



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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ADVERSE DETERMINATION LETTER

BY FACSIMILE & CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

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

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

Dear Mr. Hrouda:

From February through November 2008, United States Food and Drug Administration (FDA) investigators inspected twelve American National Red Cross (ARC) Blood Services facilities and observed significant violations of the law, regulations, and the Amended Consent Decree of Permanent Injunction (Decree), entered on April 15, 2003. 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 Paragraph IV.B.1. of the Decree and Title 21, Code of Federal Regulations (CFR), § 211.22(d).

Paragraph IV.B.1. of the Decree requires ARC to establish and submit to FDA a problem management standard operating procedure (PM SOP) to detect, investigate, evaluate, correct, and monitor all problems, trends, and systemic problems.<sup>1</sup> The Decree directs that the PM SOP include specific instructions to implement and document problem management requirements at ARC's Biomedical Headquarters (BHQ) as well as at the regional and laboratory facilities. As FDA informed ARC in a July 22, 2003 Adverse Determination Letter (ADL), FDA regards the PM SOP "as a first and indispensable step to enable ARC to comply with current good manufacturing practice."

<sup>1</sup> Decree 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*." Decree 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*." Decree 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*." (The italics in the quotations from the Decree are in the original and indicate that the italicized word was defined in Paragraph III of the Decree.)

ARC subsequently developed and submitted to FDA a PM SOP consisting of directives, work instructions, job aids, standards, and forms. After FDA reviewed and accepted the PM SOP, ARC implemented it on October 1, 2004.

In 2005, FDA conducted its first comprehensive evaluation of ARC's implementation of the PM SOP, with an inspection of the New York Penn Region. FDA investigators' review revealed many deviations from the PM SOP, indicating that the Region had not properly implemented and did not consistently follow the PM SOP and that BHQ did not exercise adequate control, because it had not detected the Region's widespread PM SOP deviations. FDA issued an ADL to ARC on November 21, 2006, and ordered ARC to take steps to comply with the problem management requirements of Decree paragraph IV.B.1. ARC promised corrective actions.

Beginning in February 2008, FDA conducted twelve inspections to evaluate the effectiveness of ARC's corrective actions and to assess ARC's compliance with the Decree.

The twelve inspections referred to above revealed significant violations similar to those observed during the 2005 New York Penn Region inspection. The deviations included, but are not limited to, failure to promptly conduct adequate investigations, failure to develop and implement adequate corrective actions, and failure to ensure their effectiveness to prevent recurrence of problems.

The inspections were conducted at the following ARC facilities:

ARC Biomedical Headquarters, 2025 E Street, N.W., Washington, DC, from February 5 to July 3, 2008  
Great Lakes Region, 1800 E. Grand River Avenue, Lansing, MI, from March 3 to March 21, 2008  
River Valley Region, 520 E. Chestnut Street, Louisville, KY, from April 14 to April 25, 2008  
Greater Alleghenies Region, 250 Jari Drive, Johnstown, PA, from August 29 to September 16, 2008  
Greater Chesapeake and Potomac Region, 4700 Mount Hope Drive, Baltimore, MD, from May 5 to June 23, 2008  
Lewis and Clark Region, 6616 South 900 East, Salt Lake City, Utah, from April 14 to May 23, 2008  
Penn Jersey Region, 700 Spring Garden Street, Philadelphia, PA, from July 21 to 29, 2008  
Southeastern Michigan Region, 100 Mack Avenue, Detroit, MI, from May 27 to July 2, 2008  
Portland National Testing Laboratory, 12124 NE Ainsworth Circle, Portland, OR, from July 21 to 25, 2008  
New York Penn Region, 825 John Street, West Henrietta, NY, from July 28 to September 26, 2008  
Heart of America Region, 405 W John H Gwynn Avenue, Peoria, Il, from September 10 to October 17, 2008  
New England Region, 209 Farmington Avenue, Farmington, CT, from November 12 to 24, 2008

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

**1. Failure to promptly implement adequate corrective actions to prevent recurrence of failure to control suspect<sup>2</sup> blood or blood components. FDA has repeatedly cited ARC for this deviation, including in letters issued pursuant to paragraph VI.A. of the original Consent Decree of**

<sup>2</sup> 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." (b) (4)

**Permanent Injunction entered on May 12, 1993, and in numerous 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.<sup>3</sup> For example:**

a. FDA inspected ARC's Biomedical Headquarters (BHQ) and issued an FDA 483 on July 3, 2008. The inspection revealed that, despite repeated promises to implement corrective actions to prevent problems involving distribution of suspect blood or blood components, from December 2006 through April 2008, ARC opened 116 such problems and retrieved 218 of the blood products associated with those problems.<sup>4</sup> These problems occurred in multiple ARC facilities. The associated blood or blood components were suspect because they were involved in deviations such as whole blood number mix-ups, ABO/Rh discrepancies, inadequate donor suitability determinations, potential air contamination during collection, incomplete blood product quality control and validation testing, distribution without required record reviews, and incorrect or incomplete collection records.<sup>5</sup> (FDA 483 observation 1.a) For example:

- i. (b) (4) was discovered on January 21, 2008, when ARC's Arizona Region learned that a whole blood number mix-up had not been investigated. Collection staff re-labeled the units without determining whether test results were properly associated with the correct unit and whether the units could be traced to the correct donor. Associated components of these units were improperly distributed.
- ii. (b) (4) was discovered on January 30, 2008, in the New England Region when two double Red Blood Cell units that required additional quality control testing were not controlled and were distributed without those tests having been performed.
- iii. (b) (4) was discovered on March 12, 2008, when ARC's Pacific Northwest Region learned that an incorrect donor gender was recorded on an electronic blood donation record causing the incorrect gender specific high risk behavior health history questions to be asked of the donor. The unit of whole blood was not controlled and two associated components were distributed.
- iv. (b) (4) was discovered on April 8, 2008, when ARC's Southern Region failed to place an electronic hold on a unit of blood that was designated to be discarded and the unit was distributed.
- v. (b) (4) was discovered on April 21, 2008, when ARC's Northern Ohio Region learned that a whole blood unit was potentially contaminated by exposure to air during collection and the associated products were shipped before the collections staff reported the error.

<sup>3</sup> See Attachment B for details of compliance history related to failure to control suspect blood or blood components.

<sup>4</sup> These data are not all-inclusive. They include only problems entered into ARC's current automated problem management system. (APMS) (b) (4) Problems entered into ARC's (b) (4) are not included. Beginning in 2006 (b) (4) was used concurrently with and eventually was replaced by (b) (4)

<sup>5</sup> See Attachment C for a complete list of problems and components identified during the BHQ inspection.

During the inspection, ARC provided the investigator with an April 25, 2008 memorandum that included bar charts indicating that between the second quarter of 2007 and first quarter of 2008, ARC identified 150 problems involving failure to control blood or blood components that ARC knew to be suspect and erroneously distributed. ARC's memorandum also identified an additional 659 similar failures to control such blood products, but which did not result in distribution of the suspect blood products.

ARC's August 21, 2008 response to FDA's observation from the BHQ inspection stated that it recognizes the need to control suspect blood and blood components, although it characterizes distribution as "uncommon." It also stated that it completed an analysis of problems associated with managing suspect blood products and in March 2008 opened system-wide problem (b) (4) and that training and workflow are root causes of the problem. The promised corrective actions include training and establishing core teams to manage suspect blood and blood components. However, FDA's review of reports required by Decree paragraphs X.D. and X.E. found that the problem persists. From December 1, 2008, through February 6, 2009, ARC reported to FDA 37 additional failures to control suspect blood or blood components that resulted in their distribution. These reports demonstrate that this significant problem continues.<sup>6</sup>

**b. FDA inspected ARC's Greater Alleghenies Region in September 2008 and issued an FDA 483 on September 16, 2008. The inspection revealed multiple failures to take steps to control suspect blood or blood components and one failure to promptly log, investigate, or correct such a problem. (FDA 483 observation 1) Specifically,**

i. Three whole blood units were individually identified at the collection site as overweight on January 24, 2008, January 28, 2008, and August 25, 2008.<sup>7</sup> Three components manufactured from those units were distributed on January 31, 2008, February 4, 2008, and August 27, 2008. The Region was unaware that the three components had been distributed until the FDA investigator identified the violations during the inspection. After the FDA investigator discovered that the components had been distributed, ARC notified the consignees and learned that they had been transfused.

ii. On April 25, 2008, the Region discovered that collection staff did not correctly manage an instrument alarm<sup>8</sup> on April 19, 2008, and did not take steps to control the associated suspect Red Blood Cells, (Apheresis) unit and prevent its distribution. The component was distributed on April 25, 2008. The Region failed to log the problem into the automated problem management system (APMS), investigate, or develop a corrective action plan until July 11, 2008, more than two months after the problem was initially discovered.

<sup>6</sup> A list of the problems with a summary of relevant facts is included as Attachment D.

<sup>7</sup> Collecting overweight units of blood is a potential risk to donor safety. It may also affect product quality because the anticoagulant present in the blood bag must be proportional to the amount of blood collected in order to prevent clotting. FDA classifies the health hazard associated with overweight units as "a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote." See 21 CFR § 7.3(m)(2).

<sup>8</sup> Collection equipment alarms may indicate that a unit of blood requires additional quality control testing prior to distribution, such as white blood cell counts or hematocrit determinations. In the instance cited, the collection machine alarms indicated the entire contents of the AS-3 blood collection bag had emptied into the reservoir bag. (b) (4)

In its November 20, 2008 response to FDA's inspectional observations from the Greater Alleghenies Region, ARC stated that the Region and BHQ each opened an investigation to determine appropriate corrective action for the distribution of suspect blood or blood components. The Region also held staff meetings and promised to provide additional training and instructions intended to increase control of suspect blood and blood components.

**c. FDA inspected ARC's Great Lakes Region and issued an FDA 483 on March 21, 2008. The inspection revealed that the Region failed to control suspect blood and blood components when it was notified on January 17, 2008, by ARC's Detroit National Testing Laboratory of a potential donor blood sample tube mix-up. The Region distributed two components on January 22, 2008, without first investigating whether the mix-up affected their suitability. The components were recalled more than a month later, on February 28, 2008. Although ARC assigned a major risk indicator to problem (b) (4) and documented the discovery date as January 30, 2008, as of the March 21, 2008 conclusion of the inspection, and more than three months after the initial discovery date, the Region had still not developed a formal corrective action plan, as required by ARC's PM SOP. (FDA 483 observation 1)**

In its July 30, 2008, response to the Great Lakes Region FDA 483, ARC promised to provide training regarding handling donor sample tube discrepancies and management of suspect blood products. The response also promised to "review all incidents of gaining control of products to determine whether actions taken are timely. Any further instances of unacceptable time delays in gaining control will be addressed as potential mismanagement of suspect products and each will be thoroughly investigated."

**d. FDA inspected ARC's Heart of America Region and collected records pertaining to a failure to control suspect blood products that ARC had reported to FDA under Decree paragraphs X.D. and X.E. Review of the records revealed that minor risk problem (b) (4) (b) (4) was discovered on May 6, 2008, when a reviewer observed that a collection trip scale was not identified as having been subjected to a required quality control function check.<sup>9</sup> The scale was used to collect five whole blood units on May 5, 2008. The reviewer failed to gain control of the units or associated components. That failure was discovered on June 16, 2008. The Region opened major risk problem (b) (4) to address the failure to control seven components that were manufactured from the five units of whole blood and distributed after the reviewer discovered that the quality control function check had not been performed on the scale. ARC recalled the seven components.**

**e. FDA inspected ARC's New York Penn Region and issued an FDA 483 on September 26, 2008. The inspection revealed that at least since September 2006, the Region has had a recurring problem related to failure to control suspect products (not distributed).<sup>10</sup> As of the time of the inspection, ARC was managing this major risk problem as part of a division-level problem but the problem had still not been corrected to prevent recurrence.**

<sup>9</sup> 21 CFR § 606.60(b) requires that blood scales be "observed, standardized, and calibrated" as necessary.

<sup>10</sup> Although no suspect blood products were distributed in several of these instances, the fact that necessary steps to gain control of such products were not taken or were not taken in a timely manner indicates that ARC's process continues to present the potential for distribution of suspect blood and blood components.

**(FDA 483 observation 1.a) In addition, failure to control suspect product had been previously cited as a violation in the November 2006 ADL that was issued after a 2005 FDA inspection of the New York Penn Region. For example:**

- i. Major risk trend problem (b) (4) was discovered on September 26, 2006, and closed on July 30, 2007, after the the Region deemed the corrective action successful. The Region identified the root cause of the trend problem as lack of staff understanding of the procedure for gaining control of suspect blood products, and ARC's lacks an adequate procedure.
- ii. Major risk problem (b) (4) was discovered on July 2, 2007, when blood components were labeled prior to review and approval of relevant records before distribution.<sup>11</sup> The problem was closed on September 11, 2008.
- iii. Major risk problem (b) (4) was discovered on August 29, 2007, upon discovery that a broken blood collection bag was placed in a manufacturing location instead of a disposal location. A corrective action plan was approved by the Region's Quality Assurance staff on October 11, 2007, more than 30 days after discovery. The problem was closed on February 11, 2008, after the Region deemed the effectiveness check was deemed successful.
- iv. Major risk problem (b) (4) was discovered on October 19, 2007, when blood transit time discrepancies<sup>12</sup> were noted and the associated products were not controlled. A corrective action plan was approved by Regional Quality Assurance on November 21, 2007. The problem record indicates that on July 10, 2008, nine months after the problem was discovered, the Quality Assurance staff determined that the effectiveness check was not performed in accordance with the approved corrective action plan. The problem was closed on August 20, 2008.
- v. Major risk problem (b) (4) was discovered on July 18, 2008, for failure to control a blood component associated with an Apheresis Production Record that lacked volume information and that had a special handling tie tag attached indicating it required additional evaluation. Because the component was not controlled, it was distributed without the required evaluation and resolution of the deviations. The corrective action plan was approved by the Region's Quality Assurance staff on September 11, 2008, almost two months after discovery of the problem.

Despite having identified the trend problem in September 2006, the Region has not implemented corrective actions adequate to prevent recurrence.

In its November 18, 2008 response to the New York Penn inspection, ARC acknowledged problems with control of suspect blood and blood components, but stated

<sup>11</sup>Blood and blood components that have not had a batch release review are suspect in that their suitability has not been confirmed through that review.

<sup>12</sup> Blood and blood components must be transported under conditions that ensure maintenance of product-specific temperatures. Transit times are determined during validation of blood containers to determine the maximum transit time at which blood or blood components will be maintained at the acceptable temperature when packed according to validated procedures.

the numbers of occurrences have been reduced. It stated that ARC opened another System Problem in February 2008, released a training document on May 30, 2008, and issued instructions to implement core teams by November 28, 2008. Additionally, ARC stated that a division-level corrective action plan that was developed in June 2008 required more oversight at monthly division meetings and that ARC initiated a checklist pilot.

**f. FDA inspected ARC's New England Region and issued an FDA 483 on November 24, 2008. The inspection identified two failures to control suspect blood or blood components. In these incidents, Red Blood Cells had been previously distributed, and the consignees notified the Region that they had been incorrectly packed for shipping. The Region did not take action to place an electronic hold on the components to ensure they were not re-issued. One of the components was returned to the Region by the consignee. Although the components were not re-issued in these incidents, the Region failed to follow ARC's Work Instruction (b) (4) which is a critical step to ensure that an unsuitable blood component that is returned to ARC by a consignee is not erroneously re-distributed. The Region determined that the root cause of the problem was inadequate training for the responsible employee. (FDA 483 observation 2) Specifically,**

**i. Moderate risk problem (b) (4) was discovered on March 20, 2008, when a consignee notified the Region that it received a shipping container of 16 Red Blood Cells packed in a shipping container without the required coolant. Major risk problem (b) (4) (b) (4) was discovered on September 9, 2008, when the Region discovered no electronic hold had been placed on the Red Blood Cells.**

**ii. Moderate risk level problem (b) (4) was discovered July 17, 2008, when a consignee notified the Region that it received a shipping container of 23 Red Blood Cells packed in a shipping container without the required coolant. Major risk problem (b) (4) (b) (4) was discovered on July 18, 2008, when the Region discovered it failed to place an electronic hold on the Red Blood Cells.**

In its January 29, 2009 response, the Region stated it was investigating why its Quality Assurance and Problem Management staff did not identify the failure to apply an electronic hold during management of the original two problems. The Region also reported that effective November 26, 2008, ARC implemented a requirement to establish core teams to manage suspect blood products. The Region also promised to ensure that responsible staff are trained and understand the importance of immediately gaining control of suspect blood and blood components.

**g. FDA inspected ARC's Lewis & Clark Region, Salt Lake City facility, and issued an FDA 483 on May 23, 2008. The inspection revealed that the Region failed to place electronic holds on unsuitable blood components that had already been distributed, but were subsequently designated for disposal by ARC's Material Review Board. (The Material Review Board decision was based on the discovery that the components had been electronically converted and labeled as irradiated, when in fact they had not actually been irradiated.) As stated in item 1.f, above, electronic holds must be placed on such units to**

ensure proper disposal. The Region identified the problem but took more than six months to develop a corrective action. Specifically, major risk problem (b) (4) was discovered on January 5, 2007, and the corrective action plan was not approved for implementation until July 17, 2007, more than six months later. (FDA 483 observation 8.d)

In its September 26, 2008 response to the Lewis & Clark FDA 483, ARC promised additional problem management training and increased oversight and monitoring in the Region and at BHQ.

**2. Failure to promptly, thoroughly, and adequately investigate and correct problems in accordance with the Decree and with ARC's PM SOP. In addition to the examples cited in item 1, above, FDA observed the following numerous examples:**

a. ARC failed to log into its APMS, to investigate, and to correct all problems involving collecting overweight whole blood units. Instead, in June 2006, ARC categorized such problems as "business issues" and stated that it tracked the problems outside of the APMS. Specifically,

i. FDA inspected ARC's Greater Chesapeake and Potomac Region and issued an FDA 483 on June 23, 2008. The inspection revealed that from November 2006 through May 2008, the Region collected 197 overweight units of whole blood but logged only 95 of them as problems in the APMS. In addition to not logging the other 102 occurrences, ARC did not investigate and correct them, as required. (FDA 483 observation 1) Failure to log problems into the APMS prevents effective and accurate facility and system-wide trending because this is the system used to create Monthly Summary Problem Reports (MSPR). The decree requires ARC to log all problems into APMS, and also requires both trending and the MSPRs.<sup>13</sup>

Approximately 18 months earlier, on January 30, 2006, FDA issued an FDA 483 to the Region that also cited its failure to correct and prevent the collection of overweight units. The Region's March 30, 2006 response to that observation promised corrective action.

During the June 2008 inspection, the Region informed FDA that on June 26, 2006, it received instructions from ARC BHQ stating that all overweight units need not be managed as problems. The written instruction stated that when overweight units were detected and documented in Collections before the unit is released by Collections, "entry of a problem in APMS is not required. These are business issues and are managed in a separate system." ARC BHQ's June 2006 instructions did not comply with Decree requirements for problem management. Collecting overweight units is a deviation from ARC's own SOPs and from the collection set manufacturer's Instructions for Use; therefore, each occurrence meets the Decree definition of "problem" and must be managed accordingly.

<sup>13</sup> Decree paragraph IV.B.1.a. requires ARC to have a "...*Problem Management System* that shall be used for logging, tracking, and trending all *problems*...In addition, each *ARC region and laboratory* shall, every 30 days, submit a *Summary Problem Report* to *ARC Biomedical Headquarters*. The *Summary Problem Report* shall, at a minimum, include each category of *problems* that occurred since the *last Summary Problem Report*...The categories shall be specific enough to enable *ARC Biomedical Headquarters* to determine whether a *trend* exists." Decree paragraph IV.B.1.b requires ARC Biomedical Headquarters to analyze and investigate Summary Problem Reports "to discover trends and system (*systemic*) problems."

In its August 29, 2008 response letter, the Region stated that ARC issued its June 2006 instructions “in good faith.” However, FDA notes that in November 2007, ARC submitted to FDA a *proposal* to modify the PM SOP to exclude certain “self-identified” problems from the Decree Definition of “problem.” ARC *proposed* excluding discrepancies that occurred during blood collection and “...the discrepancy is detected and controlled or corrected...before or during a prescribed process review.”<sup>14</sup> ARC did not inform FDA that it had already implemented this *proposed* exclusion for overweight units of blood. The Region’s August 29, 2008 response also stated that ARC issued new instructions to begin logging overweight units into the APMS effective September 30, 2008.

Additionally, on January 30, 2009, ARC reported to FDA that for an undetermined length of time, the Region had been excluding another category of problems from the PM SOP requirements (ARC Significant Corrective Action Report (b) (4)). Those problems involved autologous or directed units of blood that have labeling discrepancies. The number of occurrences is undetermined, and the Region has not maintained documentation related to the discrepancies or its communications with consignees.

ii. During the September 2008 inspection of ARC’s Greater Alleghenies Region referenced in item 1.b above, FDA discovered that from January 1, 2008, through August 31, 2008, the Region collected 75 overweight whole blood units and failed to log in the APMS, investigate, correct, and trend any of those problems. (FDA 483 observation 2.a) As stated in item 2.a.i. above, ARC BHQ had instructed Regions in June 2006 to cease managing overweight units as problems when they were discovered at the collection site.

In its November 20, 2008 response, the Region stated that ARC BHQ issued a June 2006 directive to cease logging overweight units identified at collection sites unless the overdraw was due to an equipment malfunction. ARC said the instructions were issued “in good faith with the belief that this was a self-detected error that did not need to be captured as a problem.” However, as discussed in item 2.a.i, above, in November 2007, ARC submitted a *proposal* to modify the PM SOP to exclude certain “self-identified” problems from the PM SOP requirements, but did not inform FDA that it had already implemented that exclusion for overweight units of blood.

The Region also stated in its response that it had investigated the 75 overweight units and determined that 59 of them were within the collection set manufacturer’s weight range; therefore, they do not meet the Decree definition of a “problem.” However, the Region did not provide any details or evidence to support its determination that the units met weight specifications at the time of distribution. Additionally, the determination is inconsistent with the statement made during the inspection by the Region’s Quality Director (RQD) to the FDA Investigator. The FDA Investigator asked the RQD whether the 75 units were truly overweight, and the RQD informed the Investigator that they were overweight.

<sup>14</sup> See ARC’s November 28, 2007 submission at Bates pages 0865269. In its October 15, 2008 submission ARC modified its *proposal* to include overweight units as an example of a “self-detected” discrepancy that is a “problem,” as defined in the Decree and which must be managed in accordance with the PM SOP. (See Bates page 086703.)

**b. ARC failed to promptly and thoroughly investigate problems. For example:**

i. During the October 2008 inspection of ARC's Heart of America Region referenced in item 1.d above, FDA discovered that ARC had not thoroughly investigated a system-wide problem related to entering incorrect donor gender into its electronic blood donation records (eBDR) system.<sup>15</sup> Specifically, ARC has not documented its investigation and conclusion regarding feasibility of a retrospective donor record review to identify donors assigned incorrect gender. (FDA 483 observation 1)

The ARC system-wide incorrect donor gender problem originated with the January 2006 implementation of eBDR. The entry of incorrect donor gender resulted in an undetermined number of problems and distribution of an unknown number of blood components that were collected from donors whose suitability to donate had not been properly evaluated. At Bates page 085359 of its December 14, 2007, Quality Assurance Report submitted to FDA, ARC stated, "While many problems in completing the BDR were eliminated through the introduction of automation, the Red Cross continues to have problems with fields on the BDR that require manual documentation.... If the gender of a donor is incorrectly entered into eBDR, an issue occurs where all required questions for a donor's true gender are not displayed. This issue resulted in 209 Violative BPD reports being filed between January 2006 and September 2007." At Bates page 087266, of its December 15, 2008 Quality Assurance Report, ARC stated, "This issue is unique to the use of eBDR in that if the gender is incorrectly entered into eBDR, all the required questions for the donor's true gender will not be displayed in eBDR. This problem may also occur due to an erroneous gender selection in (b) (4) (b) (4) from a prior donation. To date this problem has resulted in 437 Violative BPD Reports being filed due to the fact all the required health history questions were not asked of the donor. Often these problems are not discovered until the donor returns to donate at a later date."

On May 12, 2008, ARC implemented a software revision to prevent recurrence of gender errors; however, its investigation of the problem has not addressed its full scope, such as the number of unsuitable blood products distributed and the number of incorrect donor records created since 2006. ARC has not documented whether it took steps to determine the feasibility of a retrospective donor record review, and it has not documented its rationale for not performing such a review. Instead, it is relying on identifying such errors upon return of the donors. Therefore, these problems go undetected until the next donation or completely undetected if donors never return to donate. For example:

A. Moderate risk problem (b) (4) was discovered on April 9, 2008, when the donor returned and it became apparent that incorrect gender-specific health history questions were asked on the previous donation. Two components from a June 2007 donation were distributed and recalled by ARC.

<sup>15</sup> 21 CFR § 640.3(a) requires that whole blood donors be evaluated for suitability by means of medical history, as well as other means. 21 CFR § 606.160(a)(2)(i) requires a record of "donor selection, including medical interview and examination." ARC's eBDR automatically generates gender-specific health history questions based on the gender entered into eBDR during the donation process. One of the gender-specific questions for male donors pertains to sexual contact with other males. FDA's current policy regarding such high risk behavior is that such donors must be permanently deferred from donation.

B. Although not listed on the FDA 483, the inspection also included a review of moderate risk problem (b) (4) which was discovered on April 10, 2008, when the donor returned and it became apparent that incorrect gender-specific health history questions were asked on the previous donation. Two components from an April 2006 were distributed and recalled.

C. Moderate risk problem (b) (4) was discovered on May 30, 2008, when the donor returned and it became apparent that incorrect gender-specific health history questions were asked on the previous donation. Two blood components from a November 2007 donation were distributed and recalled by ARC.

D. Moderate risk problem (b) (4) was discovered on June 26, 2008, when the donor returned and it became apparent that incorrect gender-specific health history questions were asked on the previous donation. Two blood components from an April 2008 donation were distributed and recalled by ARC.

The Region's December 5, 2008 response acknowledged that ARC conducted no retrospective review. It stated, "The Red Cross (b) (4) (b) (4) do not contain information that would allow the identification of a donor with an incorrect gender. Verification of gender information would require contacting all donors to confirm their information. Given the number of records in the (b) (4) donor database, this undertaking is not feasible. A record review was considered and determined to be infeasible, but the decision and rationale was not documented." The response is inadequate because it provides no details regarding how ARC investigated and concluded that a retrospective record review is not feasible, including who was involved in the discussion, who made the decision, and what options were examined for performing the retrospective review. The response further asserted that there is no medical risk associated with incorrectly evaluating donor suitability using the wrong gender-specific health history questions.<sup>16</sup>

However, FDA classifies the health hazard associated with transfusable blood products collected from donors who have not been asked the correct gender-specific questions as "a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote." See 21 CFR § 7.3(m)(2). Additionally, 21 CFR § 606.100(b)(i) requires ARC to have a written procedure establishing the criteria used to determine donor suitability, including acceptable medical history criteria, and 21 CFR § 211.100(b) requires ARC to follow such written procedures. According to 21 CFR § 640.3(b), blood donors must also be determined to be free from any disease transmissible by blood transfusion, insofar as can be determined by history and examination.

<sup>16</sup> In support of that assertion, the response stated that during a March 2006 Blood Products Advisory Committee meeting, ARC and two other blood banking organizations requested that FDA change the permanent deferral requirement to a 12 month deferral for males who provide a "yes" answer to a question regarding sexual contact with another male. FDA has not changed its policy requiring permanent deferral for donors who provide an "yes" answer to that health history question.

FDA also notes that after the May 12, 2008 implementation the eBDR software revision, ARC has reported recurrences of distribution of unsuitable blood products due to the recording of incorrect donor gender.<sup>17</sup>

ii. FDA inspected ARC's River Valley Region and issued an FDA 483 on April 25, 2008. The inspection revealed that the Region failed to promptly investigate and develop a corrective action plan for a trend problem discovered on January 24, 2008. Specifically, moderate risk trend problem (b) (4) was discovered for incomplete, incorrect, or not reviewed Apheresis Alarm Logs. The inspection found that the problem investigation had not been completed, three months after initial discovery of the problem. (FDA 483 observation 1.b)

The Region's July 17, 2008 response stated that corrective actions were "recently" approved and were scheduled to be implemented in August 2008. It also reported that the Region did not have enough staff trained to perform problem trending. The response further stated that a staffing deficiency was addressed by May 29, 2008.

iii. FDA's June 2008 inspection of the Greater Chesapeake and Potomac Region revealed that it failed to conduct a thorough investigation to determine the root cause for the improper distribution of units that were associated with a whole blood number mix-up.<sup>18</sup> (FDA 483 observation 4.b.i) Specifically, major risk problem (b) (4) was discovered on December 18, 2007 when the Region was notified by a consignee of a whole blood number mix-up. The Region's investigation did not determine why the mix-up had not been detected during verification steps required in ARC's SOP, (b) (4) (b) (4)

The Region's August 29, 2008 response stated that by September 30, 2008, ARC reviewed whole blood number mix-ups to determine whether a system-wide corrective action was warranted. It also stated that ARC is holding current Good Manufacturing Practice workshops for supervisors and that by August 31, 2008, it will designate separate areas for labeling supplies, labeling area, and labeled collection sites.

**c. ARC failed to comply with the PM SOP Work Instruction (b) (4) (b) (4) which requires ARC to develop a formal corrective action plan for all trends and for moderate and major risk problems. Without FDA's approval, ARC implemented the use of "non formal CAPs" in 2006. In November 2007, ARC submitted to FDA a proposal to modify the Work Instruction, but did not inform FDA that it had already implemented the modification in 2006. For example:**

<sup>17</sup> See Attachment E for a list of donor gender problems reported to FDA from December 2008 and January 2009.

<sup>18</sup> Whole blood number mix-ups present a significant potential health hazard to blood recipients because blood and blood components collected from a donor who subsequently is determined to be unsuitable for donation must be traceable. The whole blood number assigned to each donation is the method of maintaining that traceability. For example, if a donor has a positive viral marker test, but the incorrect whole blood number was placed on a blood component, the positive component could be distributed and transfused. Relating the correct donor to the correct unit is a critical step in blood collection and processing. 21 CFR §606.160(b)(1)(vii) requires the maintenance of records to relate the donor with each previous donation from that donor. 21 CFR § 606.140(c) requires adequate identification and handling of all test samples so that they are accurately related to the specific unit of product being tested, or to its donor, or the specific recipient. 21 CFR § 606.121(c)(3) requires the blood container label to include the donor, pool, or lot number relating the unit to the donor. 21 CFR § 640.4(e) requires each unit of whole blood to be marked or identified by number or symbol to relate it to the individual donor.

i. During the June 2008 inspection of the Greater Chesapeake and Potomac Region referenced in item 2.a.i above, the FDA Investigator reviewed four major risk problems involving distribution of suspect blood components. The components were each distributed prior to a review of pertinent records, as required by 21 CFR § 606.100(c). ARC did not perform an adequate investigation of the four problems and did not develop formal corrective action plans for three of the problems, as required by the WI (b) (4) (FDA 483 observation 3) Specifically,

A. Major risk problem (b) (4) was discovered on December 31, 2007, for ten Red Blood Cells, Leukoreduced, Irradiated units that were distributed without a required second person review on November 22, 2007.<sup>19</sup> The Region did not perform a root cause analysis and did not develop a formal corrective action plan. Quality Assurance staff approved and closed the problem on March 4, 2008. Additionally, the investigation was inadequate because it did not address why the supervisor did not discover that lack of review until nine days after distribution. In its August 29, 2008 response, the Region promised corrective action.

B. Major risk problem (b) (4) was discovered on May 14, 2007, for an ABO discrepancy associated with a whole blood number mix-up. The Region's initial investigation did not address whether responsible staff performed a label verification step that is required by ARC's Work Instruction (b) (4) (b) (4) and Work Instruction (b) (4) (b) (4). On November 29, 2007 (six months after the discovery date), the Region opened a second investigation that did address the label verification. The Region did not develop a formal corrective action plan. Quality Assurance staff approved and closed the problem on January 24, 2008. The Region's August 29, 2008 response stated that it identified no additional whole blood number mix-ups that occurred at apheresis collections.

C. Major risk problem (b) (4) was discovered on October 1, 2007, for failure to perform required record reviews resulting in failure to discover that quality control function checks were not performed on three collection scales. The scales were used during collection of 122 platelets units, of which 12 were distributed. The investigation was inadequate because it did not include a root cause analysis, as required by ARC's Work Instruction, (b) (4) (b) (4) and it did not address why the 12 units were distributed before the errors were detected by supervisory record review. Supervisory review of quality control records is required before releasing components to labeling, according to ARC's (b) (4) (b) (4). Additionally, the Region did not develop a formal corrective action plan. Quality Assurance staff approved and closed the problem on January 27, 2008.

<sup>19</sup> 21 CFR 606.100 (c) requires that "All records pertinent to a lot or unit maintained pursuant to these regulations shall be reviewed before the release or distribution of a lot or unit of final product."

The Region's August 29, 2008 response stated that the problem represents an isolated incident; however, FDA notes that items 2.b.i.A and 2.b.i.B, above also involve failure to perform required record reviews prior to product distribution. Additionally, FDA had issued an ADL to ARC on June 3, 2008, citing failure to review manufacturing records prior to distribution of blood products in two other ARC Regions.

ii. During the same inspection of the Greater Chesapeake and Potomac Region, FDA discovered that in November 2006 the Region identified an adverse trend in whole blood number mix-ups, but failed to develop a formal corrective action to prevent recurrence. (FDA 483 observation 4.a and 4.b.ii) Additionally, during this inspection FDA learned that the failure to develop formal corrective action was a result of the 2006 system-wide modification to the PM SOP that ARC had not previously disclosed to FDA, as stated above. (FDA 483 observation 6) Specifically,

A. Trend problem (b) (4) was identified in November 2006 for whole blood number mix-ups. ARC's investigation of this trend problem was not adequate because it did not determine why the mix-up had not been identified during the verification steps required by ARC's standard operating procedure, (b) (4). Additionally, the Region did not develop a formal corrective action plan. The Region's justification for not developing a formal corrective action plan was "(b) (4) (b) (4) query for the time period 11012006 through 12222006, there have been no further occurrences of this type...." However, FDA's record review found that 15 such mix-ups occurred after the trend had been identified.

B. Major risk problem (b) (4) was discovered on February 14, 2008 for a whole blood number mix-up. The Region did not develop a formal corrective action.

The Region's August 29, 2008 response stated that it assembled a team to address whole blood number mix-ups in collections and manufacturing. It promised to "reduce number of WBN mix-ups and increase the likelihood of detecting them should they occur." It referred to the proposed PM SOP modifications it submitted to FDA and stated that on August 13, 2008, discussions were held with Regional and Division Quality Assurance staff regarding when a formal corrective action may not be necessary. However, the response did not acknowledge that in letters dated June 13, 2008, and July 22, 2008, FDA informed ARC that it did not concur with ARC's *proposal* to cease developing formal corrective actions for each major and moderate risk problem.

iii. During the March 2008 inspection of ARC's Great Lakes Region referenced in item 1.c, the Investigator found that the Region failed to develop a formal corrective action plan for a major risk problem involving an employee competency assessment failure. Specifically, minor risk problem (b) (4) was discovered on May 30, 2007, when an employee failed the competency assessment for donor hematocrit determination.

Six months later, on December 3, 2007, Quality Assurance staff reviewed the problem and determined that the scope of the record review and investigation was inadequate and that the problem should have been assigned a major risk indicator. On December 3, 2007, the region opened major risk problem (b) (4) for the same problem but still did not develop a formal corrective action plan. The problem record states the problem is related to specific staff and that the employee had ongoing performance problems. Additionally, the problem record indicates the Region had difficulty determining the scope of the problem. No formal corrective action had been proposed for the problem as of March 7, 2008, more than 11 months after initial discovery of the problem. (FDA 483 observation 3)

The Region's July 30, 2008 response to the FDA 483 described corrective actions, including organizational changes, filling vacancies, developing guidelines, coaching, and immediately convening Material Review Boards to define the scope of problems. The response did not address failure to develop formal corrective actions.

iv. FDA inspected ARC's Portland National Testing Laboratory (NTL) and issued an FDA 483 on July 25, 2008. The Portland facility failed to develop formal corrective actions for two major risk problems involving invalid test results due to technician errors. No associated blood products were distributed. (FDA 483 observation 1) Specifically,

A. Major risk problem (b) (4) was discovered December 25, 2007, for an invalid HIV/HCV nucleic acid test (NAT). The NAT was invalidated because the incubation time was exceeded. The problem investigation determined that the error was an isolated incident due to the Christmas shift and staff being "over-tired." The corrective action was to transfer the staff member to part-time. However, because the facility did not develop a formal corrective action plan, no effectiveness check was planned to ensure that merely transferring the employee prevented recurrences of such errors. The facility Quality Assurance staff closed the problem on January 4, 2008.

B. Major risk problem (b) (4) was discovered May 9, 2008, for an invalid ABO/Rh/TP/CMV test due to a technician error. An invalid whole blood number was manually entered into an (b) (4) analyzer. Laboratory quality control staff did not detect the incorrect whole blood number, approved the batch, and received a duplicate result message. The problem investigation attributed the error to an isolated performance issue and the NTL did not develop a formal corrective action plan.

The facility's September 11, 2008 response indicated that ARC was working to resolve a conflict in the PM SOP related to formal corrective actions. It referred to a proposed modification submitted to FDA. However, on June 13 and July 22, 2008, FDA issued letters to ARC rejecting those modifications.

**d. ARC failed to promptly develop and implement corrective actions and ensure that corrective actions are adequate to prevent recurrence of the problem.<sup>20</sup> For example:**

<sup>20</sup> Decree Paragraph IV B.1 requires ARC to promptly correct problems to prevent their recurrence. ARC's Work Instruction (b) (4) requires that it develop corrective action plans within 30 days of discovery of major risk, moderate

i. During the March 2008 inspection of ARC's Great Lakes Region referenced in items 1.c and 2.c.iii, the Investigator found that the Region failed to promptly implement corrective actions related to a whole blood number mix-up. Specifically, ten months after initial discovery of major risk problem (b) (4) it was still open, pending completion of a corrective action plan. The problem was discovered on May 4, 2007, when a consignee notified the Region of an ABO/Rh discrepancy that was determined to have resulted from a donor sample tube mix-up or blood unit mix-up. As of March 8, 2008, the Region had no documentation of having completed corrective actions, including recording the correct ABO/Rh in the donor electronic records. Quality Assurance staff approved the corrective action plan on August 30, 2007. In November 2007, an extension was requested to complete the corrective action implementation until December 2007. However, the corrective action only involved reviewing the problem with the staff member and monitoring performance. Additionally, there is no information in the problem record indicating that the Region considered that the ABO/Rh in the donor electronic records should be corrected. (FDA 483 observation 4)

The Region's July 30, 2008 response to the FDA 483 stated that corrective actions were implemented and a training session was held with staff. The ABO/Rh test results were changed in the donor record on March 10, 2008, after the Investigator had brought the matter to ARC's attention. The response also promised additional guidelines for problem management oversight.

ii. During the April 2008 inspection of ARC's River Valley Region referenced in item 2.b.ii, the Investigator discovered that the Region failed to perform an additional investigation and develop additional corrective actions following a failed effectiveness check for a problem discovered on February 23, 2007. The problem had not been corrected as of April 17, 2008, approximately 14 months after ARC initially discovered it. Specifically, moderate risk trend problem (b) (4) was discovered on February 23, 2007, for an incomplete or incorrect Apheresis Donor Continuous Record. The corrective action plan was developed and approved by Quality Assurance on April 6, 2007. Although the effectiveness check was completed on June 14, 2007, and did not meet success criteria, the Region took no further action. The problem was still open and uncorrected more than a year after discovery. (FDA 483 observation 1.a)

The Region's July 17, 2008 response to the FDA 483 promised additional problem management oversight and a retrospective review to identify other uncorrected problems with unsuccessful effectiveness check results.

iii. During the May 2008 inspection of the ARC's Lewis & Clark Region Salt Lake City facility referenced in item 1.g, FDA found that the Region had failed to promptly develop a corrective action plan for a moderate risk trend problem discovered on December 19, 2006. The corrective action plan was approved by Quality Assurance six months after discovery of the problem. The problem remained open at the time of the inspection, approximately 17 months after its discovery. Specifically, trend problem (b) (4) was discovered on December 19, 2006 for problems involving incomplete or

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risk, and trend problems. Work Instruction (b) (4) requires that ARC develop and perform effectiveness checks for major risk, moderate risk, and trend problems.

incorrect collection site daily set-up function check forms. Quality Assurance rejected the corrective action plan, but the problem manager was not made aware of the rejection. No additional action was taken until June 2007. The corrective action plan was approved on June 15, 2007 and implemented in August and September 2007. The problem was still open as of May 2008. The Region's September 26, 2008 response to the FDA 483 stated that a workshop was held on August 29, 2008, to address timeliness of corrective actions. (FDA 483 observation 2)

iv. The Lewis & Clark Region Salt Lake City inspection also revealed that the Region had failed to promptly correct problems due to repetitive cycles of granting extensions for the 30 day time frame for developing corrective action plans and subsequently rejecting those plans. (FDA 483 observation 7) For example:

A. Major risk problem (b) (4) (staff performing blood donation record review without receiving required training) was discovered on December 26, 2006. An extension was granted by the Region's Quality Assurance staff to exceed the 30 day time frame to develop a corrective action plan. The corrective action plan was submitted to Quality Assurance in May 2007 and rejected twice. Five months after initial discovery of the problem, the Region approved the corrective action plan on May 29, 2007, and implemented it in September 2007. The problem was closed in November 2007.

B. Moderate risk problem (b) (4) (product quality control deviations) was discovered on February 4, 2007. The corrective action plan was rejected three times and finally approved on April 4, 2007, two months after ARC initially discovered the problem. However, no corrective action is described in the problem record. The record states the staff now knows how to do the task. Although the effectiveness check results met ARC's success criteria, the problem was not closed until October 2, 2007, six months after initial discovery of the problem.

C. Major risk problem (b) (4) (a whole blood number mix-up) was discovered on August 21, 2007. The corrective action plan was submitted to Quality Assurance CAP and rejected in September 2007. It was re-submitted to Quality Assurance and approved in December 2007, approximately six months after ARC initially discovered the problem. The Region's September 26, 2008 response to the FDA 483 promised increased oversight and problem management monitoring.

v. FDA inspected ARC's Southeast Michigan Region and issued an FDA 483 on July 2, 2008. The inspection revealed that the Region did not complete effectiveness checks in a timely manner to ensure that corrective actions were effective to prevent recurrence of problems. (FDA 483 observation 2) For example:

A. Moderate risk problem (b) (4) (failure to verify expiration dates prior to release of seven leukoreduced Red Blood Cell units) was discovered on July 3, 2007. The target date for the effectiveness check was November 5, 2007, but the problem manager did not review the effectiveness check documentation until

March 6, 2008. It was sent to Quality Assurance for approval on June 5, 2008, seven months after the target date.

B. Major risk problem (b) (4) (when a consignee received a pooled platelet with a label lacking the number of units in the pool<sup>21</sup>) was discovered on November 23, 2007. The effectiveness check target date was April 30, 2008. It was not completed as of June 13, 2008, more than one month after the target date.

C. Moderate risk problem (b) (4) (four blood components released prior to supervisory review of the irradiation batch record) was discovered on June 15, 2007. The effectiveness check was due on January 14, 2008, but was not completed until June 5, 2008, more than five months after the target date. The problem was still open as of June 9, 2008.

The Region's September 12, 2008 response stated that effectiveness checks were completed as of August 1, 2008. The Region conducted a review to identify other late effectiveness checks and completed those by August 31, 2008. Since June 30, 2008, the Region began monitoring effectiveness checks using its APMS. Since July 29, 2008, the Region has been generating routine reports. As of July 3, 2008, ARC BHQ directed all facilities to use that method to monitor effectiveness check completion.

vi. The inspection of the Southeast Michigan Region also revealed failures to promptly develop corrective action plans. FDA found that time frames to develop corrective action plans were not met due to repetitive cycles of granting extensions for the 30 day time frame for developing corrective action plans, reviewing the corrective action plans in an untimely manner, and subsequently rejecting those proposed plans. (FDA 483 observation 1.a, 1.b, 1.c) Specifically,

A. Major risk problem (b) (4) (a transporter checklist that was missing whole blood number ranges) was discovered on February 26, 2008. Four associated blood components were not placed on hold and were distributed. (The Region thus failed to control suspect blood and blood components.) The Region granted itself time frame extensions for corrective action plan development and its Quality Assurance staff rejected the proposed plans. The problem was still open on June 6, 2008, more than three months after ARC initially discovered the problem.

B. Major risk problem (b) (4) (post-donation information was received from an autologous donor and the unit was not placed in quarantine) was discovered on December 12, 2007. The Region's Medical Director determined that the unit should be discarded. The proposed corrective action plan was rejected by Quality Assurance staff, re-submitted, and approved on March 19, 2008, more than three months after ARC initially discovered the problem.

<sup>21</sup> The number of units in the pool must be on the label to aid in identifying all whole blood numbers in a pool in order to maintain traceability.

C. Moderate risk problem (b) (4) (a platelet pool with an initial positive bacterial test result) was discovered on February 27, 2008. No assertions were applied to the donors' (b) (4) records to indicate that they were potentially implicated in the initial positive test result. The proposed corrective action plan was rejected twice by the Quality Assurance staff. As of June 16, 2008, more than four months after ARC initially discovered the problem, no corrective action had been approved.

The Region's September 12, 2008 response to the FDA 483 stated that corrective action plans for these problems were approved by July 31, 2008. Beginning on July 18, 2008, the Region has been documenting agreed-upon re-submission dates for rejected corrective action plans and ensuring appropriate oversight for rejected plans. ARC BHQ issued a communication regarding target dates to re-submit corrective action plans.

vii. FDA inspected ARC's Penn Jersey Region and issued an FDA 483 on July 29, 2008. The inspection revealed that the Region failed to promptly develop corrective action plans for three moderate risk trend problems that had occurred between nine and five months earlier. The Region granted itself time frame extensions and Quality Assurance staff rejected corrective action plans. As of July 29, 2008, the Region had taken no further actions to correct the problems. (FDA 483 observation 1) For example:

A. Trend problem (b) (4) (plasma preparation tubes without gel separator) was discovered on October 30, 2007.

B. Trend problem (b) (4) (apheresis collection device defects) was discovered on March 4, 2008.

C. Trend problem (b) (4) (unacceptable or undocumented donor temperatures) was discovered on March 4, 2008.

The Region's September 30, 2008 response to the FDA 483 stated that it took steps to strengthen its problem management process in the Region, including establishing biweekly meetings for PM staff. The Region promised to develop a plan by November 1, 2008, to increase oversight of problem management PM in the Region, including setting specific performance goals.

viii. During the inspection of the Great Lakes Region, FDA observed that the Region failed to develop a corrective action plan within 30 days of discovering that it had not applied an electronic hold to a suspect blood component and notified consignees within 48 hours of initially learning that it had distributed an unsuitable blood component, as required by Decree paragraph X.E. Specifically, on December 4, 2007, the Southern California Region notified the Great Lakes Region that it received post-donation information regarding a blood donor's suitability to donate. The Great Lakes Region had transferred a unit of Fresh Frozen Plasma from the Southern California Region and distributed it on July 13, 2007. Great Lakes did not apply a hold to the unit on December 4, 2007. The Region also did not notify the consignee. The Region opened major risk problem (b) (4) on January 1, 2008. As of March 4, 2008, the Region had not

developed a corrective action plan. Regional Quality Assurance staff granted an extension to develop the corrective action plan to allow for additional “discussion with staff.” Quality Assurance then rejected the plan on February 28, 2008.

The problem investigation determined the root cause was “Staff involved did not think this situation applied to the procedure for consignee notification and gaining control of the unit.” The rejected corrective action plan was to review procedures and provide a training session. Additionally, neither the investigation, nor the rejected corrective action plan addressed verifying consignee notification when ARC blood or blood components are transferred between Regions. Further, neither ARC’s investigation, nor the proposed CAP, addressed the lack of an SOP requiring verification of consignee notification and retrieval in such instances. (FDA 483 observation 2.c)

The Region’s July 30, 2008 response to the FDA 483 stated that ARC was revising its SOP pertaining to transferred blood and blood components and consignee notification. It also promised to provide system-wide training for controlling suspect blood products by May 30, 2008. The response disputed the lateness of the corrective action plan; however, the Decree Paragraph IV.B.1. requires prompt correction of problems and ARC’s record does not justify providing multiple time frame extensions.

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

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## ORDERS

Paragraph VIII of the Decree provides that “[i]n the event that FDA determines, based upon inspection... review of ARC records, or other information that comes to FDA’s attention ... that ARC is not following any SOP that may affect donor safety or 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 ... FDA may order ARC to come into compliance with the law, ARC SOPs, or this Order, assess penalties, and/or take any step that FDA deems necessary to bring ARC into compliance with the law, ARC SOPs, and this Order.” FDA directs ARC to do the following:

1. Commencing with the first full calendar month following receipt of this letter, provide to FDA each month thereafter a summary of problems involving failure to control suspect blood products. Such reports shall identify the responsible Region; provide a factual description of the occurrence, the dates of occurrence and discovery, the number of affected blood products, and the corrective action plan; state whether and when consignees were notified; and include a copy of the corrective action plan.
2. Within 30 days of receipt of this letter, provide to FDA all records related to System Problem (b) (4) opened in March 2008 to address failure to control suspect products. Also report to FDA the status of all corrective actions associated with System Problem (b) (4) and provide current statistics involving mismanaged suspect blood product, including the number of erroneously distributed units of blood or blood components.
3. Perform a retrospective review to identify all overweight units collected in each region beginning with the date that BHQ instructed the Regions that overweight units do not need to be managed as

problems in accordance with the Decree. Report the results of that review to FDA within 90 days of receipt of this letter. Also, report whether ARC has excluded other problem categories from the Decree problem management requirements. If there have been other exclusions, perform a similar retrospective review and provide the results to FDA within 120 days of receipt of this letter.

4. Conduct a study to determine the feasibility of a retrospective review of the (b) (4) (b) (4) and Blood Donation Records to identify donors whose gender was incorrectly entered and who were not screened correctly as a result of that error. The scope of the retrospective review must include January 2006 through implementation of (b) (4). Report the results of the feasibility study to FDA within 60 days of receipt of this letter. Additionally, provide a list of all donor gender-related problems that have occurred after the May 12, 2008 (b) (4) implementation date.

\* \* \*

For the reasons stated above, FDA has determined that ARC did not comply with the law, ARC SOPs, and the Decree. FDA regards the violations discussed in this letter to be significant. We are continuing our evaluation of fines and alternate or additional regulatory measures, and our decision on those matters will be communicated to you separately. However, we decided to send you this ADL at this time to notify you of the violations that we found so that you would take appropriate action to address them and to issue the orders set forth above.

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., Acting Director, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852.

Sincerely yours,



Evelyn Bonnin  
Director, Baltimore District

Attachments

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