Fatalities Reported to FDA Following Blood Collection and Transfusion

Annual Summary for Fiscal Year 2014

I. Background

As mentioned in the previous annual summaries of fatalities reported to the Food and Drug Administration (FDA), the blood supply is safer today than at any time in history. Due to advances in donor screening, improved testing, automated data systems, and changes in transfusion medicine practices, the risks associated with blood transfusion continue to decrease. Overall, the number of transfusion related fatalities reported to the FDA remains small in comparison to the total number of transfusions. In 2011, for example, there were approximately 21 million blood components transfused.[1] During the proximate period of Fiscal Year (FY) 2011, there were 58 reported transfusion related and potentially[2] transfusion related fatalities, with subsequent reports of 65 in FY2012, 59 in FY2013 and 56 in FY2014.

FDA's Center for Biologics Evaluation and Research (CBER) is distributing this summary of transfusion fatality reports received by the FDA to make public the data received in FY2014, to provide the combined data received over the last five fiscal years, and to compare the FY2014 report to the fatality reports received in the previous four fiscal years.[3] We also include information on the infrequent reports of post-donation fatalities. Throughout this report we note changes over time, but the reader should interpret these changes cautiously, given the small numbers of reports and inherent variations in reporting accuracy. The significance of shifts in numbers derived from small populations may appear to be greater than they really are.

Refer to Sections 606.170(b) and 640.73 of Title 21, Code of Federal Regulations (21 CFR 606.170(b) and 21 CFR 640.73), for fatality reporting requirements. For information regarding the notification process, see our web page, Notification Process for Transfusion Related Fatalities and Donation Related Deaths, http://www.fda.gov/biologicsbloodvaccines/safetyavailability/reportaproblem/transfusiondonationfatalities/default.htm. For further information, see our *Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion*, September 2003.[4]

A team of CBER medical officers reviews the documentation submitted by the reporting facilities and obtained by FDA investigators, to assess the relationship, if any, between the blood donation or transfusion and the reported fatality.

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[1] Report of the US Department of Health and Human Services. The 2011 national blood collection and utilization survey report. Washington, DC: US Department of Health and Human Services, Office of the Assistant Secretary of Health, 2012.
[2] Transfusion could not be ruled out as the cause of the fatality.
[3] The FY2005 - FY2009 data are not discussed in this report, but are available at: http://www.fda.gov/biologicsbloodvaccines/safetyavailability/reportaproblem/transfusiondonationfatalities/default.htm.
[4] Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion, September, 2003. http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm074947.htm

If you have questions concerning this summary, you may contact us using any of the three following options:

1. Email us at fatalities2@fda.hhs.gov,
2. Call us at 240-402-9160, or
3. Write us at:

   Food and Drug Administration
   Center for Biologics Evaluation and Research
   Document Control Center
   10903 New Hampshire Avenue, Bldg. 71, Rm. G112
   Silver Spring, MD 20993-0002
   ATTN: OCBQ, Fatality Program Manager

II. Results

During FY2014 (October 1, 2013, through September 30, 2014), we received a total of 68 fatality reports. Of these reports, 59 were transfusion recipient fatalities and 9 were post-donation fatalities.

Of the 59 transfusion recipient fatality reports, we concluded:

a) 3 (5%) of the fatalities were unrelated to the transfusion,
b) 26 (44%) of the fatalities were cases in which transfusion could not be ruled out as the cause of the fatality,
c) 30 (51%) of the fatalities were transfusion-related.

Of the 9 post-donation fatality reports, we concluded:

a) 2 of the fatalities were unrelated to the donation,
b) 6 of the fatalities were donations which could not be ruled out as the cause of the fatality,
c) 1 of the fatalities was related to the donation.

We summarize the results of our review in the following sections. Sections A through D of this document present the transfusion-related fatalities. Sections E and F present, respectively, the reported fatalities which were unrelated to the transfusion, and those in which we could not rule out the transfusion as the cause of death. Section G presents the post-donation fatality reports. Section H discusses forthcoming changes for evaluating transfusion and post-donation fatality reports.

A. Overall Comparison of Transfusion-Related Fatalities Reported from FY2010 through FY2014

In combined Fiscal Years 2010 through 2014, Transfusion Related Acute Lung Injury (TRALI) caused the highest number of reported fatalities (41%), followed by Transfusion Associated Circulatory Overload (TACO) (22%) and hemolytic transfusion (HTR) reactions (total of 21%) due to non-ABO (14%) and ABO (7%) incompatibilities. Microbial infections (8%) and anaphylactic reactions (6%) each accounted for a relatively smaller number of reported fatalities (Table 1 and Figure 1).

While the number of fatalities attributed to TACO has varied, TACO was the second leading cause of transfusion-related fatalities over the 5-year reporting period. There is increasing interest in TACO, as exhibited by recent articles.[5, 6, 7] The National Heart Lung and Blood Institute (NHLBI) Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) is focused on transfusion and reducing its risks. Current research includes a Phase 2 study; *Severe Transfusion Reactions Including Pulmonary Edema (STRIPE)*. This study will focus on strategies that will prevent or reduce complications related to TACO and other transfusion complications.[8, 9]

The number of reported transfusion related deaths attributable to anaphylaxis[10, 11, 12, 13, 14, 15] has remained small over the last five fiscal years. None of the 10 combined cases reported for FY2010 through FY2014 were decisively linked to IgA deficient recipients; measured IgA levels conclusively ruled out eight cases and IgA was not measured in the remaining two cases. One of the four FY2010 cases involved a haptoglobin deficiency that was possibly implicated in the patient's anaphylactic reaction. Of the two anaphylaxis cases in FY2014, testing ruled out haptoglobin deficiency in one case and in the other, neither haptoglobin nor IgA levels were determined for the recipient.

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[5] Kleinman S, Busch MP, Murphy EL et al. The National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study (REDS-III): a research program striving to improve blood donor and transfusion recipient outcomes. Transfusion. 2014 Mar;54(3 Pt 2):942-55.

[6] Narick C, Triulzi J, Yazer M. Transfusion-associated circulatory overload after plasma transfusion. Transfusion 2012;52:160-165.

[7] Tobian A, Sokoll L, Tisch D, et al. N-terminal pro-brain natriuretic peptide is a useful diagnostic marker for transfusion-associated circulatory overload. Transfusion 2008;48:1143-1150.

[8] https://reds-iii.rti.org/REDSProgram.aspx.

[9] Kleinman S, Busch MP, Murphy EL et al. The National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study (REDS-III): a research program striving to improve blood donor and transfusion recipient outcomes. Transfusion. 2014 Mar;54(3 Pt 2):942-55.

[10] Lindsted G, Larsen R, Kriegaard M, et al. Transfusion-Associated Anaphylaxis during anaesthesia and surgery – a retrospective study. Vox Sanguinis 2014;107(2):158-65.

[11] Hirayama F. Current Understanding of allergic transfusion reactions: incidence, pathogenesis, laboratory tests, prevention and treatment. British Journal of Haematology 2013;160:434-444.

[12] Savage W, Tobian A, Savage J, et al. Scratching the surface of allergic transfusion reactions. Transfusion 2013;53:1361-1371.

[13] Sandler SG1, Eder AF, Goldman M, Winters JL. The entity of immunoglobulin A-related anaphylactic transfusion reactions is not evidence based. Transfusion. 2015 Jan;55(1):199-204.

[14] Savage WJ, Tobian AA, Savage J, et al. Transfusion and component characteristics are not associated with allergic transfusion reactions to apheresis platelets. Transfusion 2015;55:296-300.

[15] Shimada E, Tadokoro K, Watanabe Y, et al. Anaphylactic transfusion reactions in haptoglobin-deficient patients with IgE and IgG haptoglobin antibodies. Transfusion 2002;42:766-773.

Table 1: Transfusion-Related Fatalities by Complication, FY2010 through FY2014

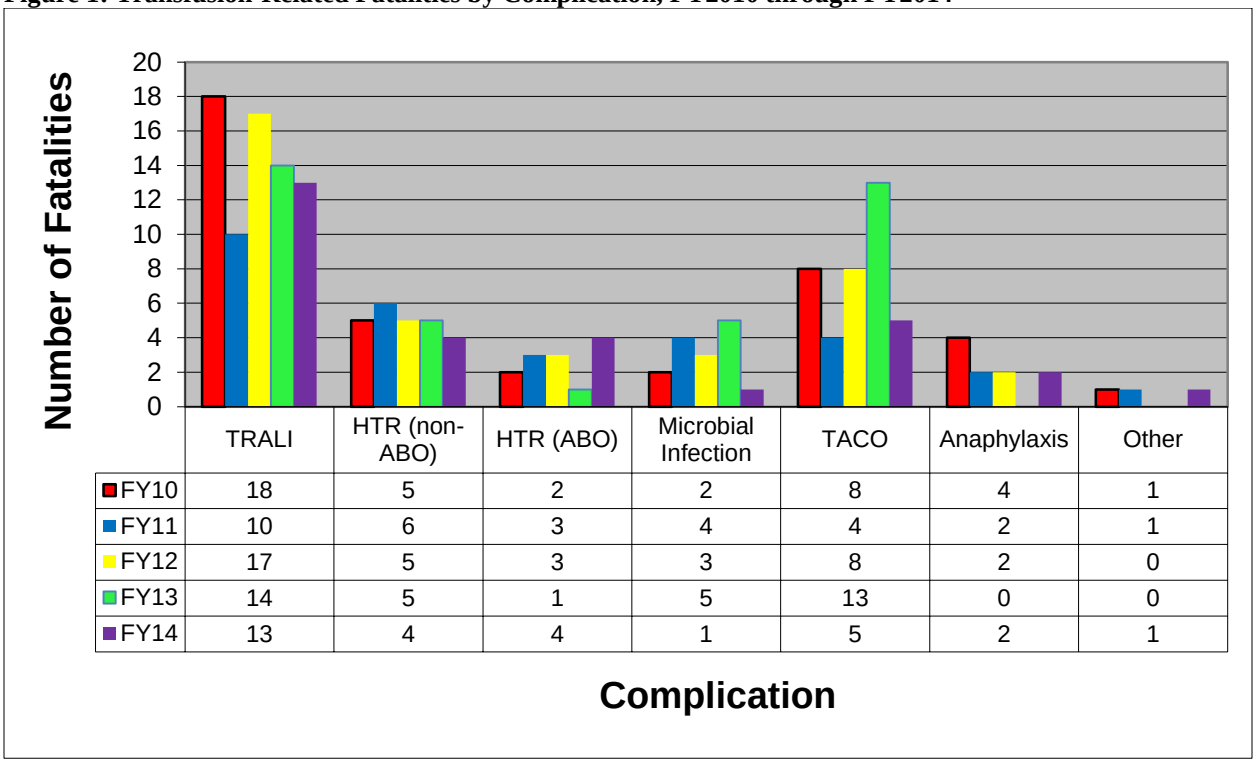
Complication	FY10	FY10	FY11	FY11	FY12	FY12	FY13	FY13	FY14	FY14	Total	Total
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
TRALI*	18	45%	10	33%	17	45%	14	37%	13	43%	72	41%
HTR (non-ABO)	5	13%	6	20%	5	13%	5	13%	4	13%	25	14%
HTR (ABO)	2	5%	3	10%	3	8%	1	3%	4	13%	13	7%
Microbial Infection	2	5%	4	13%	3	8%	5	13%	1	3%	15	8%
TACO	8	20%	4	13%	8	21%	13	34%	5	17%	38	22%
Anaphylaxis	4	10%	2	7%	2	5%	0	0%	2	7%	10	6%
Other	1**	3%	1**	3%	0	0%	0	0%	1**	3%	3	2%
Totals	40	100%	30	100%	38	100%	38	100%	30	100%	176	100%

*These numbers include both "TRALI" and "possible TRALI" cases[16, 17]

**Other:

FY2010: Graft vs. Host Disease (GVHD)
FY2011: GVHD
FY2014: Hypotensive Reaction[18]

Figure 1: Transfusion-Related Fatalities by Complication, FY2010 through FY2014



[16] Goldman M, Webert KE, Arnold DM, et al. Proceedings of a consensus conference: towards an understanding of TRALI. Transfus Med Rev 2005;19:2-31.
[17] Kleinman S, Caulfield T, Chan P, et al. Toward an understanding of transfusion-related acute lung injury: statement of a consensus panel. Transfusion 2004;44:1774-1789.
[18] Center for Disease Control and Prevention National Healthcare Safety Network, Biovigilance Component, Hemovigilance Module Surveillance Protocol, August 2014.

B. Transfusion Related Acute Lung Injury (TRALI)

TRALI represented 41% of confirmed transfusion-related fatalities reported to CBER over the last five fiscal years, and 43% in FY2014 (Table 1 and Figure 1). Figure 2 shows the overall decrease in the number of TRALI fatalities since FY2007, when the number of TRALI fatalities represented 65% (34/52) of transfusion-related fatalities. Following this decrease, the total number of TRALI fatalities, has remained relatively unchanged since FY2008. There has been an overall decrease over the last five years (FY2010 – FY 2014) in the number of TRALI fatalities associated with plasma and platelet products (Figure 3).

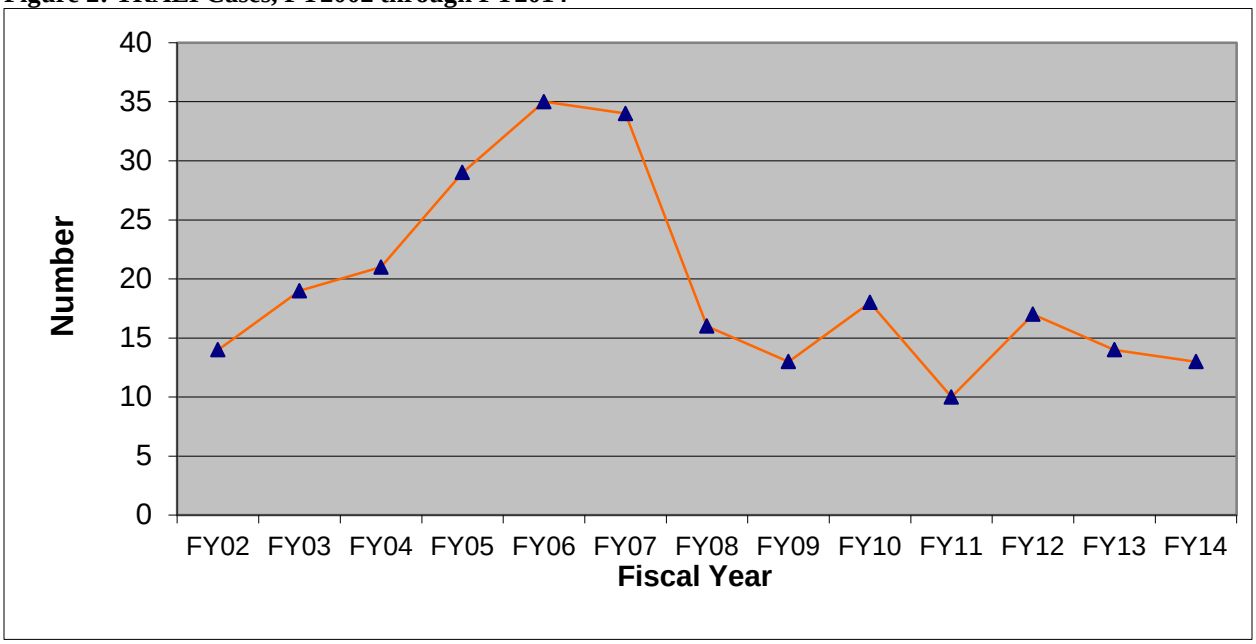
In FY2014, the 13 TRALI cases were temporally associated with products collected from 36 donors. Genders were identified for 33 of the donors, which included 19 males and 14 females. HLA/HNA antibody test results were available for 23 of these donors. In 4 of the 13 FY2014 TRALI cases, reporters who included patient testing data were able to match donor antibodies with recipient cognate antigens.

Our limited data do not elucidate the role of particular donor antibodies or donor gender in the etiology of the TRALI reactions.

Although this complication of transfusion continues to be one of the leading causes of transfusion-related fatalities reported to the FDA, the voluntary measures taken by the transfusion community to reduce the risk of TRALI have coincided with a reduction in the number of TRALI deaths. Current literature describes the results of continued international efforts to reduce the use of plasma for transfusion prepared from female donors, and other strategies to reduce the incidence of TRALI.[19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32]

[19] Muller MCA, Juffermans NP. Transfusion-related acute lung injury: a preventable syndrome? Expert Rev. Hematol. 2012;5(1):97-106.
[20] Wiersum-Osselton JC, Middleburg RA, Beckers EAM, et al. Male-only fresh frozen plasma for transfusion-related acute lung injury prevention: before-and-after comparative cohort study. Transfusion 2011;51:1278-1283.
[21] Schmidt AE, Adamski J. Pathology Consultation on Transfusion-Related Acute Lung Injury (TRALI). Am J Clin Pathol 2012;138:498-503.
[22] Saidenberg E, Petraszko T, et al. Transfusion-Related Acute Lung Injury (TRALI): A Canadian Blood Services Research and Development Symposium. Transfusion Medicine Reviews 2010;24:305-324.
[23] Arinsburg SA, Skerrett DL, Karp JK, et al. Conversion to low transfusion-related acute lung injury (TRALI)-risk plasma significantly reduces TRALI. Transfusion 2012;52:946-952.
[24] Reesink HW, Lee J, Keller A, et al. Measures to prevent transfusion-related acute lung injury (TRALI). Vox Sanguinis 2012;103:231-259.
[25] Toy P, Ognjen G, Bacchetti P, et al. Transfusion-related lung injury: incidence and risk factors. Blood 2012;119:1757-1767.
[26] Eder A, Herron Jr R, Strupp A, et al. Effective reduction of transfusion-related lung injury risk with male-predominant plasma strategy in the American Red Cross (2006-2008). Transfusion 2010;50:1732-1742.
[27] Clifford L, Singh A, Wilson G, et al. Electronic health record surveillance algorithms facilitate the detection of transfusion-related pulmonary complications. Transfusion 2013;53:1205-1216.
[28] Association Bulletin #14-02 – TRALI Risk Mitigation for Plasma and Whole Blood for Allogeneic Transfusion. http://www.aabb.org/resources/publications/bulletins/Pages/abwhatsnew.aspx.
[29] Menis M, Anderson SA, Forshee FA, et al. Transfusion-related acute lung injury and potential risk factors among the inpatient US elderly as recorded in Medicare claims data, during 2007 through 2011. Transfusion 2014;54:2182-2193.
[30] Silliman CC, Kelher MR, Khan SY, et al. Experimental prestorage filtration removes antibodies and decreases lipids in RBC supernatants mitigating TRALI in vivo. Blood 2014;123:3488-3495.

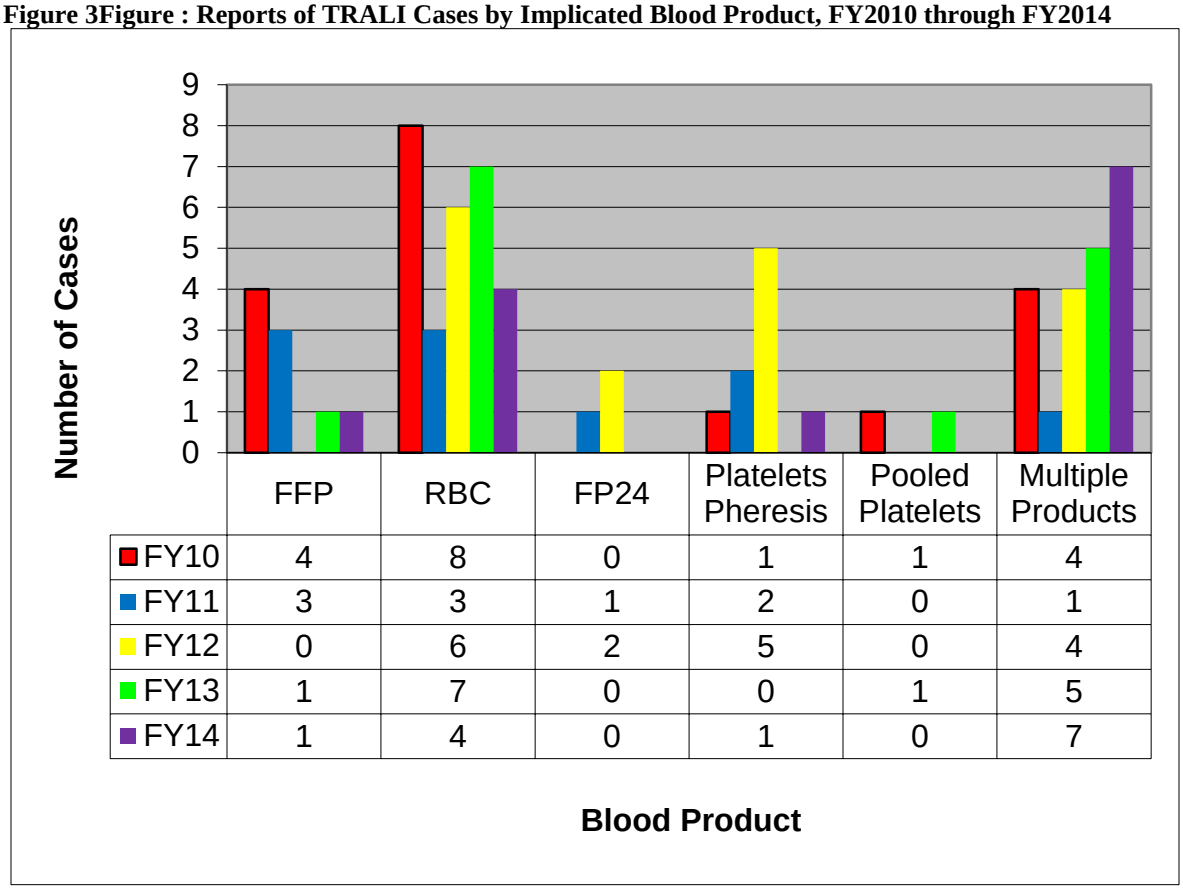
Figure 2: TRALI Cases, FY2002 through FY2014



[31] Popovsky MA. Transfusion-related acute lung injury: three decades of progress but miles to go before we sleep. Transfusion 2015;55:930-934.

[32] Peters AL, Van Stein D, Vlaar AP. Antibody-mediated transfusion-related acute lung injury; from discovery to prevention. British Journal of Haematology 2015. DOI 10.1111/bjh.13459.

Figure 3Figure : Reports of TRALI Cases by Implicated Blood Product, FY2010 through FY2014



	FFP	RBC	FP24	Platelets Pheresis	Pooled Platelets	Multiple Products
FY10	4	8	0	1	1	4
FY11	3	3	1	2	0	1
FY12	0	6	2	5	0	4
FY13	1	7	0	0	1	5
FY14	1	4	0	1	0	7

C. Hemolytic Transfusion Reactions

In FY2014, there were four reported ABO hemolytic transfusions (13% of confirmed transfusion-related fatalities) that were confirmed to be fatal, compared to one (3%) in FY2013. The four non-ABO hemolytic transfusion reactions represents a count relatively unchanged in FY2014, in comparison to the number reported in FY2013 (Tables 1 and 2, and Figure 1). The downward trend in the total number of reported fatalities due to hemolytic transfusion reactions has continued since FY2001 (Figure 4) and stabilized in recent years.

Table 2: Hemolytic Transfusion Reactions by Implicated Antibody, FY2010 through FY2014

Antibody	FY10	FY10	FY11	FY11	FY12	FY12	FY13	FY13	FY14	FY14	Total	Total
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
ABO	2	29%	3	33%	3	38%	1	17%	4	50%	13	34%
Multiple Antibodies*	3	43%	1	11%	2	25%	1	17%	0	0%	7	18%
Other**	0	0%	2	22%	0	0%	0	0%	2	25%	4	10%
Fy^a	0	0%	1	11%	0	0%	0	0%	0	0%	1	2%
Jk^b	1	14%	0	0%	1	13%	1	17%	0	0%	3	8%
Kell	0	0%	1	11%	1	13%	2	33%	0	0%	4	10%
Jk^a	0	0%	0	0%	0	0%	1	17%	1	12.5%	2	5%
c	0	0%	1	11%	0	0%	0	0%	0	0%	1	2%
Js^b	0	0%	0	0%	1	13%	0	0%	0	0%	1	2%
Co^a	1	14%	0	0%	0	0%	0	0%	0	0%	1	2%
C	0	0%	0	0%	0	0%	0	0%	1	12.5%	1	2%
Totals	7	100%	9	100%	8	100%	6	100%	8	100%	38	100%

*Multiple Antibodies:

FY2010: antibody combinations include: D+C+K+S; Jk^b+FY^a+C+E+K+Le^a+Le^b; c+E+Jk^b+K+Le^a+panagglutinin+cold agglutinin.

FY2011: anti-Jk^a+c+E+M (warm reacting).

FY2012: antibody combinations include: S+E; C+K.

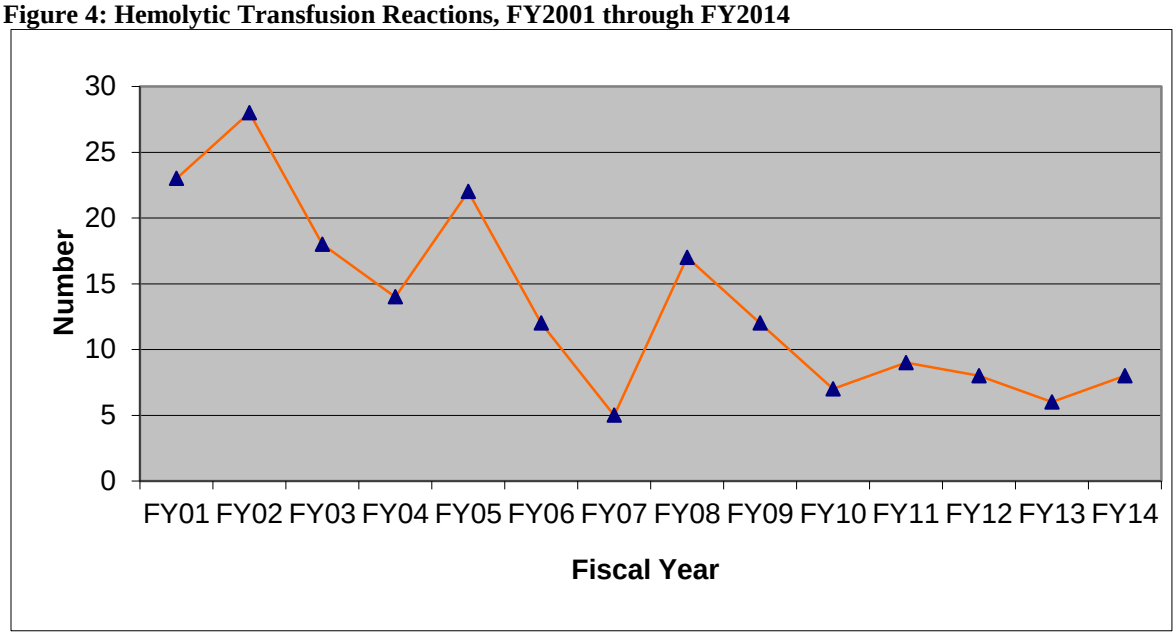
FY2013: anti-c+E

**Other:

FY2011: Includes one report of an unidentified antibody and one report of Hyperhemolysis Syndrome[33, 34].

FY2014: Includes one report of Hyperhemolysis Syndrome in which no new or additional antibody was identified.

Figure 4: Hemolytic Transfusion Reactions, FY2001 through FY2014



[33]Win N, New H, et al. Hyperhemolysis Syndrome in sickle cell disease: case report (recurrent episode) and literature review. Transfusion 2008;48:1231-1238.

[34] Santos B, Portugal R, et al. Hyperhemolysis Syndrome in patients with sickle cell anemia: report of three cases. Transfusion 2015;55:1394-1398.

The four reports of fatal hemolytic transfusion reactions which were found to be related to ABO-incompatible transfusions include one error in patient identification at the time of transfusion, one set of errors in the lab, and two cases of ABO-incompatible apheresis platelets.[35]

1. A group B RBC unit, which was correctly labeled for a patient in the step-down unit, was transfused to a group O patient in the same location. There was a failure to properly identify the patient prior to transfusion.
2. A group A RBC unit was transfused to a group O patient following errors in the laboratory. The gel tube automated instrument was off line and the wrong patient's results were selected from a instrument-generated printed report for manual entry into the lab information system. Because the patient lacked a historic ABO in the information system, SOP required an additional manual gel tube test. The firm's investigation did not reveal why the wrong results were entered for the manual test. Consequently, a group A unit was selected using an electronic crossmatch procedure, and transfused.
3. A group A patient was transfused with a unit of group O apheresis platelets. The high titer of anti-A (1:2048) was identified after the transfusion reaction.
4. A group AB patient was transfused with two units of group O apheresis platelets from the same donor. During the subsequent transfusion of a group AB RBC unit, the recipient presented with signs of a transfusion reaction. Anti-A and anti-B titers performed as part of the transfusion reaction investigation were both 1:128.

The four reports of fatal hemolytic transfusion reactions which were found to be related to non-ABO incompatible transfusions include one laboratory error, two cases of delayed hemolytic transfusion reactions with no associated errors identified, and one complex multiple-antibody case.

1. The patient had a known history of anti-Jk^a and anti-E. The transfused unit was phenotyped for the corresponding antigens, labeled negative for Jk^a and E, and documented as crossmatch compatible. Following the reported reaction, the repeat pre-transfusion and post-transfusion crossmatches were incompatible, and repeat phenotyping showed the transfused unit was Jk^a positive. The reporting firm was unable to determine whether these were procedural or clerical errors.
2. A sickle cell patient with a history of multiple antibodies, intermittent warm and cold autoantibodies, and Hyperhemolysis Syndrome[33, 34] was transfused units that were crossmatch-compatible and phenotyped negative for the corresponding antigens. Following a delayed hemolytic reaction with hyperhemolysis, no new antibodies were identified.
3. A patient with four previously identified antibodies was transfused with crossmatch-compatible units that were negative for the corresponding antigens. Following the reported reaction, anti-C was newly identified.
4. A patient with multiple medical issues (hypertension, pericarditis, Systemic Lupus Erythematosus, Raynaud's disease) and a history of multiple transfusions for symptomatic anemia secondary to dysfunctional uterine bleeding, required extensive immunohematology reference lab investigational support throughout her clinical course. The patient had two previously identified antibodies, anti-Fya and anti-Jka, plus a warm autoantibody. Least-incompatible blood was provided for transfusion after detailed evaluations that included testing

[35] Fontaine MJ, Mills AM, et al. How we treat: risk mitigation for ABO-incompatible plasma in plateletpheresis products. Transfusion 2012;52:2081-2085.

alloabsorbed patient plasma, phenotype matching for C, E and K, and finding antigen negative blood for the previously identified antibodies. After the initial transfusions, an anti-M was newly identified, but was interpreted as clinically insignificant. After the final transfusion, an acute hemolytic reaction occurred with no additional causative antibody identified.

D. Microbial Infection

In FY2014 there was one reported fatality attributed to microbial infection, compared to five in FY2013 (Table 1, Figure 1). The FY2014 report involved transfusion of a unit of pooled platelets, which was associated with sepsis due to *Serratia marcescens* (Figure 5). There were no reported fatalities associated with transfusion of apheresis platelets reported in FY2014, as compared to three in FY2013.

Over the five-year reporting period, *Babesia microti* accounted for the greatest number of the reported deaths due to microbial infection (4/15), while *Staphylococcus aureus* and *Serratia marcescens* accounted for equal numbers of fatalities (2 each). Four of the five infections associated with RBC transfusions were due to *Babesia microti*, and both of the *Serratia marcescens* infections were associated with transfusion of pooled platelets (Table 3 and Figure 5). The six deaths associated with transfusion of apheresis platelets were distributed evenly among six organisms (1 each).

Recent articles provide additional information about transfusion transmitted *Babesia*,[36, 37, 38] and reflect continuing interest in bacterial contamination of platelet products.[39, 40, 41, 42]

During the five-year reporting period, six of the implicated bacteria associated with fatal microbial infections were facultative anaerobes, and two - *Acinetobacter sp.* and *Pseudomonas fluorescens* - were obligate aerobes.

Figure 6 shows the overall downward trend in the number of bacterial infections associated with apheresis platelets since FY2001.

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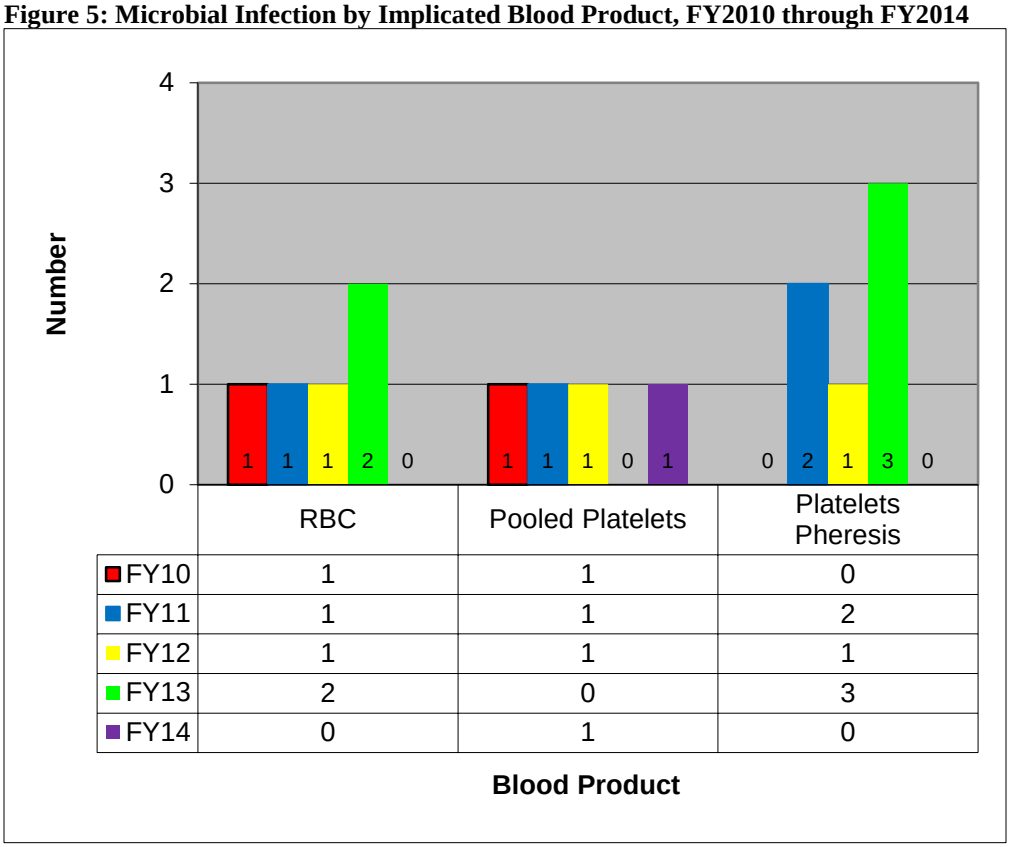
[36] Johnson ST, Van Tassell ER, et al. Babesia microti real-time polymerase chain reaction testing of Connecticut blood donors: potential implications for screening algorithms. Transfusion 2013;53:2644-2649.
[37] Young C, Chawla A, et al. Preventing transfusion-transmitted babesiosis: preliminary experience of the first laboratory-based blood donor screening program. Transfusion 2012;52:1523-1529.
[38] Simon M, Leff J, Pandya A, et al. Cost-effectiveness of blood donor screening for *Babesia microti* in endemic regions of the United States. Transfusion 2014;54:889-899.
[39] Rollins MD, Molofsky AB, Nambiar A, et al. Two Septic transfusion reactions presenting as transfusion-related acute lung injury from a split plateletpheresis unit. Crit Care Med 2012;40:2488-2491.
[40] Palavecino EL, Yomtovian RA, Jacobs MR. Bacterial contamination of platelets. Transfus Apher Sci 2010;42:71-82.
[41] Eder AF, Kennedy JM, Dy BA, et al. American Red Cross Regional Blood Centers: Limiting and detecting bacterial contamination of apheresis platelets: inlet-line diversion and increased culture volume improve safety. Transfusion 2009;49:1554-1563.
[42] Benjamin R. Bacterial contamination. ISBT Science series 2014;9:37-43.

Table 3: Microbial Infection by Implicated Organism, FY2010 through FY2014

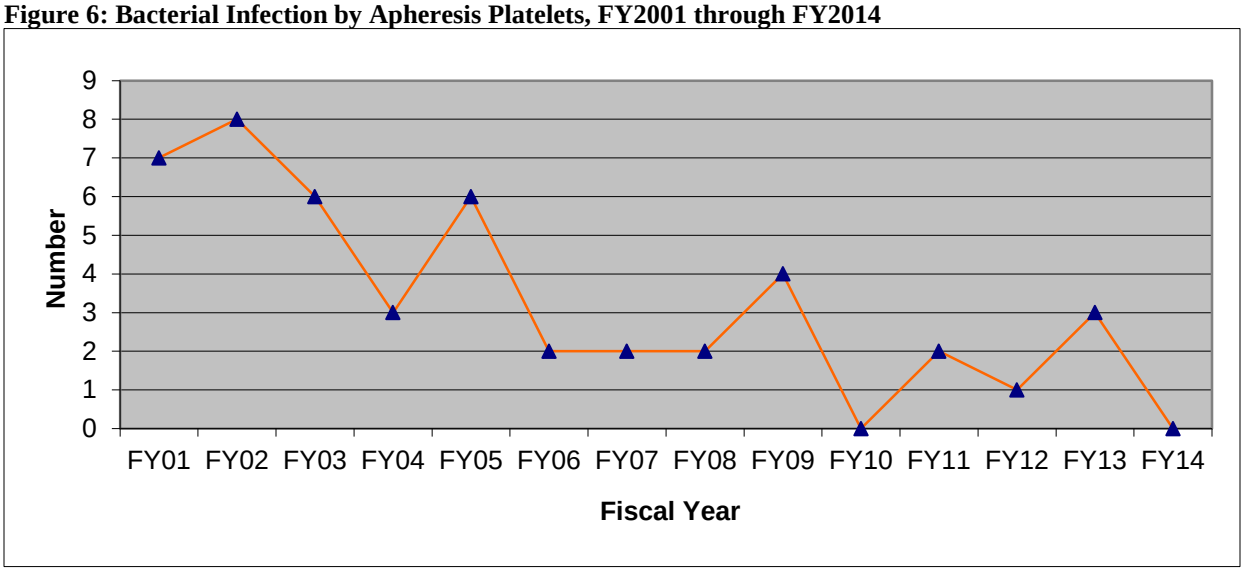
Organism	FY10	FY10	FY11	FY11	FY12	FY12	FY13	FY13	FY14	FY14	Total	Total
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Babesia microti	1	50%	1	25%	1	33%	1	20%	0	0%	4	27%
Staphylococcus aureus	0	0%	1	25%	1	33%	0	0%	0	0%	2	13%
Escherichia coli	1	50%	0	0%	0	0%	0	0%	0	0%	1	7%
Staphylococcus epidermidis	0	0%	0	0%	0	0%	1	20%	0	0%	1	7%
Morganella morganii	0	0%	1	25%	0	0%	0	0%	0	0%	1	7%
Streptococcus viridans	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Streptococcus pneumoniae	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Staphylococcus warneri	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Klebsiella pneumoniae	0	0	1	25%	0	0%	0	0%	0	0%	1	7%
Serratia marcescens	0	0	0	0	1	33%	0	0%	1	100%	2	13%
Pseudomonas fluorescens	0	0%	0	0%	0	0%	1	20	0	0%	1	7%
Acinetobacter sp.	0	0%	0	0%	0	0%	1	20	0	0%	1	7%
West Nile virus	0	0%	0	0%	0	0%	1	20	0	0%	1	7%
Total	2	100%	4	100%	3	100%	5	100%	1	100%	15	100%

Figure 5: Microbial Infection by Implicated Blood Product, FY2010 through FY2014



Red Blood Cells microorganisms: *B. microti (4), P. fluorescens (1)*
Pooled Platelets microorganisms: *S. aureus (1), E. coli (1), S. Marcescens (2)*
Platelets Pheresis microorganisms: *S. aureus (1), S. epidermidis (1), M. morganii (1), K. pneumoniae (1),* West Nile virus *(1), Acinetobacter sp. (1)*

Figure 6: Bacterial Infection by Apheresis Platelets, FY2001 through FY2014



E. Transfusion Not Ruled Out

As already noted in the results summary, 26 (44 %) of the 59 reported transfusion fatalities in FY2014 were cases in which the transfusion could not be ruled out as the cause of the fatality. In these reported fatalities, the reporting facilities were unable to identify a specific complication of transfusion as the cause of death. Often, these patients had multiple co-morbidities, and after review of the investigation documentation, our medical reviewers could neither confirm nor rule out the transfusion as the cause of the fatality (Table 4). Therefore, we did not include these reported fatalities in the analysis in Sections II.A through II.D (transfusion-related fatalities).

F. Not Transfusion Related

After reviewing the initial fatality reports and the investigation documentation, we categorized three (5%) of the 59 reported transfusion fatalities in FY2014 as "Not Transfusion Related." Our medical reviewers concluded that, while there was a temporal relationship between transfusion and subsequent death of the recipient, there was no evidence to support a causal relationship (Table 4). Thus, we did not include these reported fatalities in the analysis in Sections II.A through II.D (transfusion-related fatalities).

Table 4: Fatalities Not Related to Transfusion or Transfusion Not Ruled Out, FY2010 through FY2014

	FY10	FY11	FY12	FY13	FY14
Transfusion Not Ruled Out	24	28	27	21	26
Not Transfusion Related	7	11	9	6	3
Total	31	39	36	27	29

G. Post-Donation Fatalities

Over the five-year (FY2010 – FY2014) reporting period, there were 45 total reported fatalities associated with a variety of donated product:

- 32 Source Plasma donations
- 11 whole blood donations
- 1 apheresis platelet donation
- 1 apheresis red blood cell donation.

In the majority of the cases, it was concluded that the donations could not definitively be ruled out as being implicated in the donors' deaths.

After review each reported case was determined to fit in one of three categories.

1. Donation ruled out as cause of fatality (Table 5):
   In FY2014 there were two (2) fatalities following Source Plasma donations in which the donations were definitively ruled out as being implicated in the death of the donors. In these

cases, there was clear evidence showing the cause of death was unrelated to the donation.

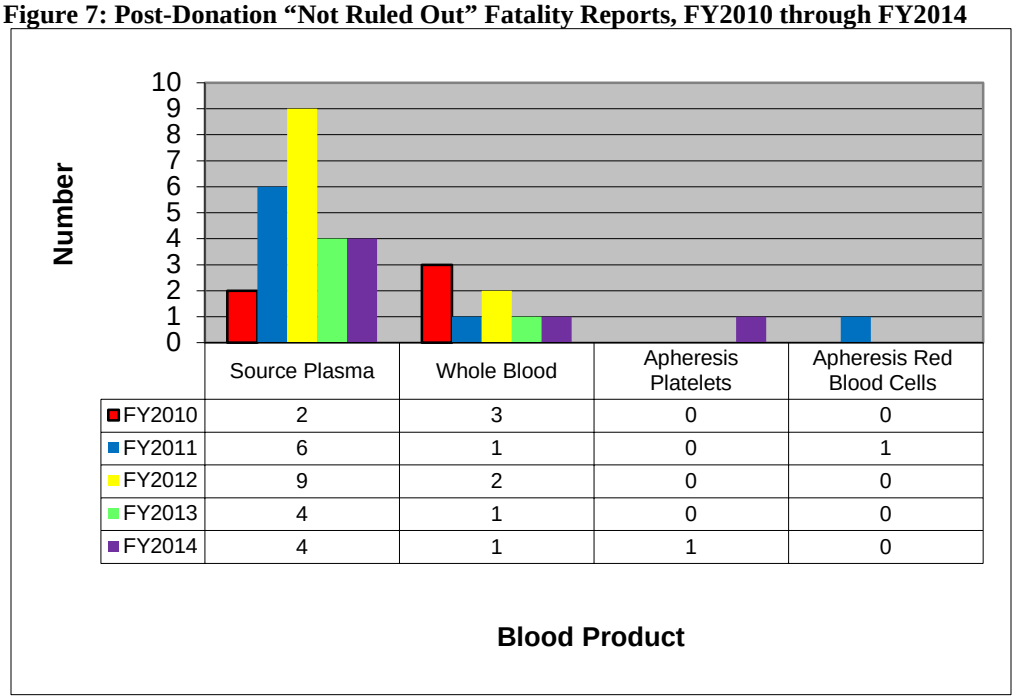
2. Donation not ruled out as cause of fatality (Figure 7):
   The most common conclusion of post-donation deaths is "donation not ruled out." In FY2014, there were four (4) fatalities following Source Plasma donations, one (1) fatality following whole blood donation, and one (1) fatality following an apheresis platelet donation in this category. For each case thorough medical review determined that the available evidence did not definitely rule out the donation being implicated in the donor's death, nor did the available evidence support a causal relationship between the donation and the post-donation death.

3. Donation implicated in fatality:
   Rarely, we determine that a causal link existed between the donation and the fatality. In FY2014 there was one such fatality following whole blood donation. After a thorough medical review of the fatality, a causal relationship between the donation and subsequent death of the donor was supported by the evidence. The individual initially complained of lightheadedness after donating a unit of whole blood and was managed conservatively with rest and oral hydration. Subsequently, after walking a short distance in the donation area, the person knelt down, and after getting back up to a standing position, fell backward. The traumatic brain injury with intracerebral and subdural hematoma that was sustained in this fall ultimately led to the donor's death. There were no conditions detected during pre-donation screening that would have contraindicated donation, or that signaled unusual risk.

Table 5: Post Donation "Ruled Out" Fatality Reports by Donated Product, FY2010 through FY2014

Donated Product	FY10	FY11	FY12	FY13	FY14	*Totals*
Source Plasma	0	1	3	1	2	*7*
Whole Blood	0	1	0	1	0	*2*
Apheresis Platelets	0	0	0	0	0	*0*
Apheresis Red Blood Cells	0	0	0	0	0	*0*
Total	0	2	3	2	2	*9*

Figure 7: Post-Donation "Not Ruled Out" Fatality Reports, FY2010 through FY2014



	Source Plasma	Whole Blood	Apheresis Platelets	Apheresis Red Blood Cells
FY2010	2	3	0	0
FY2011	6	1	0	1
FY2012	9	2	0	0
FY2013	4	1	0	0
FY2014	4	1	1	0

H. Prospective Changes in Future Fatality Report Evaluations:

Look for a change in our next annual report.

In support of the FDA's international harmonization efforts and to provide consistency between US government agencies (http://www.fda.gov/aboutfda/reportsmanualsforms/reports/ucm298576.htm), we are modifying our approach to the review and classification of fatality reports. The annual report for FY2015 will align with the case definitions and imputability criteria used by the Centers for Disease Control and Prevention (CDC)/National Healthcare Safety Network,[18] and several international organizations such as the International Society of Blood Transfusion, International Hemovigilance Network,[43] British Serious Hazards of Transfusion (SHOT)[44] and the Hemovigilance activity report of the French National Agency for Medicines and Health Products Safety (ANSM).[45] This should add greater clarity and comparability to the information we routinely share in this report.

[43] International Society of Blood Transfusion/International Haemovigilance Network Working Group on Haemovigilance. Proposed standards definitions for Surveillance of non-infectious adverse transfusion reactions, July 2011 incorporating correction to TRALI definition as adopted in June 2013.
[44] Annual Serious Hazards of Transfusion Report, 2014.
[45] French National Agency for Medicine and Health Product Safety (ANSM), 2013 Hemovigilance Activity Report.