Fatalities Reported to FDA Following Blood Collection and Transfusion

Annual Summary for Fiscal Year 2022

I. Background

FDA's Center for Biologics Evaluation and Research (CBER) is issuing this summary of fatality reports received by the FDA to make public the data received in Fiscal Year (FY) 2022 (October 1, 2021, through September 30, 2022), to provide the combined data received over the last five fiscal years, and to compare the FY22 summary to the fatality reports received in the previous four fiscal years.[1] In FY2022, there were a total of 30 fatalities evaluated by CBER to be at least possibly related to transfusion. Overall, the number of transfusion-associated fatalities reported to the FDA remains small, but relatively constant, in comparison to the total number of transfusions. In calendar year (CY) 2021, 10.8 million whole blood derived and apheresis red blood cell units, 2.2 million platelets units (approximately 96% apheresis units, 4% whole blood derived equivalents), and 3.0 million plasma units were transfused, with stable demand for red blood cells (RBCs) compared to 2019 (10.8 million).[2] Throughout this report we note changes over time in the number of reported fatalities, 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 greater than what the numbers would otherwise suggest.

We also include information on the reports of donation-associated fatalities reported to FDA. The number of donation-associated fatalities reported to the FDA also remains small in comparison to the total number of units collected. In CY 2021, U.S blood establishments collected 11.8 million whole blood derived and apheresis RBCs, and distributed 2.5 million platelet units and 3.1 million plasma units.[2] In CY 2022, there were over 46 million source plasma donations reported in North America. [3] Over the combined five-year reporting period (FY2018 – FY2022) there were 133 reported donation-associated fatalities (associated with a variety of donated products), with 32 cases since 2018 having an imputability of *definite (n=1), probable (n=6),* or *possible (n=25)*.

Fatality reporting requirements can be found under Title 21, Code of Federal Regulations 606.170(b). For information regarding the notification process, see our web page, Notification Process for Transfusion Related Fatalities and Donation Related Deaths, https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/transfusiondonation-fatalities. For further information, see our *Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion*, September 2003, updated August 2021.[4]

[1] The FY2013 - FY2021 data are available at: https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/transfusiondonation-fatalities

[2] https://pubmed.ncbi.nlm.nih.gov/37070720/

[3] Plasma Protein Therapeutics Association. *Global Plasma Updates*. Plasma Protein Forum. November 21, 2024. Washington, DC.

[4] Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion, September 2003, Updated August 2021. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/notifying-fda-fatalities-related-blood-collection-or-transfusion

If you have questions concerning this summary, you may contact us using the 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
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   10903 New Hampshire Avenue, Bldg. 71, Rm. G112
   Silver Spring, MD 20993-0002
   ATTN: OCBQ, Fatality Program Manager

II. Changes in Our Evaluation Approach:

Starting with the annual report of FY2015, in support of the FDA's international harmonization efforts, and to provide consistency among U.S. government agencies, we modified our approach to the review and classification of fatality reports to align with the case definitions and imputability criteria used by the Centers for Disease Control and Prevention (CDC)/National Healthcare Safety Network[5] (http://www.cdc.gov/nhsn/PDFs/Biovigilance/BV-HV-protocol-current.pdf), the International Society of Blood Transfusion (ISBT) in collaboration with the International Haemovigilance Network (IHN) and the AABB Donor Hemovigilance Working Group[6] (https://www.aabb.org/research/hemovigilance/Documents/Donor-Standard-Definitions.pdf), the British Serious Hazards of Transfusion (SHOT)[7], and the Haemovigilance activity report of the French National Agency for Medicines and Health Products Safety (ANSM)[8].

In fiscal years prior to FY2015, we classified fatalities in one of three imputability groups that define the strength of the evidence (causality) between the transfusion/donation and the fatality: *transfusion/donation-related, not ruled out, or not related*. Beginning in FY2015, fatalities that were previously classified either as *transfusion/donation-related*, or *not ruled out* are assigned a level of imputability, specifically *definite, probable, possible, doubtful,* and *not assessable* (Table 1). Fatalities previously defined as *not transfusion/donation related* continue to be classified as *ruled out*.

To achieve a more comprehensive review, we added three new categories of transfusion reactions beginning with FY2016: No Transfusion Reaction, Possible TRALI (previously tallied with TRALI), and Transfusion Reaction, Type Not Determined (Table 2).

[5] Centers for Disease Control and Prevention National Healthcare Safety Network, Biovigilance Component, Hemovigilance.

[6] International Society of Blood Transfusion Working Party on Haemovigilance in collaboration with the International Haemovigilance Network and the AABB Donor Hemovigilance Working Group, Standard for Surveillance of Complications Related to Blood Donation, December 2014.

[7] Annual Serious Hazards of Transfusion Report, 2014.

[8] French National Agency for Medicine and Health Product Safety (ANSM), 2013 Haemovigilance Activity Report.

Our review process includes a team of CBER physicians who conduct a detailed review of 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 fatality. Our classification approach allows the review team to conduct effective evaluations and improve consistency in case classifications, in an effort to add clarity and allow comparability with other domestic and international hemovigilance systems.

Table 1: Imputability Definitions, FY2018-FY2022

Imputability	Definition
Definite	Conclusive evidence beyond reasonable doubt for attributing the fatality to the transfusion/donation
Probable	Evidence clearly in favor of the transfusion/donation as the cause of the fatality
Possible	Evidence is indeterminate for attributing the fatality to the transfusion/donation or alternative cause
Doubtful	Evidence in favor of attributing the fatality to an alternative cause, but transfusion/donation cannot be excluded
Ruled Out	Conclusive evidence beyond reasonable doubt for attributing the fatality to cause other than transfusion/donation
Not Assessable	Insufficient information/relationship unknown

III. FY2022 Results

During FY2022, we received a total of 91 fatality reports. Of these reports, 54 were potentially associated with transfusion and 37 were potentially associated with donation.

Of the 54 potentially transfusion-associated fatality reports, we determined the imputability of the transfusions to the fatalities as follows:

a) Thirty (56%) of the fatalities were classified as either *definite, probable,* or *possible.*
b) Seventeen (31%) of the fatalities were classified as either *doubtful*, or *not assessable.*
c) Seven (13%) of the fatalities were classified as *ruled out*.

Of the 37 potentially donation-associated fatality reports, we determined the imputability of the donations to the fatalities as follows:

a) Eleven (30%) of the fatalities were classified as *definite*, *probable, or possible.*
b) Sixteen (43%) of the fatalities were classified as either *doubtful*, or *not assessable.*
c) Ten (27%) of the fatalities were classified as *ruled out*.

We summarized the results of our review in Table 2.

Table 2: Fatality Complication Breakdown by Imputability, FY2022

CATEGORY	Definite	Probable	Possible	Doubtful	Ruled Out	Not Assessable	TOTAL REPORTS
Transfusion							
Allergy/Anaphylaxis	1	1	2	-	-	-	4
Contamination (Bacterial)	1	-	-	-	-	-	1
HTR (ABO)	-	-	-	-	-	-	0
HTR (non-ABO)	3	-	3	1	-	-	7
No Transfusion Reaction	-	-	-	5	7	2	14
Other*	1	-	-	1	-	1	3
Possible TRALI	-	1	1	3	-	-	5
TACO	2	6	5	2	-	-	15
Transfusion Reaction, Type Not Determined	-	1	1	1	-	1	4
TRALI	1	-	-	-	-	-	1
Total	**9**	**9**	**12**	**13**	**7**	**4**	**54**
Donation							
Donor Fatality	**1**	**3**	**7**	**6**	**10**	**10**	**37**

TRALI = Transfusion Related Acute Lung Injury; TACO = Transfusion Associated Circulatory Overload; HTR = Hemolytic Transfusion Reaction
The Row Header refers to Imputability to Death
*Other: Includes a case with features of febrile non-hemolytic reaction complicated by post-transfusion purpura in a patient with underlying hematologic malignancy, autoimmune hemolytic anemia, and history of immune thrombocytopenic purpura.

For the purpose of comparison with previous fiscal years, the FY2018 through FY2022 imputabilities of *definite, probable,* and *possible* transfusion fatalities in the tables and figures of sections A through E of this document would most accurately compare with fatalities classified in previous years as *transfusion related*. Sections F and G present the transfusion fatalities classified respectively as *doubtful,* and *not assessable,* which would most accurately compare with fatalities classified in previous years as *transfusion not ruled out.* Section H presents the transfusion fatality reports classified as *ruled out*, which would compare with fatalities classified in previous years as *not transfusion related*. Section I presents the reported fatalities with donation.

A. Overall Comparison of Transfusion-Associated Fatalities Reported from FY2018 through FY2022

In combined FYs 2018 through 2022, TACO cases caused the highest number of reported fatalities (34%), followed by the combined TRALI and Possible TRALI (18%), HTR due to non-ABO incompatibilities (14%), microbial contamination and allergy/anaphylaxis reactions each with (10%), HTRs due to ABO incompatibilities (8%), transfusion reaction type not determined (5%), and Other (1%), (Table 3, and Figure 1).

TACO was the leading cause of reported transfusion-associated deaths for FY2018, and in FY2019, TACO and TRALI equally represented the leading causes of transfusion-associated deaths. In FY2020 through FY2022, TACO continued to be the leading cause of transfusion-associated deaths.

The number of reported transfusion-associated deaths attributable to allergy/anaphylaxis has appeared relatively steady over the last five fiscal years. Four allergy/anaphylaxis fatalities were reported in FY2022, compared to four

cases in FY2021, six cases in 2020, and three or fewer cases in the preceding two years (Table 3). For FY2018 through FY2022, 18 allergic/anaphylactic reactions were identified. While IgA and haptoglobin deficiencies have been historically implicated as a contributory factor in anaphylactic reactions[9,10], only a subset of cases was tested for IgA or haptoglobin levels, and no deficiencies were observed in any of the reported cases where testing was performed.

Table 3: Transfusion-Associated Fatalities by Complication, FY2018 – FY2022

Complication	FY18 No.	FY18 %	FY19 No.	FY19 %	FY20 No.	FY20 %	FY21 No.	FY21 %	FY22 No.	FY22 %	Total No.	Total %
Anaphylaxis	2	6%	2	5%	6	21%	4	10%	4	13%	**18**	**10%**
Contamination	7	23%	1	2%	4	14%	5	12%	1	3%	**18**	**10%**
HTR (ABO)	2	6%	4	9%	2	7%	5	12%	0	0%	**13**	**8%**
HTR (Non-ABO)	4	13%	11	25%	2	7%	2	5%	6	20%	**25**	**14%**
TACO	12	39%	12	27%	8	27%	15	36%	13	44%	**60**	**34%**
TRALI*	4	13%	12	27%	6	21%	7	16%	3	10%	**32**	**18%**
Transfusion Reaction, Type Not Determined	0	0%	2	5%	1	3%	3	7%	2	7%	**8**	**5%**
Other	0	0%	0	0%	0	0%	1	2%	1	3%	**2**	**1%**
Total	31		44		29		42		30		**176**	

Note: FY2018-FY2022 only includes cases with an imputability of *definite, probable*, or *possible*

*FY2018-FY2022 numbers combine both *TRALI* and *Possible TRALI* cases

[9] 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.

[10] 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.

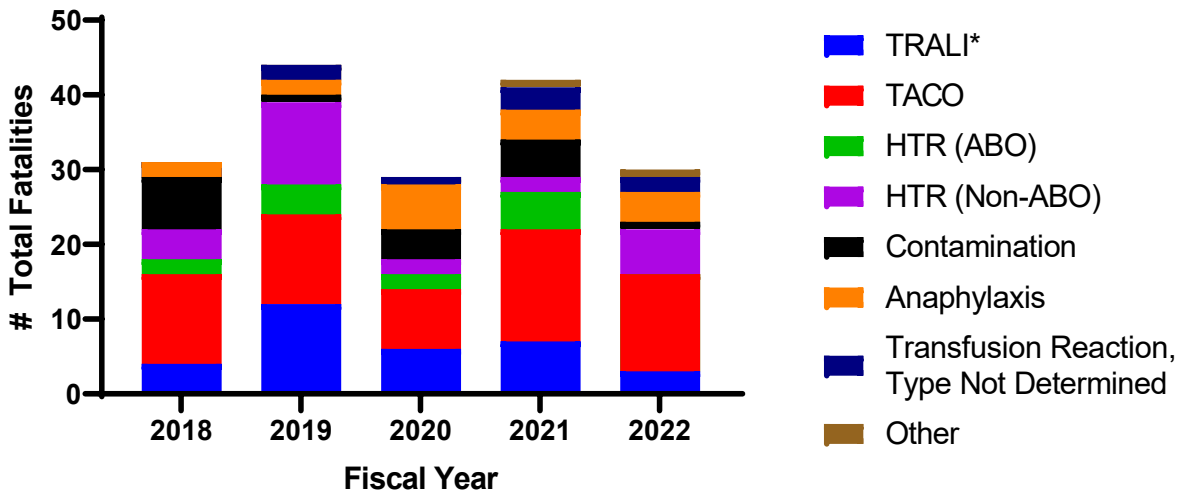

Figure 1: Transfusion-Associated Fatalities by Complication, FY2018 – FY2022

Note: FY2018-FY2022 only includes cases with an imputability of *definite, probable*, or *possible*
*FY2018-FY2022 numbers combine both *TRALI* and *Possible TRALI* cases

B. Transfusion Related Acute Lung Injury (TRALI)

In FY2022, three cases of TRALI and Possible TRALI, all associated with RBC transfusions, were reported with *definite, probable, or possible* imputability. In FY2022, there was one TRALI case where a donor of one of the implicated units tested positive for Class I HLA and HNA antibodies which matched the recipient's cognate antigens. No other instances were identified where donor antibodies could be matched with recipient cognate antigens, primarily due to negative test results or incomplete testing of donors and recipients. The limited data provided to the FDA has made it challenging to draw definitive conclusions about the specific role of donor antibodies or donor gender in the etiology of TRALI reactions.

TRALI represented 18% of transfusion-associated fatalities reported to CBER over the last five fiscal years, including FY2022 (Table 3). As documented in prior annual summaries, a rise in TRALI cases between FY2005 and FY2007 was followed by an abrupt decline in FY2008. There has been an overall downward trend since FY2013 (Figures 1 and 2), although with an uptick in FY2019, followed by a decline in FY2020, FY2021, and FY2022. Red blood cells are the most frequently implicated product since 2018 (Figure 3).

Although TRALI continues to be one of the leading causes of transfusion-associated fatalities reported to the FDA, the voluntary measures taken by the transfusion community to reduce the risk of TRALI paralleled the reduction in the number of TRALI deaths described above. Efforts to reduce the incidence of TRALI have been examined and reviewed.[11,12]

[11] Otrock, ZK, et al. Transfusion-related acute lung injury risk mitigation: an update. Vox Sang 2017;112:694-703
[12] Vossoughi S et al. Ten years of TRALI mitigation: measuring our progress. Transfusion 2019;58:2567-2574

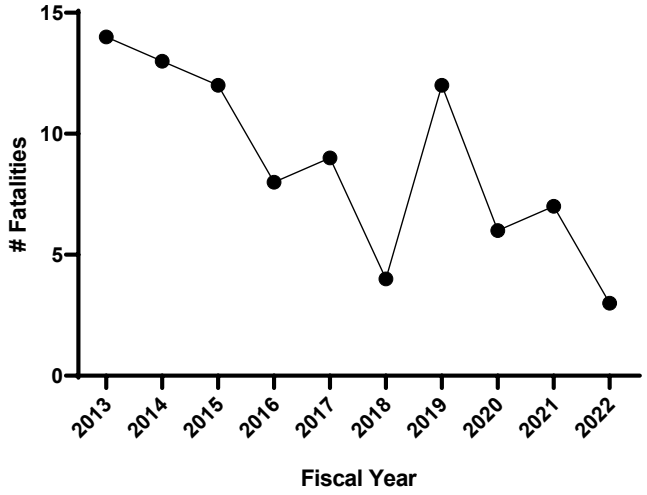

Figure 2: TRALI Fatalities, FY2013-FY2022

FY	FFP	RBC	Apheresis Platelets	Multiple Products
2013	1	7	0	5
2014	1	4	1	7
2015	3	6	1	2
2016	0	4	2	2
2017	0	4	5	0
2018	1	2	0	1
2019	1	9	0	2
2020	0	5	0	1
2021	1	3	2	1
2022	0	3	0	0

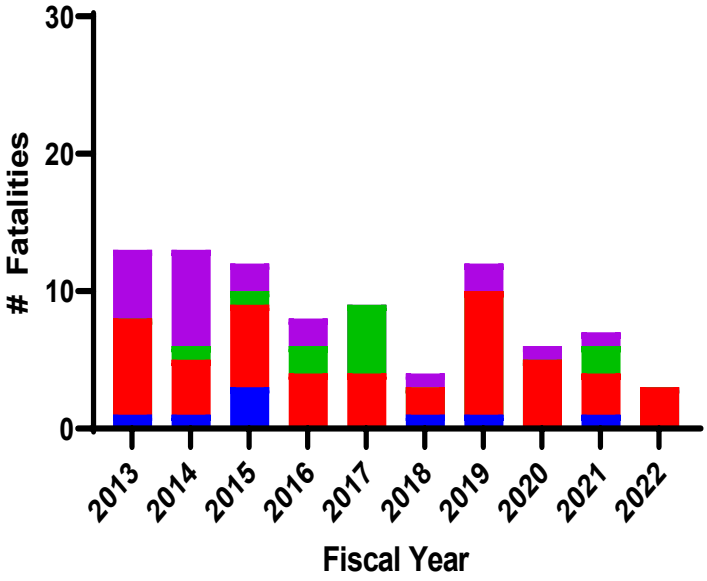

Figure 3: TRALI Fatalities by Implicated Blood Product, FY2013 – FY2022

C. Transfusion Associated Circulatory Overload (TACO)

In FY2022, TACO was the leading cause of transfusion-associated fatalities reported to FDA. There were 13 cases of TACO with an imputability of d*efinite*, *probable*, or *possible.* Among these 13 reports, 11 were associated with RBC transfusion, and two were associated with multiple blood products.

TACO has been the leading cause of transfusion-associated fatalities reported to FDA in the last five years (FY2018-FY2022). Active surveillance systems found the incidence of TACO to be approximately one case per 100 patients transfused,[13] and risk factors include cardiac, pulmonary or renal disease, older age, and pre-transfusion positive fluid balance. A revised international surveillance case definition was recently described,[14] and it is anticipated that a standardized definition may facilitate clinicians to better identify, understand, and prevent TACO. The CDC's National Healthcare Safety Network recently incorporated revised criteria to define TACO in the Hemovigilance Module in April 2021 to reflect the international effort to standardize reporting.[15]

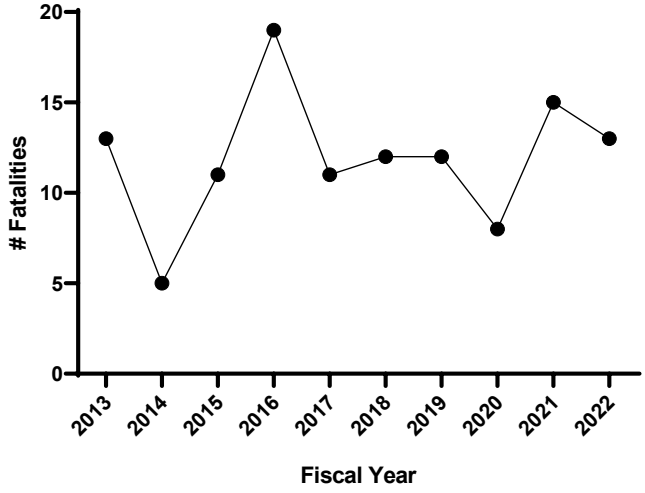

Figure 4: TACO Fatalities, FY2013-FY2022

D. Hemolytic Transfusion Reactions (HTR)

In FY2022, there were six non-ABO hemolytic transfusion fatalities with an imputability of *definite (n=3), probable (n=0),* or *possible (n=3).* These cases represented 20% of confirmed transfusion-associated fatalities (Tables 3 and 4). There were no reported ABO hemolytic transfusion fatalities in FY2022. We describe the six non-ABO hemolytic transfusion fatalities below.

[13] Roubinian NH, Hendrickson JE, Triulzi DJ, et al. Incidence and clinical characteristics of transfusion-associated circulatory overload using an active surveillance algorithm. Vox Sang. 2017;112:56–63. doi:10.1111/vox.12466.

[14] Wiersum-Osselton, Johanna C et al. Revised international surveillance case definition of transfusion-associated circulatory overload: a classification agreement validation study. The Lancet Haematology, Volume 6, Issue 7, July 2019; e350 - e358.

[15] https://www.cdc.gov/nhsn/pdfs/biovigilance/bv-hv-protocol-current.pdf

HT (non-ABO)

1. **HTR (non-ABO) – *Definite***
   A patient with multiple comorbidities and known anti-K antibody received four units of uncrossmatched O Pos RBCs via a massive transfusion protocol in the emergency department. Considering the emergent need for RBCs, ~9% prevalence of K antigen in the general population, and the potential onset of hemolysis associated with anti-K, a decision was made to transfuse the uncrossmatched units incrementally. Post-transfusion phenotyping revealed two of the four units were K antigen positive.

2. **HTR (non-ABO) – *Definite***
   A patient with sickle cell disease and a history of anti-E and warm autoantibodies underwent perioperative transfusion of two crossmatch-compatible RBCs negative for E, C, and K antigens. Four days post-transfusion, the patient presented with exacerbated pain in the back and legs. Because of a drop in hemoglobin, a subsequent unit negative for E, C, and K antigens was administered. Laboratory data showed findings consistent with a hyper hemolysis induced transfusion reaction.

3. **HTR (non-ABO) – *Definite***
   A patient with sickle cell disease and HELLP* syndrome received two units of Hemoglobin (Hgb) S negative red cells. The patient's pre-transfusion type and screen was negative. Two weeks later, the patient presented to the emergency department with symptoms initially attributed to a sickling crisis. Laboratory tests revealed severe anemia (Hgb 4 g/dL) and the presence of anti-C and anti-S antibodies. The patient received an additional crossmatched red cell unit, followed by massive transfusion protocol consisting of six red cell units and six plasma units. The patient's death was attributed to a delayed hemolytic transfusion reaction mediated by anti-C and anti-S antibodies.

4. **HTR (non-ABO) – *Possible***
   A patient with significant comorbidities and warm autoimmune hemolytic anemia (WAIHA) presented with severe anemia (Hgb 6.2 g/dL) and symptoms consistent with cardiac ischemia. The patient received two least-incompatible red cell units. Post-transfusion, the patient experienced an acute hemolytic reaction, likely due to the underlying WAIHA. The patient's death was assessed as possibly related to an acute hemolytic transfusion reaction, as ongoing hemolysis of the patient's own red blood cells was occurring simultaneously.

5. **HTR (non-ABO) – *Possible***
   A patient with significant comorbidities underwent massive transfusion protocol activation due to a gastrointestinal bleed. The patient received emergently transfused units including five units of uncrossmatched RBCs, three units of thawed plasma, one apheresis platelet unit, and one pooled cryoprecipitate unit. All units were ABO-compatible. Retrospective testing revealed an anti-E antibody, with three of the five transfused RBC units found to be incompatible due to a positive E antigen.

6. **HTR (non-ABO) – *Possible***
   A patient with a complex medical history developed hemodynamic instability following ureteral stent placement. Clinical findings suggested potential internal hemorrhage, evidenced by a significant Hgb decrease of approximately 5 g/dL over a 48-hour period, concurrent with symptoms indicative of septic shock. Two uncrossmatched RBCs were administered. The patient was later found to have anti-Jk(a) antibody and one of the transfused units was Jk(a) positive. Post-transfusion tests revealed signs of hemolysis, including elevated bilirubin, decreased haptoglobin, and antibody presence, suggestive of a hemolytic transfusion reaction.

In FY2022, no fatalities were reported due to ABO HTRs. Based on recent trends in ABO-incompatible transfusion-related fatalities, we would have expected approximately two cases per year.[16] From FY2008, there was a general downward trend in the total number of reported fatalities due to both ABO and non-ABO HTRs. However, in fiscal year 2019, there was a notable increase in non-ABO HTRs (Figure 5).

Table 4: Antibodies Identified in Fatalities due to Hemolytic Transfusion Reactions, FY2018-FY2022

Antibody	FY18 No.	FY19 No.	FY20 No.	FY21 No.	FY22 No.	Total No.
ABO	2	4	2	5	-	**13**
Multiple* Antibodies	-	1	1	1	1	**4**
Other**	2	2	-	-	1	**5**
D	-	1	-	-	-	**1**
E	-	-	-	-	2	**2**
f	-	1	-	-	-	**1**
V	-	1	-	-	-	**1**
K	-	1	-	-	1	**2**
Fy^a	1	1	-	1	-	**3**
Jk^a	-	1	-	-	1	**2**
Jk^b	1	-	-	-	-	**1**
Jk^3	-	1	-	-	-	**1**
M	-	1	-	-		**1**
Wr^a	1	-	-	-	-	**1**
Total	**7**	**15**	**3**	**7**	**6**	**38**

*Multiple Antibodies:

FY2019: antibody combinations include $Fy^a + Jk^b$
FY2020: antibody combinations include $E + Jk^a + S$
FY2021: antibody combinations include $C+E+K+Jk^b+Fy^a+Fy^b$
FY2022: antibody combinations include C+S

**Other includes:

FY2018: 1) A case with anti-Jk^b, anti-S, and hyperhemolysis syndrome
2) A case of transfused Cold Autoimmune Hemolytic Anemia
FY2019: 1) A case of transfused WAIHA
2) HTR with no definitive serological findings
FY2022: 1) A case of transfused WAIHA
2) A case with anti-E, hyperhemolysis syndrome, and a WAIHA

*A rare complication of pregnancy characterized by hemolysis, elevated liver enzymes, and low platelets.

[16] Storch, Emily K., et al. "Trends in ABO-Incompatible RBC Transfusion-Related Fatalities Reported to the FDA, 2000-2019." *Transfusion*, vol. 60, no. 12, 16 Oct. 2020, pp. 2867-2875, https://doi.org/10.1111/trf.16121.

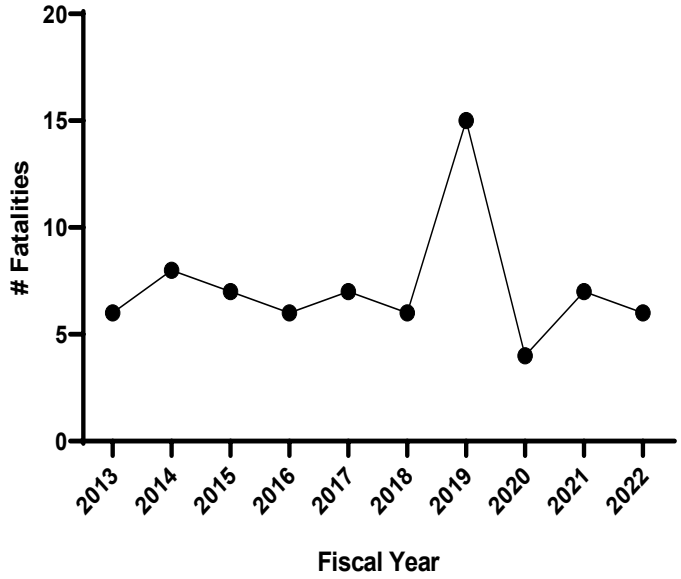

Figure 5: Hemolytic Transfusion Reaction Fatalities, FY2013 – FY2022

E. Microbial Contamination

In FY2022, there was one case of a microbial contamination-related (bacteria) fatality, attributed to a red cell unit (Tables 5 & 6).

Table 5: Contamination Breakdown, FY2022

Product	Organism(s)	Imputability
Red Blood Cells	*Pseudomonas fluorescens, Rahnella aquatilis*	Definite

1. Contamination (*Pseudomonas fluorescens, Rahnella aquatilis) - Definite*
A patient with comorbidities developed symptoms suggestive of a febrile non-hemolytic transfusion reaction after receiving two RBCs. Gram stain of one of the implicated units revealed gram-negative bacilli. First culture identified *Pseudomonas fluorescens* and *Rahnella aquatilis* and second culture grew *Rahnella aquatilis*.

Table 6: Bacterial Contamination by Implicated Organism, FY2018 - FY2022

Organism	FY18	FY19	FY20	FY21	FY22	TOTAL
Acinetobacter spp.	1	-	-	-	-	**1**
Clostridium perfringens	1	-	-	-	-	**1**
Corynebacterium striatum	-	-	-	1	-	**1**
Escherichia coli	-	-	-	2	-	**2**
Pseudomonas aeruginosa	1	-	-	-	-	**1**
Pseudomonas fluorescens	-	-	1	-	-	**1**
Pseudomonas veronii	1	-	-	-	-	**1**
Rahnella species	-	-	1	-	-	**1**
Serratia marcescens	-	1	-	-	-	**1**
Staphylococcus aureus	2	-	-	1	-	**3**
Polymicrobial*	-	-	1	1	1	**3**
TOTAL	**6**	**1**	**3**	**5**	**1**	**16**

*FY2020 case of polymicrobial contamination involved *Acinetobacter sp.*, *Leclercia adecarboxylata*, and *Staph. saprophyticus.* FY2021 case involved *Bacillus species (not Bacillus anthracis), Acinetobacter baumannii complex, Leclercia adecarboxylata, and Staphylococcus saprophyticus.* FY2022 case involved *Pseudomonas fluorescens* and *Rahnella aquatilis.*

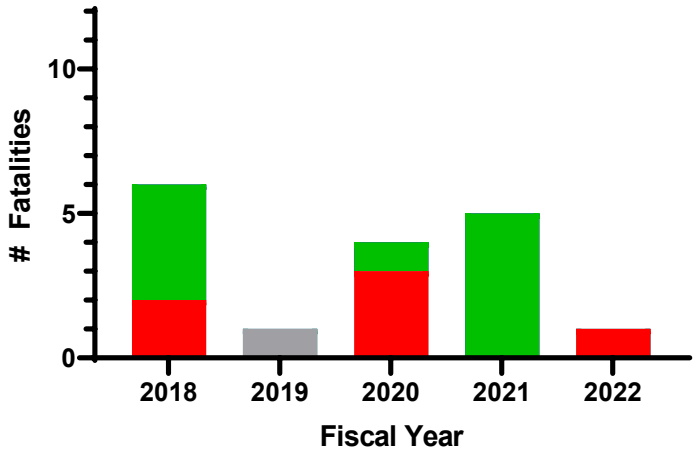

Figure 6: Contamination by Implicated Blood Product, FY2018-FY2022

FY2020 had one fatality case attributed to the transfusion transmission of *Babesia microti* from a red cell unit.

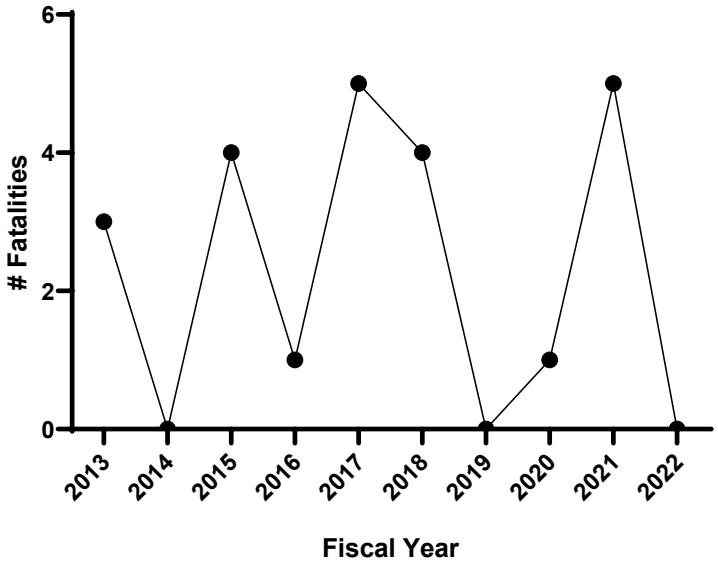

Figure 7: Contamination (bacterial) by Apheresis Platelets, FY2013 – FY2022

Figure 7 shows the trend of contamination (bacterial) associated with apheresis platelets from FY2013 to FY2022. There was one fatality report of bacterial contamination in RBCs reported in FY2022, and no cases attributed to bacterial contamination of apheresis platelets. Between fiscal years 2018 and 2021, three deaths were attributed to a common source of contamination, with one fatality occurring in each of 2018, 2020, and 2021.[17, 18] Bacterial contamination of platelet units remains a public health concern which FDA has addressed in regulation (21 CFR 606.145), with additional considerations on controlling bacterial risk provided in the guidance document "*Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion*" [19]

[17] Kracalik, Ian., et al. "Posttransfusion Sepsis Attributable to Bacterial Contamination in Platelet Collection Set Manufacturing Facility, United States." *Emerging Infectious Diseases*, vol 29, no. 10, Oct. 2023. https://doi.org/10.3201/eid2910.230869

[18] Villa, Carlos. H., et al. "Posttransfusion sepsis attributable to bacterial contamination in platelet collection set manufacturing, United States." *Transfusion*, vol 63, no. 12, pp. 2351-2357. https://doi.org/10.1111/trf.17589

[19] https://www.fda.gov/media/123448/download

F. Transfusion Doubtful as Cause of Death

We classified 13 (24%) of the 54 cases described earlier as potentially associated with transfusion recipient fatalities in FY2022 as *doubtful,* including the following classifications: No Transfusion Reaction (five), TACO (two), Possible TRALI (three), Transfusion Reaction, Type Not Determined (one), HTR (non-ABO) (one), and Other (one). Although transfusion reactions could not be excluded as a contributing factor, the evidence in each of these cases more strongly favored the patients' underlying medical conditions as the primary cause of death. Thus, we did not include these reported fatalities in the analysis in Sections III.A through III.E.

G. Transfusion Not Assessable as Cause of Death

We classified four (7%) of the 54 cases described as potentially associated with transfusion recipient fatalities in FY2022 as *not assessable*. In these cases, there was insufficient information submitted or available to determine the type of reaction and the extent of the relation between the transfusion and the death. Thus, these reported fatalities were also not included in the analysis in Sections III.A through III.E.

H. Transfusion Ruled Out as Cause of Death

We classified seven (13%) of the 54 cases described as potentially associated with transfusion recipient fatalities in FY2022 as *ruled out*. Our medical reviewers concluded that either no transfusion reaction occurred, or, while there was a temporal relationship between transfusion and subsequent death of the recipient, there was conclusive evidence beyond a reasonable doubt for attributing the fatality to a cause (e.g., underlying condition) other than transfusion. Thus, we did not include these reported fatalities in the analysis in Sections III.A through III.E.

I. Donation Fatalities

The processes of blood and plasma donation are generally safe and determining that a causal link exists between a donation and the fatality remains uncommon among reported donation fatalities. For FY2022, there was one whole blood donation fatality classified as *definite*, three classified as *probable,* and there were seven donations classified as *possible.* These numbers are slightly increased compared to those reported in recent annual summaries (Figure 8). There were six donation fatalities classified as *doubtful,* 10 donation fatalities classified as *ruled out,* and 10 donation fatalities classified as *not assessable* (Table 7).

- **Donation – *Definite***
  There was one fatality following whole blood donation where the complication was definitely related to the donation. There was unequivocal evidence establishing causal relationship between the donation and the fatality.

- **Donation – *Probable***
  There were two fatalities following Source Plasma donation and one fatality following apheresis platelet donation where the complication was probably related to the donation. The evidence was in favor for attributing the fatality to the donation.

- **Donation – *Possible***
  There were six fatalities following Source Plasma donation and one fatality following whole blood donation where the complication was possibly related to the donation; however, the evidence was indeterminate for attributing the fatality to the donation or an alternative cause.

- **Donation – *Doubtful***
  There were six fatalities following Source Plasma donations in which the relationship between the donation and subsequent death was classified as *doubtful.* In these six cases, the evidence was in favor of attributing the death to a cause other than the donation (e.g., underlying medical conditions), but the donation could not be excluded.

- **Donation – *Ruled Out***
  There were 10 fatalities following Source Plasma donation in which the donations were classified as *ruled out*. In these cases, there was evidence beyond a reasonable doubt for attributing the fatality to causes other than donation (e.g., drug overdoses, or underlying medical conditions).

- **Donation – *Not Assessable***
  There were nine fatalities following Source Plasma donation and one fatality following whole blood donation in which the donation was classified as *not assessable*. In these cases, there was insufficient information submitted/available to determine the extent of the relation between the donations and the cause of death.

Table 7: Donation Fatalities with Imputability by Product, FY2022

DONATION TYPE	Definite	Probable	Possible	Doubtful	Ruled Out	Not Assessable	TOTAL REPORTS
Source Plasma	-	2	6	6	10	9	**33**
Whole Blood	1	-	1	-	-	1	**3**
Apheresis Platelets	-	1	-	-	-	-	1
Total	**1**	**3**	**7**	**6**	**10**	**10**	**37**

The row header refers to Imputability to Death

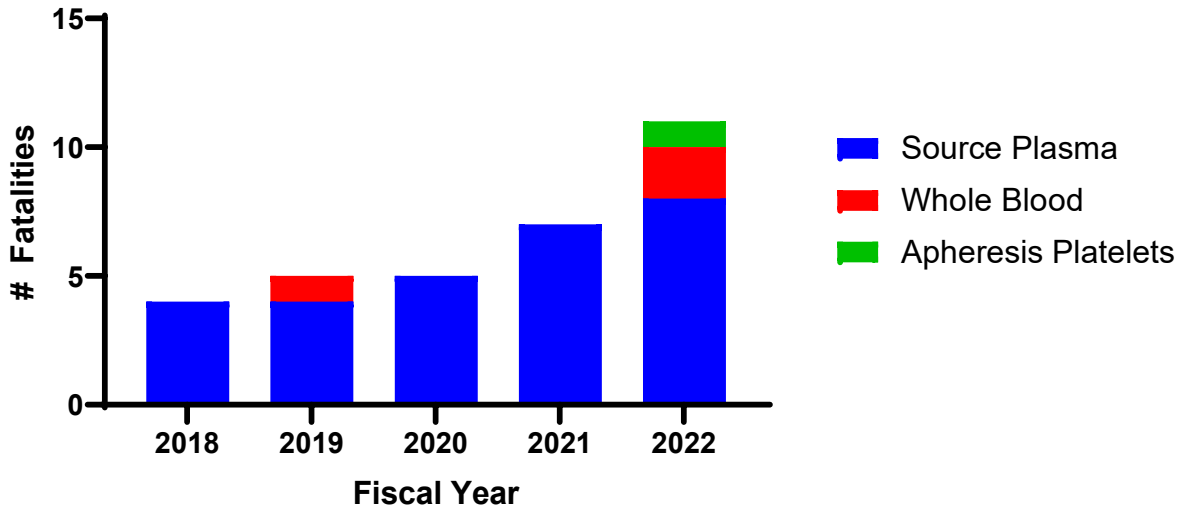

Figure 8: Donation Fatalities with Possible, Probable, or Definite Imputability by Product Type, FY2018-FY2022

Table 8: Donation with *Doubtful* or *Not Assessable* Imputability to Death by Product, FY2018-FY2022

Donated Product	FY18	FY19	FY20	FY21	FY22	TOTAL REPORTS
Source Plasma	4	8	11	17	15	**55**
Whole Blood	2	1	0	0	1	**4**
Apheresis Platelets	0	0	0	0	0	**0**
Apheresis Red Blood Cells	0	0	1	0	0	**1**
Total	**6**	**9**	**12**	**17**	**16**	**60**

Table 9: Donation *Ruled Out* by Product, FY2018-FY2022

Donated Product	FY18	FY19	FY20	FY21	FY22	TOTAL REPORTS
Source Plasma	9	6	8	7	10	**40**
Whole Blood	-	-	-	-	-	**-**
Apheresis Platelets	-	-	-	-	-	**-**
Apheresis Red Blood Cells	-	-	-	-	-	**-**
Total	**9**	**6**	**8**	**7**	**10**	**40**