Fatalities Reported to FDA Following Blood Collection and Transfusion

Annual Summary for Fiscal Year 2020

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) 2020 (October 1, 2019, through September 30, 2020), to provide the combined data received over the last five fiscal years, and to compare the FY 2020 summary to the fatality reports received in the previous four fiscal years.[1] Due to advances in donor screening, improved testing, automated data systems, and changes in transfusion medicine practices, the risks associated with blood transfusion remain low. 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 2019, 10.8 million whole blood and apheresis red blood cells, 2.2 million platelets, and 2.1 million plasma components were transfused, with a slight increase in demand for RBCs compared to 2017 (10.6 million) and reversing a decline that started in 2008.[2] However, this annual summary covers a period overlapping with the early COVID-19 pandemic, and the impact on both blood collections and transfusions during the reporting period is uncertain. For example, in the pandemic's early waves of Spring 2020, cancellation or deferral of elective procedures may have decreased the total number of transfusions[3,4]. During FY 2016 there were 43 fatalities determined to be transfusion related. The corresponding fatalities that were classified as either *definite, probable,* or *possible* were 37 in 2017, 31 in 2018, 44 in 2019, and 29 in 2020. 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.

Although donating blood is generally safe, we also include information on the infrequent 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 donations. In 2019, U.S blood establishments collected[2] 11.5 million whole blood and apheresis red blood cell units, 2.5 million platelet units, and 2.6 million of plasma components. There were 53.5 million source plasma donations made in the U.S compared to 48.7 million in 2018.[5] Over the combined five-year reporting period (FY 2016 – FY 2020) there were 92 reported donation-associated fatalities (associated with a variety of donated products), with 19 cases since 2016 having an imputability of *definite, probable,* or *possible*.

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.[6]

[1] The FY2005 - FY2013 data are available at: http://wayback.archive-it.org/7993/20171114012113/https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/default.htm

[2] https://onlinelibrary.wiley.com/doi/10.1111/trf.16449

[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7753805/

[4] https://pubmed.ncbi.nlm.nih.gov/32384164/

[5] https://www.pptaglobal.org/images/Data/Plasma_Collection/Total_Yearly_Collections_2008-2019.pdf

[6] Guidance for Industry: Notifying FDA of Fatalities Related to Blood Collection or Transfusion, September, 2003. 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:

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2. Call us at 240-402-9160, or
3. Write us at: Food and Drug Administration
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II. Changes in Our Evaluation Approach:

Starting with the annual report of FY 2015, and 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,[7] (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 Haemovigilance Working Group[8] (https://www.aabb.org/research/hemovigilance/Documents/Donor-Standard-Definitions.pdf), the British Serious Hazards of Transfusion (SHOT)[9], and the Haemovigilance activity report of the French National Agency for Medicines and Health Products Safety (ANSM)[10].

In fiscal years prior to FY 2015, 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 FY 2015, 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 FY 2016: No Transfusion Reaction, Possible TRALI (previously tallied with TRALI), and Transfusion Reaction, Type Not Determined (Table 2). In FY 2018, we added Unlikely Transfusion Reaction.

[7] Center for Disease Control and Prevention National Healthcare Safety Network, Biovigilance Component, Hemovigilance.
[8] International Society of Blood Transfusion Working Party on Haemovigilance in collaboration with the International Haemovigilance Network and the AABB Donor Haemovigilance Working Group, Standard for Surveillance of Complications Related to Blood Donation, December 2014.
[9] Annual Serious Hazards of Transfusion Report, 2014.
[10] French National Agency for Medicine and Health Product Safety (ANSM), 2013 Haemovigilance Activity Report.

Our review process includes a team of CBER medical officers 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, FY 2016-FY 2020

	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. FY 2020 Results

During FY 2020, we received a total of 77 fatality reports. Of these reports, 52 were potentially associated with transfusion, and 25 were potentially associated with donation.

Of the 52 potentially transfusion-associated fatality reports, we determined the imputability of the transfusions to the fatalities as follows:

a) Twenty-nine (56%) of the fatalities were classified as either *definite, probable,* or *possible.*
b) Thirteen (25%) of the fatalities were classified as either *doubtful*, or *not assessable*.
c) Ten (19%) of the fatalities were classified as *ruled out*.

Of the 25 potentially donation-associated fatality reports, we determined the imputability of the donations to the fatalities as follows:

a) Five (20%) of the fatalities were classified as *probable, or possible*.
b) Twelve (48%) of the fatalities were classified as either *doubtful*, or *not assessable*.
c) Eight (32%) of the fatalities were classified as *ruled out*.

We summarize the results of our review in Table 2.

Table 2: Fatality Complication Breakdown by Imputability, FY 2020

CATEGORY	Definite	Probable	Possible	Doubtful	Ruled Out	Not Assessable	TOTAL REPORTS
Transfusion							
Allergy/Anaphylaxis	4	1	1	1	-	-	7
Contamination (Bacterial)	2	-	1	-	-	-	3
Contamination (Parasitic)	-	1	-	-			1
HTR (ABO)	1	1	-	-	-	-	2
HTR (non-ABO)	-	2	-	1	-	-	3
No Transfusion Reaction	-	-	-	-	10	-	10
Not Assessable*	-	-	-	-	-	1	1
Other**	-	-	-	2	-	-	2
Possible TRALI	-	1	1	1	-	1	4
TACO	-	5	3	1	-	-	9
Transfusion Reaction, Type Not Determined	-	-	1	1	-	-	2
TRALI	2	2	-	1	-	-	5
Unlikely Transfusion Reaction	-	-	-	3	-	-	3
Total	9	13	7	11	10	2	52
Donation							
Donor Fatality	-	1	4	8	8	4	25

TRALI = Transfusion Related Acute Lung Injury; TACO = Transfusion Associated Circulatory Overload; HTR = Hemolytic Transfusion Reactions
The Row Header refers to Imputability to Death
*Category and Imputability Not Assessable
**Other: Febrile Non-Hemolytic Reaction

For the purpose of comparison with previous fiscal years, the FY 2016 through FY 2020 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 FY 2016 through FY2020

In combined FYs 2016 through 2020, TACO[11,12] cases caused the highest number of reported fatalities (34%), followed by the combined TRALI and Possible TRALI (21%), microbial contamination (13%), HTR due to non-ABO incompatibilities (13%), anaphylaxis reactions (10%), HTRs due to ABO incompatibilities (7%), and transfusion reaction type not determined (2%), (Table 3, and Figure 1).

[11] 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.

[12] http://anesthesiology.pubs.asahq.org/article.aspx?articleid=2598362

TACO was the leading cause of reported transfusion-associated deaths for FY 2016 through FY 2018, and in FY 2019, TACO and TRALI represented the leading causes of transfusion-associated death (12 cases each). In FY 2020, TACO was the leading cause of transfusion-associated death (eight cases). Prior to FY 2016, TRALI was the consistent leading cause of transfusion-associated fatalities.

Although the number of reported transfusion-associated deaths attributable to anaphylaxis has appeared relatively steady over the last five fiscal years, FY 2020 found a larger number of deaths attributed to anaphylaxis (six) compared to each of the two prior years (Table 3). For FY 2016 through FY 2020, 18 anaphylactic reactions were identified. While IgA and haptoglobin deficiencies have been historically implicated as a contributory factor in anaphylactic reactions[13,14], 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.

Transfusion-associated deaths attributable to hypotensive reactions remains rare, with only one case (FY 2016) identified in the last five years. Hypotension may be an element of the clinical presentation for other types of transfusion reactions and recognizing it as the primary cause can be challenging. In the case reported in FY 2016, all other adverse reactions presenting with hypotension were excluded.

Table 3: Transfusion-Associated Fatalities by Complication, FY 2016 – FY 2020

Complication	FY16 No.	FY16 %	FY17 No.	FY17 %	FY18 No.	FY18 %	FY19 No.	FY19 %	FY20 No.	FY20 %	Total No.	Total %
Anaphylaxis	5	12%	3	8%	2	6%	2	5%	6	21%	**18**	**10%**
Contamination	5	12%	7	19%	7	23%	1	2%	4	14%	**24**	**13%**
HTR (ABO)	4	9%	1	3%	2	6%	4	9%	2	7%	**13**	**7%**
HTR (Non-ABO)	1	2%	6	16%	4	13%	11	25%	2	7%	**24**	**13%**
Hypotensive Reaction	1	2%	0	0%	0	0%	0	0%	0	0%	**1**	**0%**
TACO	19	44%	11	30%	12	39%	12	27%	8	27%	**62**	**34%**
TRALI**	8	19%	9	24%	4	13%	12	27%	6	21%	**39**	**21%**
Transfusion Reaction, Type Not Determined	0	0%	0	0%	0	0%	2	5%	1	3%	**3**	**2%**

Note: FY 2016-FY 2020 only includes cases with an imputability of *definite, probable*, or *possible*

**FY 2016-FY 2020 numbers combine both *TRALI* and *Possible TRALI* cases

[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] 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.

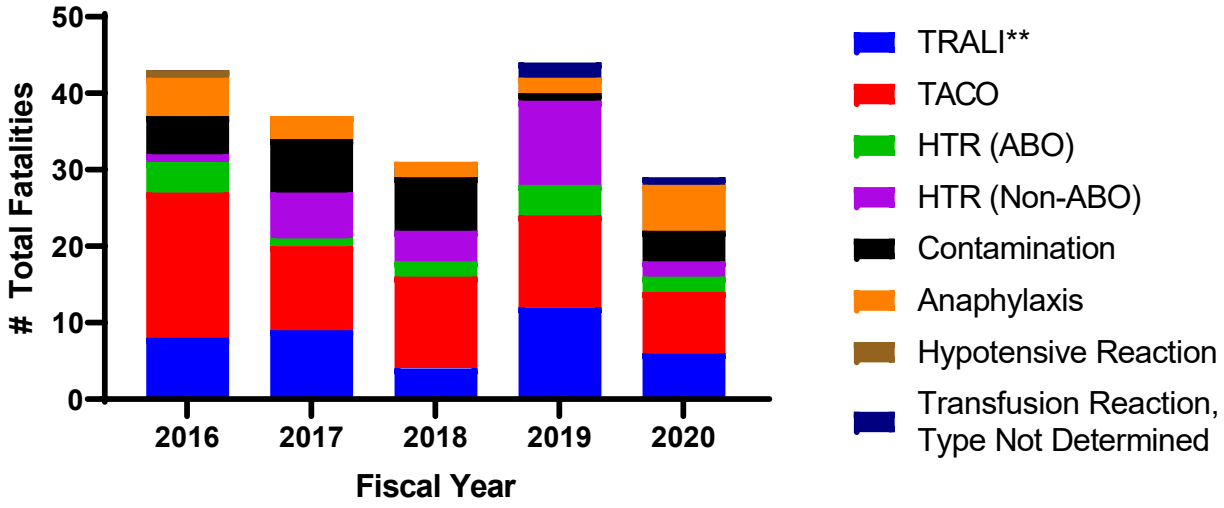

Figure 1: Transfusion-Associated Fatalities by Complication, FY 2016 – FY 2020

Note: FY 2016-FY 2020 only includes cases with an imputability of *definite, probable*, or *possible*
**FY 2016-FY 2020 numbers combine both *TRALI* and *Possible TRALI* cases

B. Transfusion Related Acute Lung Injury (TRALI)

In FY 2020, TRALI was the second leading cause of transfusion-associated fatalities (along with anaphylaxis). There was one case of Possible TRALI classified with an imputability to death of *probable*, and one case classified with an imputability of *possible*. There were also two cases of TRALI classified with an imputability to death of *definite* and two cases classified with an imputability to death of *probable*. Altogether, there were a total of six TRALI cases. For FY 2020, there were no cases where testing matched donor antibodies with recipient cognate antigens, due to either negative or incomplete donor/recipient testing. The limited data provided to FDA do not elucidate the role of particular donor antibodies or donor gender in the etiology of the TRALI reactions.

TRALI represented 21% of transfusion-associated fatalities reported to CBER over the last five fiscal years, including FY 2020 (Table 3). As documented in prior annual summaries, a rise in TRALI cases between FY 2005 and FY 2007 was followed by an abrupt decline in FY 2008. There has been an overall downward trend since FY 2010 (Figures 1 and 2), although with an uptick in FY 2019, followed by a decline in FY 2020. Red blood cells are the most frequently implicated product since 2016 (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.[15,16]

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

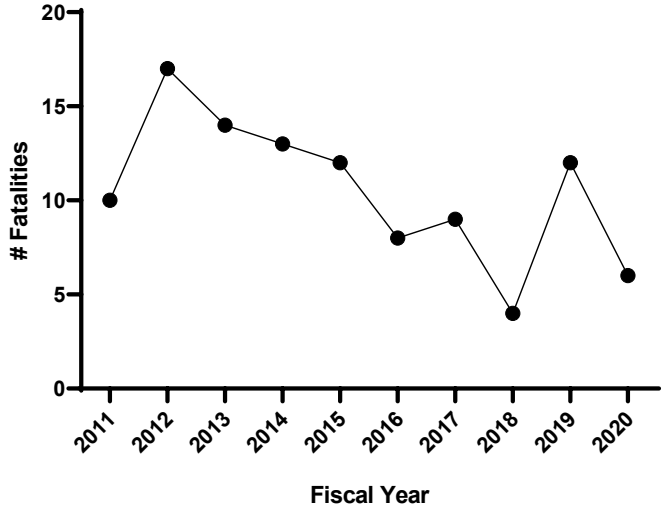

Figure 2: TRALI Fatalities, FY 2011-FY 2020

FY	FFP	RBC	Apheresis Platelets	Multiple Products
2011	3	3	2	1
2012	0	6	5	4
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

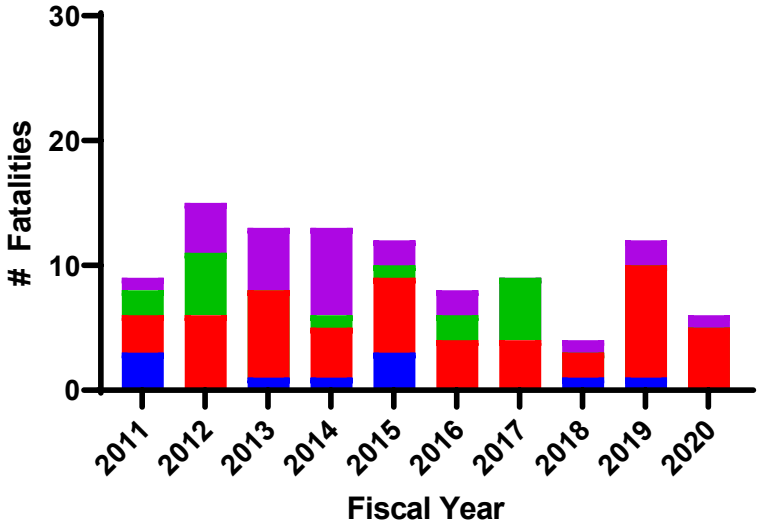

Figure 3: TRALI Fatalities by Implicated Blood Product, FY 2011 – FY 2020

C. Transfusion Associated Circulatory Overload (TACO)

In FY 2020, there were eight cases of TACO with an imputability of d*efinite*, *probable*, or *possible.* TACO was the leading cause of transfusion-associated fatalities reported to FDA. Among these eight reports, one was associated with whole blood transfusion, three were associated with RBC transfusion, and four were associated with multiple blood products.

TACO has been the leading cause of transfusion-associated fatalities reported to FDA in the last five annual reports (FY 2016-FY 2020). The number of TACO fatalities (Figure 4) has not shown significant change since FY 2016. Active surveillance systems found the incidence of TACO to be approximately one case per 100 patients transfused,[17] 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,[18] 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.[19]

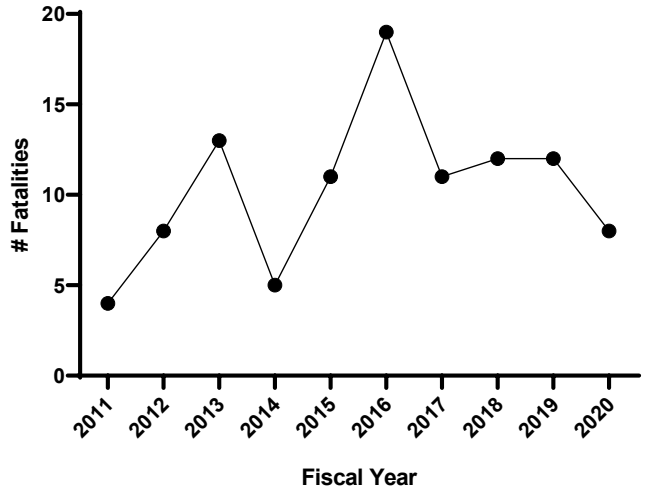

Figure 4: TACO Fatalities, FY 2011-FY 2020

D. Hemolytic Transfusion Reactions (HTR)

In FY 2020, there were two reported ABO hemolytic transfusion fatalities classified as d*efinite and probable* (7% of confirmed transfusion-associated fatalities), and two non-ABO hemolytic transfusion fatalities; with an imputability of *probable* (7% of confirmed transfusion-associated fatalities) (Tables 3 and 4).

[17] 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.

[18] 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, e350 - e358.

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

HTR (ABO)

1. **HTR (ABO) – *Definite***
   A group O patient was transfused with a unit of group A RBCs due to a blood administration error. The patient experienced a hemolytic transfusion reaction. It was subsequently determined that this error was related to administration of blood intended for another patient and failure to follow procedures for two-person verification at the patient bedside prior to transfusion.

2. **HTR (ABO) – *Probable***
   A group O patient was transfused with group A RBCs due to a labeling error that occurred in the blood bank. The patient experienced a hemolytic transfusion reaction. Upon further review, it was discovered that the recipient's sample was received with a non-barcoded label and the blood bank erroneously affixed the sample with another patient's (group A) blood bank label. Additionally, the unit was issued prior to receiving a second ABO confirmation sample.

HTR (non-ABO)

1. **HTR (non-ABO) – *Probable***
   A patient with a history suggestive of a warm autoantibody received two uncrossmatched RBCs under emergency release prior to completion of the antibody workup. The patient immediately developed signs of a hemolytic transfusion reaction. It was subsequently determined that the patient had anti-Jk(a), anti-S, and anti-E antibodies, in addition to the warm autoantibody. The first transfused unit was antigen positive for S and Jk(a), and the second unit was antigen positive for S, E, and Jk(a). Both units were determined to be incompatible. The patient also had multiple co-morbidities which may have contributed to the death.

2. **HTR (non-ABO) – *Probable***
   A patient with Sickle Cell Disease received multiple RBCs. The patient developed clinical evidence of a hemolytic transfusion reaction. While an antibody screen on the post transfusion sample was positive, no specific antibodies were identified. The findings were consistent with sickle cell crisis complicated by hyperhemolysis.

The number of hemolytic transfusion reactions has remained low in recent years, particularly ABO HTRs, where the error is most frequently preventable misidentification of the patient or the patient's sample. From FY 2008, there was an overall downward trend in the total number of reported fatalities due to HTRs (both ABO and non-ABO) until FY 2019, where there was a relative increase, particularly with non-ABO HTRs. However, there a was a sharp reduction in FY 2020 (Figure 5).

Table 4: Antibodies identified in fatalities due to hemolytic transfusion reactions, FY 2016-FY 2020

Antibody	FY16 No.	FY17 No.	FY18 No.	FY19 No.	FY20 No.	Total No.
ABO	4	1	2	4	2	**13**
Multiple* Antibodies	-	1	-	1	1	**3**
Other**	-	2	2	2	-	**6**
D	-	-	-	1		**1**
c	1	-	-	-	-	**1**
e	-	1	-	-	-	**1**
f	-	-	-	1	-	**1**
V	-	-	-	1		**1**
K	-	-	-	1	-	**1**
Fy^a	-	1	1	1		**3**
Jk^a	-	-	-	1	-	**1**
Jk^b	-	-	1	-	-	**1**
Jk3	-	-	-	1	-	**1**
M	-	-	-	1		**1**
U	-	1	-	-	--	**1**
Wr^a	-	-	1	-	-	**1**
Total	**5**	**7**	**7**	**15**	**3**	**37**

*Multiple Antibodies: FY 2017: antibody combinations include: Jk^a+M
FY 2019: antibody combinations include Fy^a + Jk^b
FY 2020: antibody combinations include E + Jk^a + S

**Other: FY 2017: Includes one report of Hyperhemolysis Syndrome in which no new or additional antibody was identified, and one case of a hemolytic transfusion reaction where no new or additional antibody was identified
FY 2018: 1) The case with anti-Jk^b also demonstrated anti-S and a Hyperhemolysis Syndrome
2) A case of transfused Cold Autoimmune Hemolytic Anemia
FY 2019: 1) Likely WAIHA 2) HTR with no definitive serological findings.

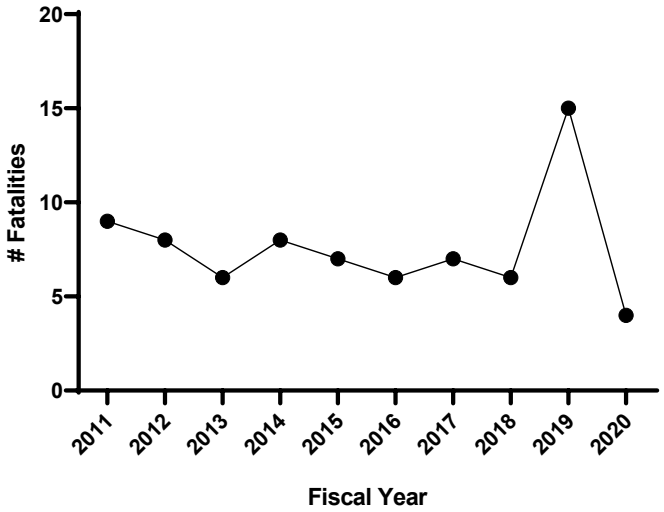

Figure 5: Hemolytic Transfusion Reaction Fatalities, FY 2011 – FY 2020

E. Microbial Contamination

In FY 2020, there were four cases of a contamination-related fatalities, with three attributed to bacterial contamination and one attributed to parasitic contamination (Tables 5 & 6). The bacterial contamination cases were associated with two red blood cells (*Pseudomonas fluorescens and Rahnella* species*),* and one associated with an apheresis platelet *(Leclercia adecarboxylata, Acinetobacter baumannii complex,* and *Staphylococcus saprophyticus).* The parasitic contamination case was associated with red blood cells *(Babesia microti).*

Table 5: Contamination Breakdown, FY 2020

	Organism	Imputability
Apheresis Platelets	*Acinetobacter baumannii complex, Leclercia adecarboxylata,* and *Staphylococcus saprophyticus*	Definite
Red Blood Cells	*Pseudomonas fluorescens*	Definite
Red Blood Cells	*Rahnella* species *(Enterobacteriaceae)*	Possible
Red Blood Cells	*Babesia microti*	Probable

1. Contamination (*Acinetobacter baumannii* complex species, *Leclercia adecarboxylata and Staphylococcus saprophyticus) - Definite*

The patient developed symptoms of a septic reaction on receipt of the implicated platelet unit. Cultures of the implicated unit (which was processed with a pathogen reduction device) grew *Acinetobacter baumannii* complex species*, Leclercia adecarboxylata and Staphylococcus saprophyticus.* The patient's blood culture also grew the same organisms. Of note, a platelet co-component also grew the same organisms but was not implicated in a transfusion reaction. This case has been separately reported in published literature[20].

2. Contamination (*Pseudomonas fluorescens*) - *Definite*

The patient received a unit of red blood cells and *Pseudomonas fluorescens* was identified in the red cell unit and in the patient. Additional testing confirmed that the organism from the patient and implicated red blood cell unit were related.

3. Contamination (*Rahnella sp.*) – *Possible*

A patient received two units of irradiated red blood cells and *Rahnella* species was identified in the second unit and in the patient's blood culture. While we considered the case to likely represent transfusion-transmission of *Rahnella sp.*, when considering the severity of the patient's underlying illness, the imputability of the reaction to death was classified as *possible*.

[20] Fadeyi EA et al. Fatal sepsis associated with a storage container leak permitting platelet contamination with environmental bacteria after pathogen reduction. Transfusion 2021;61:641-648.

4. Contamination (*Babesia microti*) – *Probable*

A patient received four red blood cell units and *Babesia microti* was identified in the patient. Post donation testing showed that one donor tested positive for antibodies to Babesia and a negative NAT result. However, the patient had multiple co-morbidities and significant clinical deterioration; therefore, imputability of the reaction to death was classified as *probable*.

Figure 6 show microbial contamination events by product type. *Babesia microti* infections were associated with four of the 10 RBC transfusions implicated in reported fatalities over the last five years. In 2019, FDA issued the final guidance document "Recommendations for Reducing the Risk of Transfusion-Transmitted Babesiosis".[21]

[21] https://www.fda.gov/media/114847/download

Figure 7 shows the trend of contamination (bacterial) associated with apheresis platelets from FY 2004 to FY 2020. While there was only one fatality report of bacterial contamination in apheresis platelets reported in FY 2020, bacterial contamination of platelet components 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*".[22] The effect of apheresis technology on bacterial contamination has been described.[23]

Table 6: Contamination by Implicated Organism, FY 2016 – FY 2020

	FY16	FY17	FY18	FY19	FY20	TOTAL
Bacteria						
Acinetobacter spp.	-	-	1	-	-	**1**
Anaplasma phagocytophilum	-	1	-	-	-	**1**
Clostridium perfringens	-	2	1	-	-	**3**
Coagulase-negative staphylococci	1	-	-	-	-	**1**
Enterobacter aerogenes	1	-	-	-	-	**1**
Klebsiella pneumoniae	-	1	-	-	-	**1**
Pseudomonas aeruginosa	-	-	1	-	-	**1**
Pseudomonasfluorescens	1	-	-	-	1	**2**
Pseudomonas veronii	-	-	1	-	-	**1**
Rahnella species	-	-	-	-	1	**1**
Serratia marcescens	-	-	-	1	-	**1**
Staphylococcus aureus	-	-	2	-	-	**2**
Staphylococcus epidermidis	-	1	-	-	-	**1**
Polymicrobial*	-	-	-	-	1	**1**
Parasites						
Babesia microti	2	-	1	-	1	**4**
Viruses						
West Nile virus	-	2	-	-	-	**2**
TOTAL	**5**	**7**	**7**	**1**	**4**	**24**

FY 2020 case of polymicrobial contamination involved *Acinetobacter spp.*, *Leclercia adecarboxylata*, and *Staph. saprophyticus

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

[23] Eder AF, et al. Fatal sepsis correlates with bacterial contamination of platelets and reported septic transfusions reactions. Transfusion 2017;57:2969-2976

FY	RBC	Pooled Platelets	Apheresis Platelets	Plasma
2016	3	0	1	1
2017	1	0	5	1
2018	2	0	4	0
2019	0	1	0	0
2020	3	0	1	0

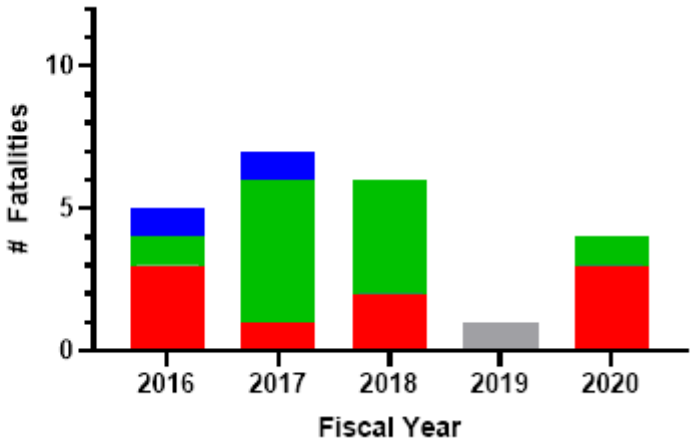

Figure 6: Contamination by Implicated Blood Product, FY 2016-FY 2020

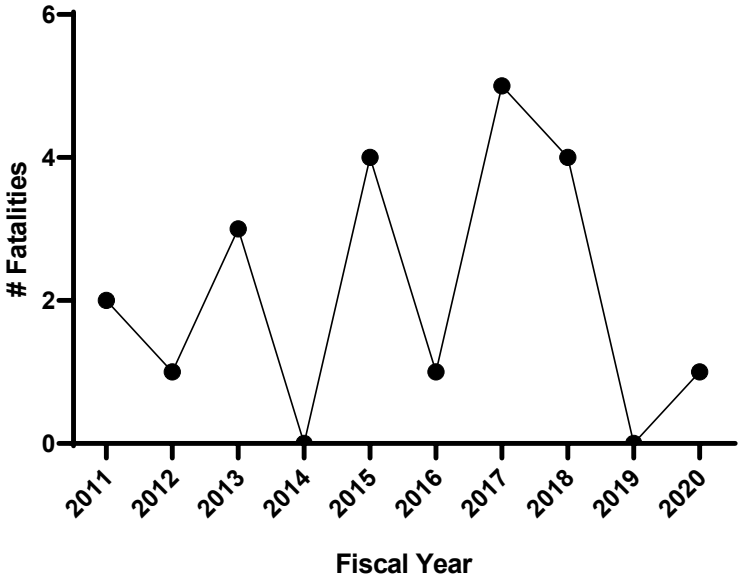

Figure 7: Contamination (bacterial) by Apheresis Platelets, FY 2011 – FY 2020

F. Transfusion Doubtful as Cause of Death

We classified 11 (21%) of the 52 cases described earlier as potentially associated with transfusion recipient fatalities in FY 2020 as *doubtful,* including one anaphylaxis case, one HTR (non-ABO), one TACO, one Possible TRALI, one TRALI, one Transfusion Reaction, Type Not Determined, three Unlikely Transfusion Reaction cases, and two cases classified as Other. Although transfusion could not be excluded as a contributing factor, the evidence in each of these cases more strongly favored the patient's underlying medical condition(s). 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 two (4%) of the 52 cases described as potentially associated with transfusion recipient fatalities in FY 2020 as *not assessable*. In these cases, there was insufficient information submitted/available to determine the type of reaction and the extent of the relation between the transfusions 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 10 (19%) of the 52 cases described as potentially associated with transfusion recipient fatalities in FY 2020 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 FY 2020, there were no donation fatalities classified as *definite*, one classified as p*robable,* and there were four donations classified as *possible.* These numbers are similar to those reported in recent annual summaries (Figure 8). There were eight donation fatalities classified as *doubtful,* eight donation fatalities classified as *ruled out,* and four donation fatalities classified as *not assessable* (Table 7).

- **Donation – *Probable***
  There was one fatality following Source Plasma donation where the complication was probably related to the donation. The evidence was clearly in favor for attributing the fatality to the donation.

- **Donation – *Possible***
  There were four fatalities following Source Plasma 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 eight fatalities following Source Plasma donations and one fatality following Red Blood Cell donation, in which the relationship between the donation and subsequent death was classified as *doubtful.* In these eight 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 eight fatalities following Source Plasma donation in which the donations were classified as *ruled out*. In these cases, there was clear 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 four fatalities following Source Plasma 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, FY 2020

DONATION TYPE	Definite	Probable	Possible	Doubtful	Ruled Out	Not Assessable	TOTAL REPORTS
Source Plasma	-	1	4	7	8	4	**24**
Whole Blood	-	-	-	-	-	-	-
Apheresis Platelets	-	-	-	-	-	-	-
Apheresis Red Cells	-	-	-	1	-	-	1
Total	**-**	**1**	**4**	**8**	**8**	**4**	**25**

The row header refers to Imputabilility to Death

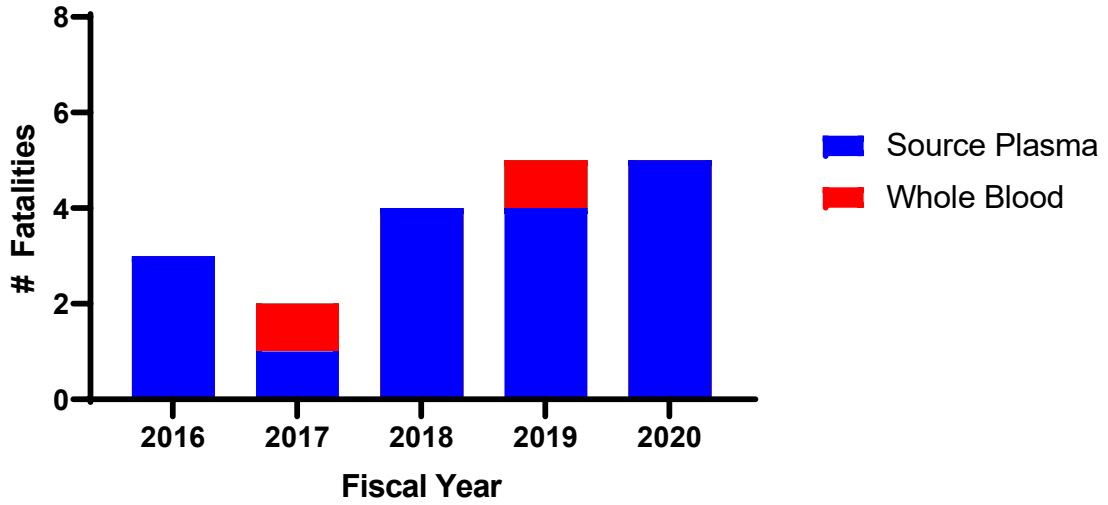

Figure 8: Donation Fatalities with *Possible, Probable, or Definite* Imputability by Product Type, FY 2016-FY 2020

In years prior to FY 2016, and in most donation cases, the donation could not be definitively ruled out as the cause of the donor's death following a thorough medical review which determined that the available evidence did not definitively rule out the donation, nor did the available evidence support a causal relationship between the donation and the donor's death.

For FY 2020, the cases classified as *doubtful*, and *not assessable* would most accurately compare to the *donation not ruled out* cases from years prior to FY 2015 (Table 8).

Table 8: Donation with *Doubtful* or *Not Assessable* Imputability to Death by Product, FY 2016-FY 2020

Donated Product	FY16	FY17	FY18	FY19	FY20	TOTAL REPORTS
Source Plasma	5	6	4	8	11	**34**
Whole Blood	2	1	2	1	0	**6**
Apheresis Platelets	0	0	0	0	0	**0**
Apheresis Red Blood Cells	1	0	0	0	1	**2**
Total	**8**	**7**	**6**	**9**	**12**	**42**

Finally, the number of donation fatalities definitively ruled out as being implicated in the donor's death is markedly smaller than the combination of cases classified as *donation not ruled out, doubtful*, and *not assessable* in FY 2016 to FY 2020. These reported donation fatality cases have been classified in years prior to FY 2015 as *donation ruled out* (Table 9).

Table 9: Donation *Ruled Out* by Product, FY 2016-FY 2020

Donated Product	FY16	FY17	FY18	FY19	FY20	TOTAL REPORTS
Source Plasma	3	5	9	6	8	**31**
Whole Blood	-	-	-	-	-	**-**
Apheresis Platelets	-	-	-	-	-	**-**
Apheresis Red Blood Cells	-	-	-	-	-	**-**
Total	**3**	**5**	**9**	**6**	**8**	**31**