to review and document the review of all records necessary to determine whether distribution of units of unsuitable blood or blood components in fact occurred and to identify all related units of unsuitable blood or blood components that were, may have been, or may be distributed.

2009. Exception E-0664458 (Issue I-0020096-FC) was created on 9/30/09 for missed 48 hour consignee notification and missed follow up timelines. Corrective action plan development extensions were approved by QA on 10/20/09, 12/1/09, and 4/28/10. The justification for the 4/28/10 extension was "staff issues and lack of good tracking mechanisms...." No investigation of the trend problem was documented until 5/18/10. QA approved the corrective action plan on 7/6/10, ten months after discovery of the trend. The root causes are cited as "poor work practices/work flow including poor follow-up, insufficient reviews, and oversight." The described corrective action plan included restructuring the DCSC into functional teams and revising work flows to standardize gain control activities. Approximately one year after discovery of the trend, the corrective action plan has not been fully implemented. Functional teams were not implemented at the Philadelphia DCSC as late as June 2010 and at the Charlotte DCSC as late as September 2010, as described in the Issue report. The status of the work flow revisions is not documented. The trend problem remained open as of 10/1/10, twelve months after identifying the trend.

ii. On 9/24/10, ARC identified a trend for MI-00-01-23 (recall/market withdrawal records incorrect/incomplete/not timely, including late follow up letters to consignees) in August 2010. Exception E-0878847 was created on 9/27/10. The problem description refers to the June 2009 MI-00-01-19 trend being managed under Exception E-0664458, as described in the item above. The trend problem remained open as of 10/1/10, twelve months after identifying the trend, with no documentation of an investigation or corrective action.

***Decree Violations*: Problem Management [Lookback Investigations]**

e. During the inspection of the DCSC, FDA observed that ARC had discovered problems related to the management of lookback cases dating back to 3/15/10, but failed to promptly correct those problems. When a person donates blood early in an infection, screening and testing may not detect the presence of an infectious agent (the "window period"). After the infection is discovered, it is important to identify and "lookback" at prior donations that might have been collected during the "window period" in order to identify, notify and test any recipient of a transfusion of blood or blood components collected during the "window period." Such process is necessary for the protection of blood product recipients. For example,

i. Issue I-0019746-FC was created 4/26/10 to implement a formal corrective action for 17 different problems involving management of lookback investigations. The oldest of those problems was discovered on 3/15/10, yet a corrective action plan was not approved by QA until 6/25/10, more than three months after the initial date of discovery. The root causes of these problems are identified as "supervisors are not consistently reviewing with their staff the open cases report generated from the Access Lookback Log" and "Operations Staff of the involved Supervisors may not have been trained to generate and use reports in the Lookback log database." The effectiveness checks were not due until 12/10/10, nine months after the oldest problem was discovered.

ii. A trend related to the management of lookback investigations was discovered on 6/30/10. Exception E-0831094 (Issue I-0011220-NF) was created on 6/30/10 and was closed on 8/2/10. No formal corrective action plan was required by ARC and the Issue report references the formal corrective action implemented in Issue I-0019746-FC discussed in the item above. However, Issue I-0019746-FC remained open at the time of the September-October 2010

inspection because the effectiveness checks were not due until 12/10/10, nine months after the oldest problem involving the management of lookback investigations was discovered.

iii. On 8/31/10, ARC discovered another trend related to the management of lookback investigations. Exception E-0864242 (Issue I-0011479-NF) was created on 8/31/10. The Issue report also referenced the formal corrective action implemented in Issue I-0019746-FC, discussed in the item above, which remained open at the time of the September-October 2010 inspection, because the effectiveness checks were not due until 12/10/10, nine months after the oldest problem involving the management of lookback investigations was discovered.

***Decree Violations*: Problem Management [Failure to Meet Established Timeframes]**

f. During the DCSC inspection, FDA investigators requested a search of ARC's automated problem management system for the period 1/1/10 through 9/22/10. A review of the results revealed that the DCSC does not always meet the established time frames required in ARC's PM SOP and in the Decree. For example, FDA observed that the query showed 90 problems in which the DCSC failed to comply with the paragraph X.E requirement to notify consignees within 48 hours "after initially learning that a unit of unsuitable blood or blood component has been distributed."

g. During an inspection of the Indiana-Ohio Region in July 2010, FDA discovered that ARC failed to promptly correct a problem related to the late entry of a donor into the NDDR. For example, a donor was confirmed positive for anti-HTLV on 1/6/10, but the result was not promptly entered into ARC's National Biomedical Computer System until 4/4/10 and was not promptly submitted for entry into the NDDR by the DCSC until 4/5/10. Exception E-0781884 was opened on 4/6/10. It was merged with 27 other problems (in Issue I-0019116-FC, created 3/11/10) involving similar occurrences in other regions. The investigation determined the root causes were a lack of defined processes and misinterpretation of timeframes for reconciliation of test results. QA approved the corrective action plan on 5/11/10, yet there was no documentation that the corrective action plan was implemented as of 7/16/10, four months after Issue I-0019116-FC was created. The corrective action plans that were approved by QA did not adequately address the identified root causes and the effectiveness checks were not adequate to assess effectiveness of the corrective action plan.

***Decree Violations*: Problem Management [Overweight Units]**

h. During an inspection of the Heart of America Region in June-August 2010, FDA's review of monthly trend records for BPD code BC-43-03 (overbleed; not discovered prior to component preparation) in December 2009 revealed that ARC did not follow Work Instruction 10.3.013, *Trend Identification by Facilities*, Version 2.1, when analyzing data for the effectiveness checks for the corrective action plans implemented for Exception E-0717565 (discovered in December 2009) (Issue I-0018377-FC). For example, the effectiveness check query found 13 additional overweight units during the queried period. ARC eliminated six of those occurrences from its effectiveness check calculation because their failure modes were "unknown." ARC deemed the corrective action plan effective and closed the trend problem. FDA requested a query for March through June 2010 and found there were five additional occurrences of overweight units.

***Decree Violations*: Failure to Follow Standard Operating Procedure**

7. Failure to comply with paragraph IV.A.1., which requires "continuous compliance with this Order, *the law*, and *ARC SOPs*." For example, during an inspection of the Southwest Region in July-August 2010, FDA observed that ARC did not follow its written procedures pertaining to consignee notification in order to determine the final disposition of a blood product. The region held 25 imported components out of controlled storage in excess of 30 minutes. The region opened Exception E-0748767 (Issue I-0004237) and Biological Product Deviation Report E-0748767 was opened on 2/12/10 and the region notified the DCSC to manage the components. The DCSC placed holds on the components and notified consignees. FDA's review of the (b) (4) file from the DCSC found that the DCSC had no final disposition for five components and two components had a final disposition of "Q" (quarantine). According to Work Instruction 11.3.011, *Sending Retrieval Letters and Notifications*, Version 1.5, if the consignee does not respond to the first notification, a second notice must be sent in order to obtain the final disposition of the recalled component. The DCSC failed to send the second letters. Additionally, FDA noted during a subsequent review of the records that the Component Status Change Record for the recall found that it had not been process-verified five months after being created.

## ***GMP VIOLATIONS:***

***GMP Violations*: Inadequate System for the Distribution or Receipt of Blood Products**

8. Failure to establish and maintain a distribution and receipt procedure that includes a system by which the distribution or receipt of each unit of blood can be readily determined to facilitate its recall, if necessary [21 CFR § 606.165(a)]. This procedure is necessary to ensure that unsuitable products are promptly recalled and not transfused. For example,

a. During an inspection of the Heart of America Region in June-August 2010, FDA discovered that on 12/15/08, ARC changed the manner in which it assigns a unique number to the label of each unit of pooled cryoprecipitate. Prior to that date, each unit was assigned a four digit number, and after that date a nine digit number was assigned. The nine digit unique number is applied to the label on each unit of pooled cryoprecipitate; however, the computer record for each such unit continued to use the four digit format. ARC's relevant written procedures still do not provide adequate instructions to ensure that staff responsible for blood product retrieval and consignee notification consider whether the unit was distributed prior to or after the change to the numbering format.

Beginning February 2009, the Heart of America Region's donor management functions, including blood component retrieval and consignee notification, were consolidated with the DCSC. FDA's review of records pertaining to consignee notification for units of pooled cryoprecipitate found that the DCSC notified consignees using the incorrect unit number format for four units. For example, pooled cryoprecipitate unit 2399 was distributed on 5/30/08. It was subsequently determined to require retrieval by ARC due to high risk behavior by one of the donors. On 12/2/2009, the DCSC notified the consignee of that unit by letter, using the erroneous nine-digit number 040C02399. The DCSC documented the unit's final disposition on a Component Status Change Record (CSCR) as discarded; however, the FDA investigator was informed during the inspection that the documentation to support that final disposition was misplaced. During the inspection, ARC again notified the consignee with the correct four digit unit number and the consignee responded that the unit had been transfused into a patient on 6/26/08.

During the inspection, ARC reported to FDA that as a result of this observation, it had opened an investigation and identified an additional 62 cases that were managed by the DCSC using the wrong unit number format. Those cases involved regions other than the Heart of America. In its 9/8/10 response to the FDA 483, ARC stated that the problem was caused by a procedural gap and that it was a system-wide problem.

b. During an inspection of the Northern California Region in September 2010, FDA discovered that the DCSC was unable to locate documentation for the final dispositions of 31 Red Blood Cell units that were subject to retrieval. A Material Review Board decided to retrieve the products after it was discovered that the storage temperature of the units, documented at the time of receipt, was unacceptable. ARC contacted the consignee of the units to request a copy of the missing notification documentation. The CSCR form documented that all 31 units were destroyed. However, the consignee reported that eight units had been transfused into patients. The CSCR, with the incorrect dispositions, had been process-verified by the DCSC on 3/4/10, but the discrepancies were not detected.

***GMP Violations*: Failure to Follow Manufacturer's Instructions**

9. Failure to ensure that supplies are used in a manner consistent with the manufacturer's instructions, as required at 21 CFR § 606.65(e); and failure to prepare the phlebotomy site using a method that gives maximum assurance of a sterile container of blood [21 CFR § 640.4(f)]. For example,

During an inspection of the Southern California Region in August-September 2010, FDA observed collection staff placing hand warmers directly on Whole Blood donors' arms over prepared phlebotomy sites. Only a piece of gauze separated the hand warmer from the area where the venipuncture was performed. This action may have compromised sterility during the collection procedure. FDA's review of the manufacturer's instructions for the hand warmer found that they specifically stated, "***Do not use***on parts of the body other than the hand***." ARC's 11/4/10 response to the FDA 483 acknowledged that this use of hand warmers was inappropriate and could burn donors' skin.

***GMP Violations*: Failure to Maintain and/or Follow Written Procedures**

10. Failure to establish, maintain and follow written procedures that include all steps to be followed in the collection, processing, compatibility testing, storage, and distribution of blood and blood components for transfusion and further manufacturing purposes [21 CFR § 606.100(b)]. For example,

a. During the inspection of the DCSC, FDA reviewed ARC's management of recipient complication cases, in which a patient had difficulty with a blood transfusion. ARC's Job Aid 11.4.ja056, *Timing Guidelines for Recipient Complication Investigations*, Version 1.0, requires that the DCSC complete a recipient complication case investigation within three months of it being opened or document why the case remains open. In addition, the Job Aid requires that a monthly review of each opened case file be performed, to ensure that actions are being appropriately managed. However, FDA reviewed nine recipient complication investigations during the inspection of the Philadelphia DCSC facility and discovered the following:

i. Case ID DCSC-P-053-TR-TRL00375 was opened on 11/04/09 and was closed 5/25/10, 202 days later. The case file did not have a justification for exceeding the 90 day time frame documented in the case notes until 2/16/10, the date ARC documented why the case was

open for more than three months. The file also contained no documentation that the case was reviewed on a monthly basis to "ensure that actions are being appropriately managed."

ii. Case ID DCSC-P-053-TTI-HBV00429 was opened on 12/28/09 and was closed 5/25/10, 158 days later. The case file did not have a justification for exceeding the 90 day time frame documented in the case notes until 5/25/10, the date ARC documented why the case was open for more than three months. The file also contained no documentation that the case was reviewed on a monthly basis to "ensure that actions are being appropriately managed."

iii. Case ID DCSC-P-053-TTI-HBV00651 was opened on 4/28/10 and was closed during the inspection on 10/6/10, 157 days later. The case file contained no justification for exceeding the 90 day time frame documented in the case notes until 8/12/10, the date ARC documented why the case was open for more than three months.

b. During an inspection of the Southeastern Michigan Region in August – September 2010, FDA reviewed 26 transfusion reaction/recipient complication cases and discovered 11 that were not managed according to ARC's written procedures. For example,

i. The DCSC opened a transfusion reaction/recipient complication case on 7/9/09 and closed it on 5/22/10, without justification for why the case was open for more than three months.

ii. The DCSC documented inaccurate final component dispositions on CSCRs. Form 11.4.frm9, *Component Status Change Records*, Version 1.1, provides a component final disposition section and states that if used, it must be completed with "a valid disposition to the final disposition." DCSC-C-013-TR-ORX00246 indicates that one component was marked destroyed, but had in fact been shipped to a consignee. Another component was marked as expired in-house, but in fact had been destroyed by the consignee.

c. During the inspection of the DCSC, FDA discovered that the DCSC has not established adequate procedures to ensure that donor health history deferred reports are generated daily and that failure to generate such reports will be detected promptly. According to the DCSC management, it has been operating with only draft work flows for the health history deferred report review process. During the inspection of the Philadelphia DCSC facility, FDA requested health history deferral records for July 2010 for three regions. The DCSC informed FDA that it had failed to generate five requested reports; therefore, it failed to conduct a review of each listed donor with prior donations for potentially unsuitable blood components requiring quarantine, retrieval, and consignee notification, when necessary. Upon discovery during the inspection, the DCSC opened Exception report E-0869169 to address the problem and review the omitted reports. Their review found that, due to the omission, prior donations from five donors had not been managed appropriately. In addition, ARC discovered an additional 18 omitted donor health history reports.

d. During an inspection of the Greater Alleghenies Region in September 2010, FDA observed that during the blood donation process, the region provided donors with hand warmers prior to collecting a blood sample using the finger stick method. The blood samples were collected for hemoglobin determination as part of the donor health assessment to determine suitability for donation. The region's management said the hand warmers are used in the winter with the (b) (4) (b) (4) . ARC has not established a written standard operating procedure for use of hand warmers to

increase blood flow when a donor's hands are cold. In addition, ARC has not provided training to the collections staff regarding their use.

e. During an inspection of the Heart of America Region in June-August 2010, FDA observed that ARC does not consistently follow Work Instruction 10.3.011, *External Customer Complaint Management*, Version 1.1 and Directive 10.2.9, *Managing Customer Concerns*, Version 1.0. For example, ARC's recruitment staff distributes "Blood Drive Sponsor Satisfaction Survey" forms to mobile blood drive coordinators and/or chairpersons. A portion of the survey requests feedback regarding the ARC blood drive staffing level. It also includes a space for comments. FDA's review of survey forms found that complaints related to FDA-regulated functions were not investigated as concerns or complaints, in accordance with established written procedures as required by 21 CFR § 211.100(b) and 21 CFR § 606.100(b). For example,

Survey cards for two mobile blood drives conducted on 11/4/09 and 12/11/09 reported complaints pertaining to a donor sprayed with blood and pertaining to donor injuries during phlebotomy.

During the inspection, ARC informed the FDA investigator that it believes complaints on the survey cards are not complaints because they are solicited information and that Directive 10.2.9 only applies when the donor takes the initiative to inform the staff of the complaint. Yet, Work Instruction 10.3.011 states that a complaint is "any written, electronic, or oral communication that alleges deficiencies related to the identity, durability, reliability, safety, effectiveness, or performance of any device, blood component, blood product, process, procedure, or employee performance that impacts donor or product safety." ARC also solicits donor feedback through the internet and does not evaluate those to determine whether there is an issue that should be managed as a concern or complaint, in accordance with its written procedures and regulations. In its 9/8/10 response to the FDA 483, ARC maintains that the surveys are "proactive methods to improve business," that they are not "designed to assess regulatory compliance," and that they are "outside the scope of the Problem Management SOPs." The response further states that subsequent to the Heart of America inspection, it modified the survey to remove the comment section and to add a statement directing the user to report donor issues to the collections lead and to provide a contact number. ARC's response does not state how it modified the survey with respect to complaints about staffing or how it will address staffing complaints that may appear on future surveys.

f. During the inspection of the Penn Jersey Region in May-June 2010, FDA observed a failure of the DCSC to follow written procedures to obtain final dispositions (January 2009 and March 2010) for four components that were subject to retrieval because they were collected from a male donor who was registered as a female. The DCSC also had no documentation to support the final dispositions for the components. One CSCR had been process-verified, but the errors were not detected by the staff performing the verification.

g. During inspections of nine ARC regions and the Philadelphia DCSC, FDA discovered multiple failures by ARC to follow written procedures pertaining to managing adverse donor reactions, as required by 21 CFR § 606.170(a). For example,

i. During an inspection of the Heart of America Region in June-August 2010, FDA discovered that the region failed to conduct a thorough investigation of each reported adverse reaction, as required by 21 CFR § 606.170(a). For example, on 5/20/10, ARC received a report of an adverse donor reaction from a high school blood drive coordinator regarding a blood drive

on 5/19/10. During the blood drive, a 16-year-old donor's hemoglobin test result was unacceptable and a second blood sample was collected to re-test the donor's hemoglobin level. The donor was accepted for donation based on the results of the second test. The donor lost consciousness and hit his/her head after a unit of blood was collected. The report included injuries sustained by the donor subsequent to falling in the canteen area. In an ARC document, a collection staff member stated he/she had concerns about the donor's weight and was aware of the loss of consciousness, but did not believe a DRIR was necessary. Even after the region received the report from the high school coordinator on 5/20/10, it failed to document the event on a DRIR and investigate the adverse reaction. It was not until 6/29/10, after FDA reviewed the complaint from the high school, that the region addressed the adverse reaction and the failure to document and investigate it. At that time, the region opened a problem report to investigate the failure to initiate a DRIR upon receipt of the 5/20/10 report, but the problem report did not address the failure of the collection staff to initiate a DRIR on 5/19/10, when the event occurred at the collection site. ARC's 8/9/10 response to the FDA 483 states the root cause of the failure to initiate a DRIR at the collection site is that the staff was focused on providing care to the donor, which caused the failure to document the reaction. The root cause of the failure of staff at the region to initiate a DRIR on 5/20/10 is that they "may not be familiar with recognizing all aspects of a donor reaction. These staff members focus primarily on the customer service aspects of the concern and do not consistently identify a potential donor reaction."

ii. During the inspection of the Heart of America Region, FDA also reviewed Concern/Complaint forms for 2009 and 2010 and observed that eight of the forms included complaints related to adverse donor reactions. There were no DRIRs initiated in response to those complaints and there were no investigations of the reported adverse reactions. The reports pertained to bruising and swelling at the venipuncture site, painful needle sticks, and injury to arms and back subsequent to a donor fainting. In its 9/8/10 response, ARC stated that staff responsible for investigating the donor reaction "may not be familiar with recognizing all aspects of a donor reaction. These staff members focus primarily on the customer service aspects of the concern and do not consistently identify a potential donor reaction."

iii. During the inspection of the Heart of America Region, FDA also reviewed DRIRs completed during the period 3/1/10 through 5/2/10, and found three that had an untimely Medical Director's review and/or final quality review. For example, a donor experienced a large hematoma after donating on 3/15/10. The final quality review was not performed until 6/25/10. The donor donated three more times before that final quality review was performed and experienced another hematoma following one of those donations.

iv. During an inspection of the Badger Hawkeye Region in April 2010, FDA reviewed DRIRs initiated in 2009, and found 13 without the final quality review and five missing the Medical Director review and the final quality review. On 5/3/2010, ARC reported a Significant Corrective Action (Issue I-0010881-NF) following its investigation of this FDA 483 observation issued to the Badger-Hawkeye Region in April 2010. ARC reported to FDA in this Significant Corrective Action that the DCSC facility in Charlotte had a backlog of approximately 2,000 DRIRs open for more than 60 days, demonstrating that the violations observed in the Badger Hawkeye Region were only a small part of a larger issue. ARC's corrective action was to assign and train more staff, to approve overtime, to do a time study, and to change the filing system.

v. During an inspection of the Great Lakes Region in April 2010, FDA reviewed 47 DRIRs initiated during November 2009, and discovered that three had no final quality review and two had untimely reviews.

vi. During an inspection of the Indiana-Ohio Region in July 2010, FDA reviewed 24 DRIRs and discovered that three had no Medical Director review and eleven with no final quality review.

vii. During an inspection of the Appalachian Region in August 2010, FDA's review of DRIRs found five initiated in 2010 with no Medical Director's review or final quality review. An additional 12 DRIRs (two initiated in 2009 and ten initiated in 2010) had no final quality review.

viii. During an inspection of the Northern Ohio Region in August-September 2010, FDA reviewed DRIRs initiated in 2010 and discovered that six had no final quality review. Additionally, one DRIR was not reviewed by a supervisor and a Medical Director and had no final quality review until eight months after the donor reaction. Only one attempt was made by the DCSC to re-contact the donor, eight months after the reaction.

ix. During an inspection of the Arizona Region in September 2010, FDA reviewed records related to a potential donor complication that involved a phlebotomist who stuck herself with a needle, then stuck a donor with the same needle and collected a unit of blood. For more than a month, the DCSC did not notify a Medical Director and the donor was not deferred. In its 10/29/10 response to the FDA 483, ARC stated the DCSC staff member who managed the DRIR associated with this incident was not aware of the need to immediately notify a Medical Director.

x. During the inspection of the Arizona Region in September 2010, FDA also reviewed 13 DRIRs and discovered that 11 had no final quality review or an untimely final quality review. Four DRIRs also had an untimely or late Medical Director's review

xi. During an inspection of the Greater Alleghenies Region in September 2010, FDA discovered five DRIRs that were initiated in 2010 and had no final quality review. Another DRIR had the final quality review six months after the donor reaction.

xii. During an inspection of the Southeastern Michigan Region in August-September 2010, FDA reviewed DRIRs for the period 11/18/09 through 2/13/10, and discovered that 22 had no final quality review.

xiii. During the DCSC inspection, FDA reviewed 13 DRIR case files that were opened in the DCSC in January, February, and March 2010, but had not been process-verified as of September 2010, as required by ARC's written procedures. FDA also found that six of the DRIRs had no final quality review and six had no Medical Director review.

***GMP Violations*: Inadequate Training and Staffing Levels**

11. Failure to ensure that the personnel responsible for the collection, processing, compatibility testing, storage, or distribution of blood or blood components are adequate in number, educational background, training, and experience to assure competent performance of their assigned functions and to

ensure that the final product has the safety, purity, potency, identity, and effectiveness it purports or is represented to possess [21 CFR § 606.20(b)]. For example,

a. During an inspection of the Heart of America Region in June-August 2010, FDA's review of adverse donor reaction procedures and cases revealed that ARC permitted Medical Director designees located in the DCSC, who had no apparent medical training, to perform the required Medical Director's review for major donor complications. The Medical Director's review includes a determination regarding donor suitability and a decision as to whether product quarantine or retrieval is necessary as required in Form 15.4,frm015, *Donor Reaction and Injury Record*, Version 1.2. Job Aid 14.4.ja164, *Final Case and Donor Suitability Assessment Code and Case Types*, Version 1.0, permits designees to perform the Medical Director's review. For example, ARC permitted DCSC staff with no medical degree, certificate or medical training to perform the Medical Director's reviews for the following adverse donor reactions:

i. An adverse donor reaction that was reported on 9/17/09, and included seizures/convulsions.

ii. An adverse donor reaction that occurred on 12/3/09, and included a long loss of consciousness and loss of bowel/bladder control.

iii. An adverse donor reaction that occurred on 1/28/10, and was reported to ARC as a large hematoma (6"x3").

In its 9/8/10 response, ARC states that when it began consolidating donor management functions in the DCSC, it decided to eliminate the requirement to have a Medical Director review all DRIRs because minor reactions account for most of the post-donation reports. ARC further states that it trained DCSC case investigators to serve as Medical Director designees for adverse reactions, including minor complications, arterial punctures, large hematomas, and long loss of consciousness. However, ARC states that, at the recommendation of the BHQ Medical Office, it decided to require a Medical Director's review of all major complications, except large hematomas. The implementation of that requirement was scheduled for 9/15/10.

FDA also notes that despite permitting designees with no medical training, certification, or experience to perform the reviews, ARC's 9/8/10 response states, "The practice of medicine requires physicians to use available resources as necessary to make their medical assessment that may or may not include an assessment of prior reactions or other medical history. Medical evaluation of donor reactions requires a case-by-case approach and medical judgment; consequently, medical practice is not defined in ARC procedures."

b. During an inspection of the Detroit National Testing Laboratory (NTL) in May-June 2010, FDA discovered that ARC did not thoroughly investigate a problem that it had detected. For example, proficiency test records for January–December 2009 were found by ARC to lack the signature of two employees on attestations that they had received the training. The NTL opened a minor risk problem (Exception E-0744002). FDA review of the records for that period found an additional 13 employees had not signed attestations. FDA also found an additional seven employees had not signed their attestations for the period 11/1/08-12/31/08.

c. During an inspection of the Detroit NTL in May-June 2010, FDA discovered that annual competency reviews[18] and/or QA reviews did not detect that employees were not correctly performing all steps of testing blood samples. One test was repeatedly performed incorrectly by many employees beginning 2007, and another test was repeatedly performed incorrectly by many employees since April 2008. FDA's review of the competency assessments for those employees performing those tests found that none failed the assessment. FDA's review of the quality process review for one of the tests found that the errors were not detected.

d. In addition to understaffing issues noted during review of records at the Philadelphia DCSC during the September-October 2010 inspection discussed in paragraphs 2(d) and (e) above, FDA observed collection staffing issues during inspections at the Heart of America Region in June-August 2010. For example, FDA observed donor survey cards for three mobile blood drives conducted on 11/6/09, 1/12/10 and 1/13/10, each of which reported dissatisfaction with ARC's staffing levels. FDA's review of the operation reports and staffing matrices for those three drives found that staffing for both was below the staffing matrices.

***GMP Violations*: Inadequate Recordkeeping**

12. Records are not maintained and/or not as detailed as necessary to contain a complete history of work performed as required by 21 CFR § 606.160. For example,

During the August-September 2010 inspection of the Southern California Region, FDA reviewed reports of potential duplicate donors and determined that investigations of potential duplicate donors are incomplete and/or not fully documented and lack documentation necessary to assess whether corrections were made. Duplicate donors are of concern because multiple donor records for the same donor may result in the release for distribution of unsuitable blood products. Therefore, it is very important to correct duplicate records as soon as possible because each day the incorrect information remains in the system increases the likelihood that an unsuitable blood product will be released. For example, Soundex Reports for 2/1/10-2/8/10, 2/9/10-2/16/10, 2/2/10-2/9/10, 3/22/10-3/29/10, 2/8/10-2/15/10, 3/8/10-3/15/10, 1/31/10-2/6/10, 2/10/10-2/17/10, and 2/4/10-2/11/10 state multiple donor pairs were determined to be false duplicates based on review of BDRs. The specific information noted during ARCs review of the related BDRs and used as the basis for the false duplicate determination is not documented.

This is not intended to be an all-inclusive list of violations in ARC facilities.

* * *

## 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

[18] Paragraph IV.C.5 requires competency reviews to "be conducted and documented, at least annually, to evaluate each employee's job performance including, when appropriate, actual performance of testing and data entry in controlled situations."

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." FDA directs ARC to do the following:

1. Within 60 days of receipt of this letter, provide a status report of each issue noted during internal audits of the DCSC since the beginning of consolidation in May 2008 and whether each issue has been effectively corrected. Please provide a justification for any open problems created as a result of an internal audit. Explain why they were not addressed promptly when the auditors found each issue.

2. Within 30 days of receipt of this letter, provide a list and a complete description of each functional team in the DCSC, including a complete list of all supplemental sites assisting with Philadelphia and Charlotte DCSC activities. Provide a status report of the staff hiring plan described in your 12/15/10 response to the Philadelphia DCSC FDA 483 issued on 10/29/10.

3. Within 90 days of receipt of this letter, re-examine the DCSC response to the ARC BHQ audit observations related to training. Report to FDA what ARC is doing to strengthen its DCSC training program given the audit observation and the lack of a corrective action plan to address training at that point in time. Explain why obvious training deficiencies were not addressed promptly and adequately at the time of their discovery by the auditors. Also, explain ARC's methodology for evaluating the adequacy of its DCSC training program.

4. Within 45 days of receipt of this letter, provide a thorough description of ARC's system for determining the staffing levels for the mobile collection drives and submit the written procedure that describes this system.

5. Within 60 days of receipt of this letter, provide a thorough description of the DCSC's operation for answering donor eligibility calls from collection sites, including the number of staff assigned to this function. Explain the use of inexperienced DCSC personnel answering donor eligibility calls from collections sites. Describe what controls ARC has implemented to ensure DCSC personnel provide accurate answers to donor eligibility calls.

6. Within 45 day of receipt of this letter, establish and implement a time frame for the Medical Director's review of DRIRs. A timely review is critical to donor safety due to the seriousness of some donor reactions. In order to ensure that the safety of the donor is not compromised, the Medical Director's review should be completed prior to allowing a donor who has experienced a donor reaction to return for additional donations.

7. Within 45 days of receipt of this letter, communicate to all collection staff personnel and management the regulatory and procedural requirements for managing and documenting donor adverse reactions. Ensure that all collection staff is adequately trained to perform this task. Report to FDA your plan to accomplish this order.

8. Within 60 days of receipt of this letter, develop a work around to assess whether a donor has prior names in the NDDR to ensure that unsuitable blood products are not distributed from donors who have prior names in the NDDR.

9. Within 60 days of receipt of this letter, perform a retrospective review of survey cards, since the time they were first issued to the date of this letter, to identify all complaints or concerns that are related to FDA regulated functions and, as required by the Decree, manage any regulated complaints/concerns

as problems. Identify all regions that issue such survey cards. Additionally explain how ARC manages such complaints and concerns that are received through the internet.

10. Within 30 days of receipt of this letter, provide copies of all Quality Process Reviews conducted at the DCSC since the DCSC began merging of the regional donor management operations. This material was requested numerous times during the September-October 2010 Philadelphia DCSC inspection. Provide a detailed explanation why the completed Quality Process Reviews were not provided to the FDA investigators during the inspection.

11. Within 60 days of receipt of this letter, provide a status report on ARC's 12/15/10 response to the Philadelphia DCSC FDA 483 issued on 10/29/10.

12. Within 30 days of receipt of this letter, provide a copy and complete description of the Modified Compliance Improvement Strategy (MCIS) that the DCSC was placed on in January 2011, as well as the status of the MCIS.

13. Within 60 days of receipt of this letter, develop and implement an SOP to require complete documentation of all information evaluated during review of any utility report including the soundex reports. Provide a copy of this SOP to FDA and include the effective date of its implementation.

14. Within 30 days of receipt of this letter, provide an explanation for the use of BPD Code QC-90-01-05 [failure to adequately manage potentially non-confirming product (product not released)] when ARC's investigation into problems determined that blood products were actually distributed. FDA noted this during the review of Exception Reports E-0780785 and E-0790730.

15. Within 60 days of receipt of this letter, review the contents of the quarterly and annual QA reports to ensure that such reports adequately convey to ARC's Biomedical Services senior management that serious problems or deficiencies are developing and/or have occurred. This would enable senior management to be aware of the potential risk of the developing problems/deficiencies to public health and the impact on ARC's compliance with the law and the Decree.

16. Within 45 days of receipt of this letter, provide a list of all facilities using the hand warmers during the blood collection process. Include details regarding: when the facilities began utilizing the hand warmers, the purpose of their use is, and why they were in use without training and a written procedure.

17. Within 45 days of receipt of this letter, evaluate the process for performing annual competency assessments and determine the reason they consistently fail to identify employees who do not perform tasks in accordance with written procedures or manufacturer's instructions. Report to FDA what steps you plan to take to ensure the assessments are adequate.

* * *

FDA has determined that ARC did not comply with the law, ARC SOPs, and the Decree, and, under paragraph IX of the Decree, FDA is fining ARC a total of $9,592,200.[19] In previous Adverse

[19] Paragraph IX.F.5. of the Decree states that "All penalties assessed under this Order shall be based on the year in which the violative conduct occurred. The annual cap amounts described in paragraph IX.F.1 of this Order shall also be attributed solely to the year in which the violative conduct occurred." To document compliance with that provision, FDA provides the

Determination Letters (ADL), FDA fined ARC $10,000 for each day on which one or more violations occurred without regard to the number of violations that occurred on a particular day. This was the method used to calculate the fine in the October 2009 Problem Management ADL. However, as FDA noted in that letter, the Decree authorizes alternate methods of calculating fines. For example, paragraph IX.A authorizes FDA to assess penalties for "each violation." Thus, FDA can charge a per diem fine for each violation instead of the single per diem charge for all of the violations collectively. Because many of the violations continued for an extended period of time, there were many days on which several violations occurred simultaneously, and thus an assessment for each violation will be considerably higher that a single per diem rate.

For the reasons explained below, FDA is assessing per diem fines separately for each of the violations as described by the following chart:

| ADL Item | Violation | Violation Timeframe | Amount per Day | Total |
|---|---|---|---|---|
| 1.a-e | Decree: Inadequate Managerial Control | 375 days *[9/2/10 (date FDA 482 issued to the Philadelphia DCSC) back to 12/6/09 = 270 days; 9/2/10 to 12/15/10 (date of ARC's FDA 483 response) = 105 days; 270 days + 105 days = 375 days]* | $6,500 | $2,437,500 |
| 2.a-f | Decree: Inadequate Quality Assurance | 375 days *[9/2/10 (date FDA 482 issued to the Philadelphia DCSC) back to 12/6/09 = 270 days; 9/2/10 to 12/15/10 (date of ARC's FDA 483 response) = 105 days; 270 days + 105 days = 375 days]* | $6,500 | $2,437,500 |
| 3 | Decree: Failure to Comply with Reporting Requirements | 58 days *[5/10/10 (date of ARC's Suspension Report) to 7/6/10 (date of ARC's FDA 483 response) = 58 days]* | $1,000 | $58,000 |
| 4.a-b | Decree: Inadequate National Donor Deferral Register | 358 days *[8/9/10 (date FDA 482 issued to the Southern California Region) back to 11/12/09 = 270 days; 8/9/10 to 11/4/10 (date of ARC's FDA 483 response) = 88 days; 270 days + 88 days = 358 days]* | $2,000 | $716,000 |
| 5.a-b 6.a-h | Decree: Inadequate Problem Management | 375 days *[9/2/10 (date FDA 482 issued to the Philadelphia DCSC) back to 12/6/09 = 270 days; 9/2/10 to 12/15/10 (date of ARC's FDA 483 response) = 105 days; 270 days + 105 days = 375 days]* | $4,000 | $1,500,000 |
| 7 | Decree: Failure to Follow SOP | 146 days *[4/3/10 (date final notification letter should have been sent) to 8/26/10 (date of ARC's FDA 483 response) = 146 days]* | $1,600 | $233,600 |
| 8.a-b | GMP: Inadequate System for the Distribution or Receipt of Each Unit of Blood | 288 days *[12/3/09 (date the DCSC notified the consignee with the incorrect unit number) to 9/8/10 (date of ARC's FDA 483 response) = 288 days]* | $1,600 | $460,800 |
| 9 | GMP: Failure to Follow Manufacturer's Instructions | 83 days *[8/13/10 (date investigators observed use of hand warmers) to 11/4/10 (date of ARC's FDA 483 response) = 83 days]* | $1,600 | $132,800 |

following information. The penalty period described in this letter includes violations that occurred in 2007, 2008, 2009 and 2010. The penalty amounts assessed as a result of the violations for each of those years is $81,600 in 2007, $964,382 in 2008, $2,839,578 in 2009, and $5,706,640 in 2010.

| | | | | |
|---|---|---|---|---|
| 10.a-g | GMP: Failure to Maintain and/or Follow Written Procedures | 375 days<br>*[9/2/10 (date FDA 482 issued to the Philadelphia DCSC) back to 12/6/09 = 270 days; 9/2/10 to 12/15/10 (date of ARC's FDA 483 response) = 105 days; 270 days + 105 days = 375 days]* | $1,600 | $600,000 |
| 11.a-d | GMP: Inadequate Training | 357 days<br>*[9/17/09 (earliest date investigator noted personnel without medical training were permitted to review adverse donor reactions) to 9/8/10 (date of ARC's FDA 483 response) = 356 days]* | $1,600 | $571,200 |
| 12 | GMP: Inadequate Recordkeeping | 278 days<br>*[1/31/10 date of earliest report of potential duplicate donors) to 9/8/10 (date of ARC's FDA 483 response) = 356 days]* | $1,600 | $444,800 |
| | **TOTAL** | | | $9,592,200 |

In arriving at this penalty amount, we have taken the following facts into account:

First, as noted above, proper QA programs by blood establishments are essential to ensure the safety of donors and the nation's blood supply by properly and promptly investigating and addressing unsafe practices and procedures; preventing the collection, manufacture, processing, packing, holding, and distribution of unsuitable blood and blood components; and identifying and effectively fixing the causes of recurrent problems. Many of the violations discussed in this letter, when not suitably addressed and corrected, implicate these concerns.

Second, during the period 10/1/09 to 12/1/10, FDA completed 42 inspections of ARC regions, National Testing Laboratories, and the DCSC facility. Of those inspections, FDA has classified nine as Official Action Indicated (OAI) and 19 as Voluntary Action Indicated; one has not yet been classified. This is the highest proportion of OAI inspections of ARC facilities since ARC entered the Amended Consent Decree of Permanent Injunction on April 15, 2003.

Third, many of the violations recounted in this letter are virtually identical to violations charged in previous ADLs. ARC has known of these continuing problems and has failed to take adequate steps to correct them.

Fourth, ARC's Biomedical Services senior management knew or should have had full knowledge of the extent of the continuous and serious violations regarding the DCSC consolidation and the lapses in QA throughout the ARC facilities no later than October 2008 when the first internal audit of the Philadelphia DCSC occurred. (See paragraph IV.B.3 which requires internal audits to be performed and results to be reported to ARC Biomedical Services senior management.) In addition, ARC held periodic senior management meetings, QCOC meetings, and Board of Governor meetings in which the DCSC consolidation project was discussed. Quarterly and annual QA and training reports were also submitted to ARC's Biomedical Services senior management. (See paragraph IV.A.2.b. and e.) As ARC acknowledged, it "did not effectively manage consolidation of the donor management functions into the DCSC" and the methods it used to oversee the consolidation and operations of the DCSC "proved to be inadequate." (12/15/10 response to the Philadelphia DCSC FDA 483.)

You should note that we have charged a higher per diem rate for the violations related to management oversight and QA to highlight the need for ARC Biomedical Services senior management to accept greater accountability and responsibility with respect to the correction and prevention of QA problems, as well as a higher per diem rate for the substantial and recurring problem management violations.

Under the Decree, FDA could have assessed penalties under alternative schedules that would have resulted in greater fines. For example, under paragraph IX.A., FDA could have penalized ARC "up to $10,000 for each violation *and* for each day described in FDA's [ADL]." (Emphasis added.) Second, under paragraph IX.F.4 of the Decree, FDA could have penalized ARC not only for the initial violations of each line employee but also for each subsequent ARC failure to detect and correct the violations (e.g., by downstream supervisors and BHQ). Finally, the Decree authorizes a per diem maximum fine of $10,000, and, as shown in the chart above, FDA has chosen smaller per diem amounts. Please note that, in future ADLs, we may choose one of these alternate methods of calculating the fine, or we may assess a different per diem amount, including the maximum allowed under the Decree, for violations similar to the ones listed in this ADL.

As provided in the Decree, if ARC agrees with this adverse determination, it shall within 20 days of receipt of this letter, notify FDA of its intent to come into compliance with the Decree and submit a plan to do so. If ARC disagrees with FDA's adverse determination, it shall respond in writing within 20 days of receipt of this letter, explaining its reason 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 200 N, Rockville, Maryland 20852.

Sincerely yours,

Evelyn Bonnin
Director, Baltimore District

Enclosures

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**ATTACHMENT B**

## Suspect Product History

1. Observation 3.c of the FDA 483 Inspectional Observations (FDA 483) issued to ARC's Biomedical Headquarters (BHQ) on April 26, 2000, cited the firm for distribution of two unsuitable blood products. The components were not stored correctly and were quarantined. The components were inappropriately released from quarantine, and ARC had to recall them. The Establishment Inspection Report states that for the period, January 1, 1999, through February 2, 2000, the FDA investigators observed 86 reports related to distribution or potential distribution of unsuitable products. In a July 21, 2000 letter, ARC stated, "Deviation reports are reviewed to determine the frequency of release of unsuitable product. In addition, QA regional staff is required to report any unsuitable releases to BHQ within 24 hours. Each incident must be immediately and thoroughly investigated, and results reported to BHQ. All information is being closely monitored to determine the existence of any weaknesses not previously identified and verify the effectiveness of corrective actions..." In a September 29, 2000 letter, ARC stated that it released a written procedure that included "... a requirement for 24-hour coverage to gain control of non-conforming materials immediately upon discovery..."

2. On October 19, 2001, FDA issued a VI.A. letter to ARC following FDA's inspection of the Lewis and Clark Salt Lake City facility. The letter cited numerous violations, including the failure to "correct known critical deviations, such as failure to...ensure that unsuitable units of blood are physically and electronically quarantined to prevent distribution of such units." ARC stated the problem was mismanaged by the Region and that "long term corrective action to prevent recurrence of this type of problem has been undertaken by Biomedical Services Headquarters." (Bates pages 025356-025357)

3. Observations 21-24 of the FDA 483 issued to BHQ on December 20, 2002, cited the firm for distribution of unsuitable blood products. The observation describes ARC's System Problem 618 opened in January 2002 after discovering that regions were distributing unsuitable blood products. ARC stated that it implemented corrective action and that it would consider implementation effective if the number of occurrences was reduced by only (b) (4) FDA issued a VI.A. letter to ARC that stated, "ARC failed to correct and prevent deviations that resulted in release and/or distribution of unsuitable blood products." ARC's April 14, 2003 response to the VI.A. letter stated, "Red Cross recognizes and understands the importance of preventing the release of unsuitable products....Over the last several years, BHQ has spent considerable time and effort to identify the factors that contribute to the release of unsuitable products and to institute corrective actions related to these sources of information." ARC committed to further investigate, develop additional corrective actions, and increase BHQ oversight." (Bates pages 028681-028683)

4. In a December 2003 submission, ARC reported to FDA that it opened System Problem 702 because "data continues to demonstrate an adverse trend in the release of suspect products. ARC described a corrective action plan that included establishing a task force, identifying the nature of the occurrences in facilities, and assessing data to develop appropriate corrective actions. (Bates pages 030099-030101) ARC also reported that it implemented corrective actions for earlier system problems related to mismanagement of suspect products and that the effectiveness checks found that the corrective actions were ineffective. (Bates pages 030733, 031383-031389)

5. On March 28, 2005, FDA issued an Adverse Determination Letter (ADL) based on violations observed during a July-August 2004 inspection of ARC's Southern California Region. The inspection revealed that the Region had distributed 20 blood products manufactured after the Region had made the decision that they were to be discarded. Until the inspection, the Region was unaware that the blood products had been distributed. In multiple response letters, ARC described corrective actions, including implementation of new procedures. In a November 30, 2005 letter, ARC stated "Although there is some improvement in performance in this area, the initial effectiveness check did not indicate a satisfactory decline in the number of problems after implementation of the System 11 documents....ARC will continue to monitor this area and develop further system-wide corrective action based on the analysis of recent problems that have occurred in this area." (Bates pages 038567-038568) In a February 7, 2006 letter, ARC discussed the results of its monitoring. The corrective actions were evaluated to determine effectiveness. Success criteria were defined by ARC as follows: "The corrective action will be deemed effective if there are no problems associated with the release of suspect products and if there are no more than [redacted] problems associated with mismanagement of suspect products during a given month for the EC evaluation period." (Bate page 039139). ARC also included in the February 7, 2006 letter a bar chart showing that it reported to FDA 92 occurrences of having distributed suspect blood products during the nine month period following receipt of the ADL, April through December 2005. ARC stated that it developed and implemented additional procedural changes and promised to "continue to evaluate the data to ensure that all root causes for mismanagement of suspect products have been identified and appropriate corrective action taken. ARC is working at the system and individual facility level toward a goal of 'first-time right' and a continual reduction in the number of suspect products that require management." (Bates pages 039145 and 039149-039150)

6. On November 21, 2006, FDA issued an ADL to ARC following the 2005 inspection of the New York Penn Region. The ADL cited ARC for failure to control suspect blood products and for failure to comply with the Decree problem management requirements during their handling of numerous related problems. ARC promised corrective action.

7. On October 30, 2009, FDA issued an ADL to ARC following multiple inspections of ARC facilities beginning February through November 2008. The ADL cited ARC again for failure to control suspect blood products and for failure to comply with the

Decree problem management requirements during the handling of numerous related problems. ARC promised corrective action.