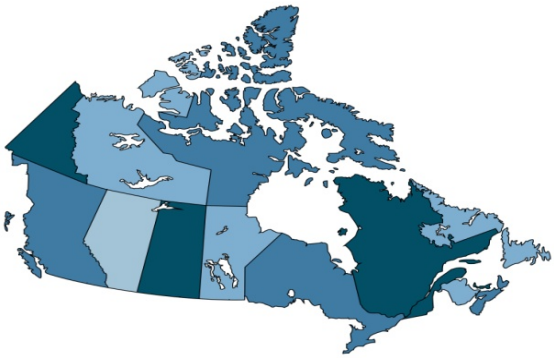
TRANSFUSION TRANSMITTED INJURIES SURVEILLANCE SYSTEM (TTISS):

2009 - 2013
SUMMARY RESULTS



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INFORMATION TO THE READER OF THE 2009-2013 TRANSFUSION TRANSMITTED SURVEILLANCE SYSTEM (TTISS) SUMMARY RESULTS

The Centre for Communicable Diseases and Infection Control (CCDIC) of the Public Health Agency of Canada (the Agency) is pleased to present *Transfusion Transmitted Injuries Surveillance System (TTISS) Summary Results, 2009-2013*. This summary report presents transfusion transmitted injuries surveillance data submitted by Canadian hospitals participating in the Transfusion Transmitted Injuries Surveillance System (TTISS).

The TTISS is a pan-Canadian surveillance system established by the Agency to capture non-nominal data on adverse transfusion reactions in Canadian hospitals providing transfusion services. The overarching goal of the TTISS is to improve patient safety in Canadian hospitals.

CCDIC in partnership with participating hospitals is responsible for the collection, management and analysis of the TTISS data, as well as the production of reports summarizing key findings. CCDIC supports the use of these data to inform public health and policy action. In addition, CCDIC supports the Agency's ongoing commitment to improving data quality, and to defining and setting surveillance standards.

Summary

Transfusion Transmitted Injuries Surveillance System (TTISS) has been monitoring adverse reactions related to the transfusion of blood components, and blood products (plasma derivatives) since 2001 in Canada. As of 2007, all provinces and the Northwest and Yukon territories participate in the TTISS. The participation rate of hospitals providing transfusion services in each of these provinces and territories (P/Ts) increased gradually over time: by 2013, it was between 80% and 100% in 11 P/Ts. Only one province had a participation rate of less than 50%. The TTISS coverage is also measured by the volume of blood components (red blood cells, granulocytes, platelets, plasma and cryoprecipitates) transfused annually and, approximately 1.5 million transfusions were given in Canada each year from 2009 to 2013. Approximately 80% of these transfusions were monitored by the TTISS network.

In addition to the overall counts and proportions of adverse reactions from transfusion of blood components and blood products (plasma derivatives), this report also provides the overall and annual risks of individual adverse reactions resulting from the transfusion of blood components during the five year period 2009-2013. These statistics could not be calculated for blood products (plasma derivatives) because of the lack of appropriate corresponding denominator data. Minor allergic reactions as well as febrile non-hemolytic reactions were excluded as a result of inconsistent reporting of adverse transfusion reactions over the years. Also, the doubtful, ruled out and missing responses for the relationship of adverse event with transfusion have not been considered in the report.

A total of 3,369 cases of transfusion-related adverse reactions were reported to the TTISS from 2009 to 2013: from 465 in 2009 to 874 in 2013, corresponding to an overall five-year increase of 88% (annual increase of 17.5%). The surveillance protocol requires participants to send comprehensive reports on the transfusion reactions such as transfusion-associated circulatory overload (TACO), Severe anaphylactic & anaphylactoid reactions - SAAR (include anaphylactic shocks), hypotensive reaction, acute and delayed hemolytic reaction, transfusion-related acute lung injury (TRALI), transfusion-associated dyspnea (TAD), IVIG associated reaction, aseptic meningitis, bacterial/viral infections, and unusual reactions of clinical significance. Each reported adverse reaction is categorized not only by its severity level (which is measured by the level of medical care/intervention required for a patient as a result of developing the reaction), but also

by their resulting outcome which assesses whether the patient sustained any physiological and/or physical consequence (damage/impairment of a body function) following the development of the reaction. The outcome varies from minor to major/long-term sequelae including death. In 2013, the TTISS recorded 6 deaths were determined to be related to the transfusion of blood components. Of these, two were deemed to be definitely related to: (i) bacterial contamination of transfused platelets with alpha-hemolytic *streptococcus* and, (ii) incompatible transfusion whereby a B Rh+ blood component (red blood cells) was transfused to an A Rh+ patient. Three deaths were determined to be possibly related to transfusion: (i) TACO, (ii) possible TRALI, and (iii) delayed hemolytic reaction. The last case with a probable link with the transfusion of blood component was determined to be a possible TRALI. There were no reported transfusion-related deaths for blood products.

1. Overall adverse transfusion-related reactions

Table 1A: Adverse reactions resulting from transfusion of blood components and blood products (plasma derivatives), TTISS 2009-2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	149	32.0%	190	30.7%	223	34.7%	220	28.6%	255	29.2%	**1,037**	**30.8%**
Acute hemolytic reaction (AHR)	25	5.4%	32	5.2%	24	3.7%	31	4.0%	51	5.8%	**163**	**4.8%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	65	14.0%	96	15.5%	61	9.5%	87	11.3%	121	13.8%	**430**	**12.8%**
Hypotensive reaction (HR)	41	8.8%	44	7.1%	37	5.8%	66	8.7%	57	6.5%	**245**	**7.3%**
Delayed hemolytic reaction (DHR)	65	14.0%	62	10.0%	71	11.1%	84	10.9%	81	9.3%	**363**	**10.8%**
Transfusion-related acute lung injury (TRALI)	10	2.2%	8	1.3%	13	2.0%	8	1.0%	3	0.3%	**42**	**1.2%**
Possible TRALI	9	1.9%	14	2.3%	9	1.4%	13	1.7%	8	0.9%	**53**	**1.6%**
Transfusion-associated dyspnea - TAD	19	4.1%	39	6.3%	19	3.0%	24	3.1%	63	7.2%	**164**	**4.9%**
IVIG-associated reaction	24	5.2%	39	6.3%	54	8.4%	105	13.7%	146	16.7%	**368**	**10.9%**
Aseptic meningitis	1	0.2%	10	1.6%	3	0.5%	13	1.7%	15	1.7%	**42**	**1.2%**
Incompatible transfusion	7	1.5%	7	1.1%	10	1.6%	10	1.3%	3	0.3%	**37**	**1.1%**
Bacterial infection	4	0.9%	7	1.1%	9	1.4%	3	0.4%	0	0.0%	**23**	**0.7%**
Other[1]	37	8.0%	52	8.4%	98	15.3%	76	9.9%	71	8.1%	**334**	**9.9%**
Unusual reactions[2]	9	1.9%	19	3.1%	11	1.7%	28	3.6%	0	0.0%	**67**	**2.0%**
Total	**465**	**100%**	**619**	**100%**	**642**	**100%**	**768**	**100%**	**874**	**100%**	**3,368**	**100%**

Over the 2009-2013 period, transfusion-associated circulatory overload (TACO), severe anaphylactic & anaphylactoid reactions (SAAR), IVIG-associated reactions and delayed hemolytic reactions were the most commonly reported adverse reactions. Collectively, they accounted for more than 65% (n=2,198) of all the reported adverse transfusion reactions (Table 1A).

[1] ***Other*** *= Transfusion-related adverse reactions which are well described (in the literature), but rarely occurred (e.g. atypical pain).*

[2] ***Unusual reactions*** *= Adverse reactions that were definitely related to transfusion, but did not fit into any other categorization. These are new and unexpected reactions/effects of clinical significance.*

Table 1B: Adverse reactions related to transfusion of blood components, TTISS 2009 – 2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	141	41. 8%	185	40. 8%	216	48. 4%	209	41.6%	243	42.9%	**994**	**43.1%**
Acute hemolytic reaction (AHR)	14	4.2%	16	3.5%	15	3. 4 %	14	2.8%	17	3.0%	**76**	**3.3%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	50	14. 8%	79	17.4%	46	10.3%	65	12.9%	106	18.6%	**346**	**15. 0%**
Hypotensive reaction (HR)	34	10. 1%	40	8.8%	30	6.7%	63	12. 5%	49	8.5%	**216**	**9.3%**
Delayed hemolytic reaction (DHR)	38	11. 3%	31	6.8%	37	8.3%	38	7. 6 %	41	7.1%	**185**	**8.0%**
Transfusion-related acute lung injury (TRALI)	8	2.4%	7	1.5%	12	2.7%	8	1.6%	3	0.5%	**38**	**1.7%**
Possible TRALI	9	2.7%	14	3.1%	8	1.8%	13	2.6%	8	1.4%	**52**	**2.3%**
Transfusion-associated dyspnea - TAD	16	4.7%	34	7. 5%	18	4.0%	20	4.0%	47	8.2%	**135**	**5.8%**
Incompatible transfusion	7	2.1%	6	1.3%	8	1.8%	10	2.0%	3	0.5%	**34**	**1.5%**
Bacterial infection	4	1.2%	7	1.5%	9	2.0%	3	0. 4%	0	0.0%	**23**	**1.0%**
Other	7	2.1%	21	4.6%	39	8.7%	36	7. 2%	53	9.2%	**156**	**6.7%**
Unusual reactions	9	2.7%	13	2.9%	8	1.8%	25	4.8%	0	0.0%	**55**	**2.3%**
Total	**337**	**100%**	**453**	**100%**	**446**	**100%**	**504**	**100%**	**570**	**100%**	**2,310**	**100%**

Adverse reactions related to the transfusion of blood components (Table 1B) accounted for 68.6% (n=2,310) of all reported adverse reactions. Transfusion-associated circulatory overload (TACO) and severe anaphylactic & anaphylactoid reactions (SAAR) were the most commonly reported and represented respectively 43.1% (n=994) and 15.0% (n=346) of the cases (Table 1B). Transfusion-related lung injury (TRALI) and possible TRALI accounted for just 4% and unlike TACO and SAAR that increased respectively by 14% and 63% in 2013, they decreased significantly by 48%.

Table 1C: Adverse reactions related to transfusion of blood products (plasma derivatives), TTISS 2009 – 2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	8	6.3%	5	3.0%	7	3.6%	11	4.2%	12	4.0%	**43**	**4.1%**
Acute hemolytic reaction (AHR)	11	8.6%	16	9.6%	9	4.6%	17	6.4%	34	11.2%	**87**	**8.2%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	15	11.7%	17	10.2%	15	7.7%	22	8.3%	15	5.0%	**84**	**7.9%**
Hypotensive reaction (HR)	7	5.5%	4	2.4%	7	3.6%	3	1.1%	8	2.6%	**29**	**2.7%**
Delayed hemolytic reaction (DHR)	27	21.1%	31	18.7%	34	17.3%	46	17.4%	40	13.2%	**178**	**16.8%**
Transfusion-related acute lung injury (TRALI)	2	1.6%	1	0.6%	1	0.5%	0	0.0%	0	0.0%	**4**	**0.4%**
Possible TRALI	0	0.0%	0	0.0%	1	0.5%	0	0.0%	0	0.0%	**1**	**0.1%**
Transfusion-associated dyspnea - TAD	3	2.3%	5	3.0%	1	0.5%	4	1.5%	16	5.3%	**29**	**2.7%**
IVIG-associated reaction	24	18.8%	39	23.5%	54	27.6%	105	39.8%	146	48.2%	**368**	**34.8%**
Aseptic meningitis	1	0.8%	10	6.0%	3	1.5%	13	4.9%	15	5.0%	**42**	**4.0%**
Incompatible transfusion	0	0.0%	1	0.6%	2	1.0%	0	0.0%	0	0.0%	**3**	**0.3%**
Other	30	23.4%	31	18.7%	59	30.1%	40	15.2%	18	5.6%	**178**	**16.7%**
Unusual reactions	0	0.0%	6	3.6%	3	1.5%	3	1.1%	0	0.0%	**12**	**1.1%**
Total	**128**	**100%**	**166**	**100%**	**196**	**100%**	**264**	**100%**	**304**	**100%**	**1,058**	**100%**

The most common of the adverse reactions related to transfusion of blood products (plasma derivatives) were IVIG-associated reactions, followed by delayed hemolytic reactions that accounted respectively for 34.8% (n=368) and 16.8% (n=178) of the cases recorded between 2009 and 2013. While the number of cases of delayed hemolytic reactions stayed almost unchanged from 2009 to 2011 and from 2012 to 2013 (Table 1C), that of IVIG-associated reactions has steadily increased significantly over time going from 24 cases per year in 2009 to 146 in 2013 (Table 1C).

2. Imputability (i.e. Relationship of adverse reactions to transfusion)

Table 2A: Relationship of adverse reaction to transfusion of blood components & blood products (i.e. imputability), TTISS 2009-2013

Type of transfusion-related adverse reaction	Definite[1]		Probable[2]		Possible[3]		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	69	6.7%	475	45.8%	493	47.5%	**1,037**	**100%**
Acute hemolytic reaction (AHR)	74	45.4%	62	38.0%	27	16.6%	**163**	**100%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	51	11.9%	278	64.7%	101	23.5%	**430**	**100%**
Hypotensive reaction (HR)	9	3.7%	77	31.7%	159	64.6%	**245**	**100%**
Delayed hemolytic reaction (DHR)	211	58.1%	109	30.0%	43	11.8%	**363**	**100%**
Transfusion-related acute lung injury (TRALI)	10	23.8%	21	50.0%	11	26.2%	**42**	**100%**
Possible TRALI	6	11.3%	13	24.5%	34	64.2%	**53**	**100%**
Transfusion-associated dyspnea (TAD)	3	1.8%	71	43.3%	90	54.9%	**164**	**100%**
IVIG-associated reactions	39	10.6%	261	70.9%	68	18.5%	**368**	**100%**
Aseptic meningitis	6	14.3%	27	64.3%	9	21.4%	**42**	**100%**
Incompatible transfusion	29	78.4%	4	10.8%	4	10.8%	**37**	**100%**
Bacterial infection	1	4.3%	4	17.4%	18	78.3%	**23**	**100%**
Other	23	6.9%	184	55.1%	127	38.0%	**334**	**100%**
Unusual reactions	1	1.5%	16	23.9%	50	74.6%	**67**	**100%**
Total	**532**	**15.8%**	**1,602**	**47.6%**	**1,234**	**36.6%**	**3,368**	**100%**

N.B. Cases for which the relationship to transfusion was missing, doubtful[4] or ruled out[5] were excluded from the analysis.

[1] ***Definite*** = *Clinical and/or laboratory event occurred within a time frame consistent with the administration of the blood, blood component, or blood product (plasma derivative) and was proven by investigation to have been caused by transfusion.*

[2] ***Probable*** = *Clinical and/or laboratory event occurred within a time frame consistent with the administration of the blood, blood component, or blood product (plasma derivative) and did not seem to be explainable by any other cause.*

[3] ***Possible*** = *Clinical and/or laboratory event occurred within a time frame consistent with the administration of the blood, blood component, or blood product (plasma derivative) but could be explained by concurrent disease(s) or by the administration of a drug or other agent.*

[4] ***Doubtful*** = *Clinical and/or laboratory event occurred within a reasonable time frame in relation to the transfusion but the preponderance of data supports an alternative explanation.*

[5] ***Ruled out*** = *Clinical and/or laboratory event occurred within a time frame inconsistent with the administration of the blood, blood component, or blood product (plasma derivative), or if it occurred within a consistent time period but was proven to have no relationship to the transfusion.*

Table 2B: Relationship of adverse reaction (imputability) to transfusion of blood components, TTISS 2009-2013

Type of transfusion-related adverse reaction	Definite		Probable		Possible		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	67	6.7%	461	46.4%	466	46.8%	**994**	**100%**
Acute hemolytic reaction (AHR)	40	52.6%	24	31.6%	12	15.8%	**76**	**100%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	30	8.7%	230	66.7%	86	24.6%	**346**	**100%**
Hypotensive reaction (HR)	6	2.8%	67	31.2%	143	66.0%	**216**	**100%**
Delayed hemolytic reaction (DHR)	125	67.9%	43	22.8%	17	9.2%	**185**	**100%**
Transfusion-related acute lung injury (TRALI)	9	21.1%	19	50.0%	11	28.9%	**38**	**100%**
Possible TRALI	6	11.5%	12	23.1%	34	65.4%	**52**	**100%**
Transfusion-associated dyspnea - TAD	3	2.2%	54	39.6%	78	58.2%	**135**	**100%**
Incompatible transfusion	29	85.3%	1	2.9%	4	11.8%	**34**	**100%**
Bacterial infection	1	4.5%	4	13.6%	18	81.8%	**23**	**100%**
Other	9	5.8%	75	47.7%	72	46.5%	**156**	**100%**
Unusual reactions	0	0.0%	13	22.2%	42	77.8%	**55**	**100%**
Total	**324**	**14.1%**	**1003**	**43.4%**	**983**	**42.6%**	**2,310**	**100%**

Overall, only 15.8% (n = 532) of the cases were definitely linked to transfusion (Table 2A), while the remaining 84.2% were deemed to be probably (n = 1,602) or possibly (n = 1,234) related to transfusion. Almost 61% (n = 324) of the cases definitely linked to transfusion were patients that received blood component (Table 2B).

Table 2C: Relationship of adverse reaction (imputability) to transfusion of blood products (plasma derivatives), TTISS 2009-2013

Type of transfusion-related adverse reaction	Definite		Probable		Possible		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	2	4.7%	14	32.6%	27	62.8%	**43**	**100%**
Acute hemolytic reaction (AHR)	34	39.1%	38	43.7%	15	17.2%	**87**	**100%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	21	25.0%	48	57.1%	15	17.9%	**84**	**100%**
Hypotensive reaction (HR)	3	10.3%	10	34.5%	16	55.2%	**29**	**100%**
Delayed hemolytic reaction (DHR)	86	48.3%	66	37.1%	26	14.6%	**178**	**100%**
Transfusion-related acute lung injury (TRALI)	2	50.0%	2	50.0%	0	0.0%	**4**	**100%**
Possible TRALI	0	0.0%	1	100%	0	0.0%	**1**	**100%**
Transfusion-associated dyspnea -TAD	0	0.0%	17	58.6%	12	41.4%	**29**	**100%**
IVIG-associated reactions	39	10.6%	261	70.9%	68	18.5%	**368**	**100%**
Aseptic meningitis	6	14.3%	27	64.3%	9	21.4%	**42**	**100%**
Incompatible transfusion	0	0.0%	3	100%	0	0.0%	**3**	**100%**
Other	14	7.9%	109	61.0%	55	31.1%	**178**	**100%**
Unusual reactions	1	8.3%	3	25.0%	8	66.7%	**12**	**100%**
Total	**208**	**19.7%**	**599**	**56.6%**	**251**	**23.7%**	**1,058**	**100%**

Of the adverse reactions from blood product/plasma derivative approximately 19.7% (n = 208) were determined as being definitely transfusion-related, 56.6% (n = 599) as being probably related to transfusion and the remaining 23.7% (n = 251) were deemed to have possible link to transfusion (Table 2C).

3. Severity of adverse transfusion-related reactions

Approximately 60% (n = 1,998) of adverse transfusion reactions reported between 2009 and 2013 were of grade 1 severity level (i.e. no permanent damage or impairment of a bodily function).

3.1. Grade 2[1] severity (or severe) adverse reactions:

Table 3A: Severe (Grade 2) adverse reactions from *transfusion of blood components*, TTISS 2009-2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	32	40.0%	79	38.3%	93	50.3%	95	43.8%	74	43.3%	**373**	**43.4%**
Acute hemolytic reaction (AHR)	1	1.3%	5	2.4%	8	4.3%	6	2.8%	7	4.1%	**27**	**3.1%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	21	26.3%	58	28.2%	35	18.9%	47	21.7%	50	29.2%	**211**	**24.6%**
Hypotensive reaction (HR)	3	3.8%	12	5.8%	8	4.3%	18	8.3%	7	4.1%	**48**	**5.6%**
Delayed hemolytic reaction (DHR)	4	5.0%	9	4.4%	8	4.3%	14	6.5%	12	7.0%	**47**	**5.5%**
Transfusion-related acute lung injury (TRALI)	5	6.3%	3	1.5%	6	3.2%	3	1.4%	0	0.0%	**17**	**2.0%**
Possible TRALI	4	5.0%	8	3.9%	4	2.2%	9	4.1%	3	1.8%	**28**	**3.3%**
Transfusion-associated dyspnea (TAD)	3	3.8%	14	6.8%	8	4.3%	6	2.8%	12	7.0%	**43**	**5.0%**
Incompatible transfusion	1	1.3%	1	0.5%	3	1.6%	4	1.8%	1	0.6%	**10**	**1.2%**
Bacterial infection	2	2.5%	5	2.4%	4	2.2%	3	1.4%	0	0.0%	**14**	**1.6%**
Other	3	3.8%	10	4.9%	7	3.8%	8	3.7%	5	2.9%	**33**	**3.8%**
Unusual reactions	1	1.3%	2	1.0%	1	0.5%	4	1.8%	0	0.0%	**8**	**0.9%**
Total	**80**	**100%**	**206**	**100%**	**185**	**100%**	**217**	**100%**	**171**	**100%**	**859**	**100%**

[1] ***Grade 2 (severe)*** = *Patient requires in-patient hospitalization or prolongation of hospitalization directly attributable to the reaction; or the adverse reaction results in persistent/significant disability or incapacity; or it necessities medical/surgical intervention to preclude permanent/significant damage or impairment of a body function.*

Over 37% (n = 859) of the 2,302 adverse reactions recorded between 2009 and 2013 from the transfusion of blood components were deemed to be of grade 2 severity i.e. the patients involved sustained a condition serious enough to require hospitalization or prolonged hospitalization, medical/surgical intervention (Table 3A). The majority of these adverse reactions have consistently been identified under TACO or severe anaphylactic & anaphylactoid reactions (SAAR) which collectively accounted for more than two third of the cases (Table 3A). As for the adverse reactions of the same severity level but from the transfusion of blood products, the most predominant were hemolytic reactions (both acute and delayed), followed by SAAR and aseptic meningitis (Table 3B).

Table 3B: Severe (Grade 2) adverse reactions from *transfusion of blood products*, TTISS 2009-2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	2	6.7%	1	1.9%	3	4.8%	5	7.9%	3	4.4%	**14**	**5.1%**
Acute hemolytic reaction (AHR)	4	13.3%	7	13.5%	7	11.3%	7	11.1%	18	26.5%	**43**	**15.6%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	4	13.3%	8	15.4%	12	19.4%	19	30.2%	7	10.3%	**50**	**18.2%**
Hypotensive reaction (HR)	2	6.7%	2	3.8%	0	0.0%	0	0.0%	1	1.5%	**5**	**1.8%**
Delayed hemolytic reaction (DHR)	14	46.7%	11	21.2%	22	35.5%	9	14.3%	14	20.6%	**70**	**25.5%**
Transfusion-related acute lung injury (TRALI)	1	3.3%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	**1**	**0.4%**
Transfusion-associated dyspnea (TAD)	1	3.3%	1	1.9%	1	1.6%	1	1.6%	1	1.5%	**5**	**1.8%**
IVIG headache	0	0.0%	0	0.0%	3	4.8%	7	11.1%	7	10.3%	**17**	**6.2%**
Aseptic meningitis	1	3.3%	8	15.4%	3	4.8%	9	14.3%	11	16.2%	**32**	**11.6%**
Incompatible transfusion	0	0.0%	1	1.9%	1	1.6%	0	0.0%	0	0.0%	**2**	**0.7%**
Other	1	3.3%	11	21.2%	10	16.1%	6	9.5%	6	8.8%	**34**	**12.4%**
Unusual reactions	0	0.0%	2	3.8%	0	0.0%	0	0.0%	0	0.0%	**2**	**0.7%**
Total	**30**	**100%**	**52**	**100%**	**62**	**100%**	**63**	**100%**	**68**	**100%**	**275**	**100%**

3.2. Grade 3[1] severity (or life-threatening) adverse reactions:

Table 3C: Life-threatening (Grade 3) adverse reactions from *transfusion of blood components*, TTISS 2009-2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	9	42.9%	14	35.9%	16	45.7%	15	36.6%	7	30.4%	**61**	**38.4%**
Acute hemolytic reaction (AHR)	0	0.0%	3	7.7%	0	0.0%	0	0.0%	4	17.4%	**7**	**4.4%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	2	9.5%	5	12.8%	4	11.4%	10	24.4%	1	4.3%	**22**	**13.8%**
Hypotensive reaction (HR)	0	0.0%	1	2.6%	2	5.7%	3	7.3%	1	4.3%	**7**	**4.4%**
Delayed hemolytic reaction (DHR)	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	4.3%	**1**	**0.6%**
Transfusion-related acute lung injury (TRALI)	1	4.8%	4	10.3%	6	17.1%	3	7.3%	0	0.0%	**14**	**8.8%**
Possible TRALI	4	19.0%	6	15.4%	3	8.6%	4	9.8%	5	21.7%	**22**	**13.8%**
Transfusion-associated dyspnea (TAD)	1	4.8%	4	10.3%	0	0.0%	1	2.4%	1	4.3%	**7**	**4.4%**
Incompatible transfusion	2	9.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	**2**	**1.3%**
Bacterial infection	0	0.0%	1	2.6%	2	5.7%	0	0.0%	0	0.0%	**3**	**1.9%**
Other	1	4.8%	1	2.6%	1	2.9%	1	2.4%	3	13.0%	**7**	**4.4%**
Unusual reactions	1	4.8%	0	0.0%	1	2.9%	4	9.8%	0	0.0%	**6**	**3.8%**
Total	**21**	**100%**	**39**	**100%**	**35**	**100%**	**41**	**100%**	**23**	**100%**	**159**	**100%**

The majority (159 of the 175) of the cases of grade 3 severity (i.e. life-threatening) adverse reactions from 2009 to 2013 was recorded from the transfusion of blood components 2013 (Table 3C). In 2013 the ascending pattern of the total number of cases

[1] ***Grade 3 (life-threatening)*** *= Patient may require major intervention following the transfusion (vasopressors, intubation, transfer to intensive care).*

reported annually observed since 2009 abruptly decreased by about 44% (from 41 in 2012 to 23 in 2013. This decline was almost entirely due to the significant reduction of the number of TACO and SAAR (Table 3C).

Table 3D: Life-threatening (Grade 3) adverse reactions from *transfusion of blood products*, TTISS 2009-2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	0	0.0%	0	0.0%	1	20.0%	2	40.0%	0	0.0%	**3**	**18.8%**
Acute hemolytic reaction (AHR)	0	0.0%	0	0.0%	0	0.0%	1	20.0%	0	0.0%	**1**	**6.3%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	1	100%	1	25.0%	1	20.0%	0	0.0%	0	0.0%	**3**	**18.8%**
Delayed hemolytic reaction (DHR)	0	0.0%	1	25.0%	0	0.0%	0	0.0%	0	0.0%	**1**	**6.3%**
Transfusion-related acute lung injury (TRALI)	0	0.0%	1	25.0%	1	20.0%	0	0.0%	0	0.0%	**2**	**12.5%**
Possible TRALI	0	0.0%	0	0.0%	1	20.0%	0	0.0%	0	0.0%	**1**	**6.3%**
Transfusion-associated dyspnea (TAD)	0	0.0%	0	0.0%	0	0.0%	1	20.0%	0	0.0%	**1**	**6.3%**
Other	0	0.0%	1	25.0%	1	20.0%	1	20.0%	1	100%	**4**	**25.0%**
Total	**1**	**100%**	**4**	**100%**	**5**	**100%**	**5**	**100%**	**1**	**100%**	**16**	**100%**

Life-threatening adverse reactions from the transfusion of blood products has been consistently limited to not more than five cases per year with 2009 and 2013 recording the lowest (n = 1) number of cases (Table 3D).

4. RATE OF OCCURRENCE OF ADVERSE TRANSFUSION-RELATED REACTIONS

Rates of occurrence of adverse reactions could be calculated only for cases that arose from the transfusion of blood components. Cases from the transfusion of blood products could not be considered because of the non-availability appropriate denominator data. Table 4 summarizes the number of units of blood components transfused from 2009 to 2013 by each Canadian jurisdiction participating in the program and corresponding to the denominators in the calculation of the different occurrence rates.

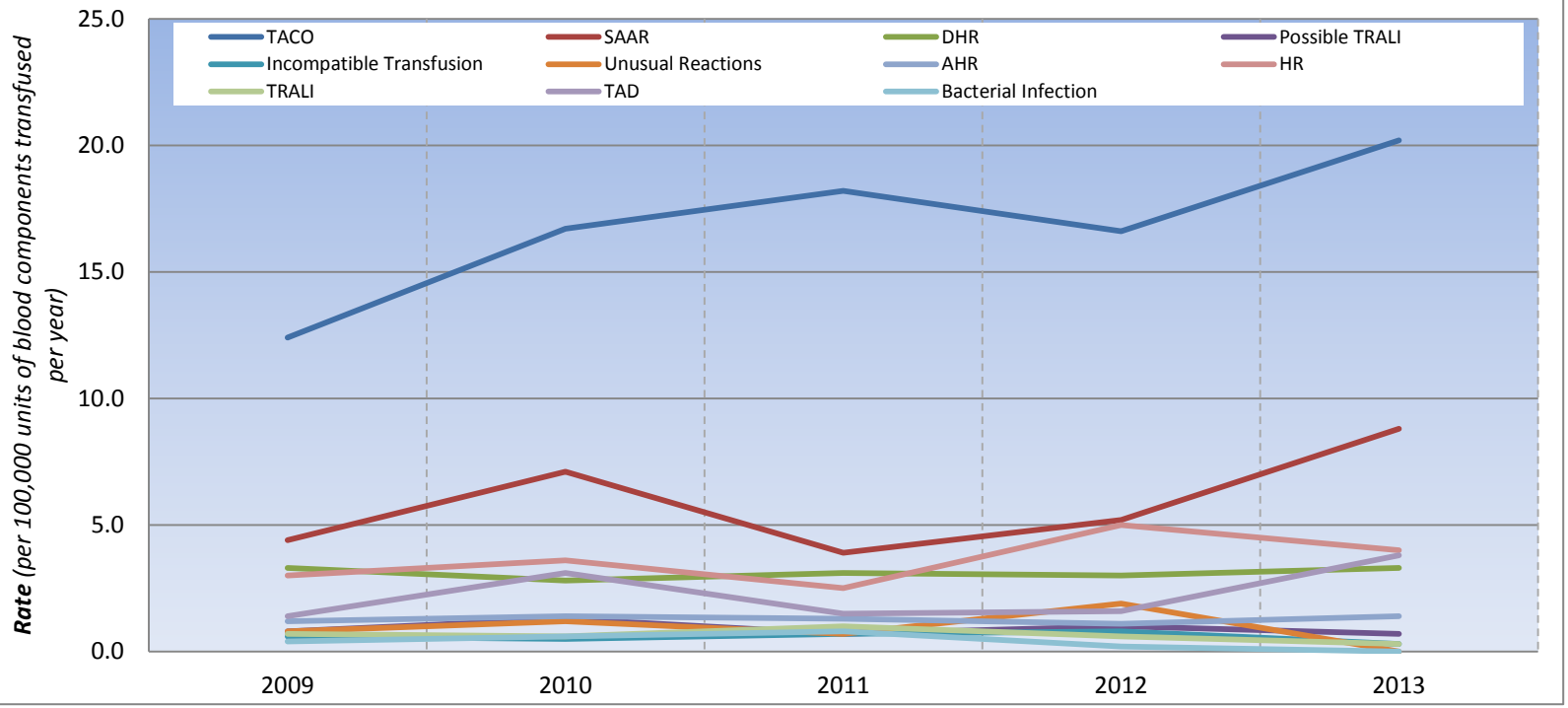
Table 4: Total units of blood components transfused by hospitals of the TTISS network from 2009 to 2013

PROVINCE/Territory	2009		2010		2011		2012		2013	
	Freq.	% within P/T	Freq.	% within P/T	Freq.	% within P/T	Freq.	% within P/T	Freq.	% within P/T
British Columbia	173,993	96.0%	172,696	96.8%	177,387	96.9%	177,299	98.0%	180,184	98.8%
Yukon Territory	590	100%	551	100%	499	100%	422	100%	809	100%
Alberta	68,561	49.4%	71,978	52.8%	114,734	83.9%	155,120	100%	140,153	95.7%
Manitoba	52,525	100%	55,317	100%	54,819	100%	59,893	100%	56,501	100%
Saskatchewan	56,082	99.7%	51,700	100%	48,182	100%	46,707	100%	42,450	100%
Ontario	351,611	64.5%	349,176	65.3%	378,422	67.0%	365,591	67.5%	357,568	66.9%
Québec	338,005	93.9%	305,220	84.1%	310,047	89.2%	346,565	99.8%	325,995	98.6%
New Brunswick	29,973	100%	31,242	100%	29,276	100%	32,597	100%	30,057	100%
Nova Scotia	39,965	100%	40,646	100%	42,893	100%	43,205	100%	37,685	100%
Prince Edward Island	4,736	100%	4,430	100%	4,607	100%	4,400	100%	4,378	100%
Newfoundland & Labrador	20,556	100%	23,549	100%	23,464	100%	23,856	100%	22,254	100%
Northwest Territories	440	100%	393	100%	348	100%	505	100%	125	100%
Total	**1,137,037**	**79.5%**	**1,106,898**	**77.9%**	**1,184,678**	**82.5%**	**1,256,160**	**87.4%**	**1,198,159**	**86.3%**

The number of units of blood components transfused annually had not changed significantly over the years (Table 4). Larger proportions were transfused in larger jurisdictions like Québec and Ontario. Though a voluntary system, data on the volume of blood

components transfused indicate that the TTISS network had 100% coverage of transfusion activities in eight of the 12 participating Canadian jurisdictions from 2009 to 2013, between 96 and 99% in three other jurisdictions and 67% in one (Table 4).

Figure 1: Annual Rate of Adverse Reactions Related to Transfusion of Blood Components, TTISS 2009-2013



The overall risk presented in Table 5 and Figure 1 was calculated by dividing the number of adverse reactions from blood components (Table1B) by the total number of units of blood components transfused by hospitals participating in the TTISS from 2009 to 2013 (Table 4). The results are given in: (i) adverse reaction per 100,000 units of blood components transfused and (ii) number of units transfused for the occurrence of an adverse event (Tables 5 and Figure 1).

Table 5: Annual rate of adverse reactions related to transfusion of blood components, TTISS 2009-2013

Type of transfusion-related adverse reaction	2009		2010		2011		2012		2013		Total	
	Per 100,000 UT[1]	*1 case per X[2] units transfused*	*Per 100,000 units transfused*	*1 case per X units transfused*	*Per 100,000 units transfused*	*1 case per X units transfused*	*Per 100,000 units transfused*	*1 case per X units transfused*	*Per 100,000 units transfused*	*1 case per X units transfused*	*Per 100,000 units transfused*	*1 case per X units transfused*
Transfusion-associated circulatory overload (TACO)	12.4	1 : 8,064	16.7	1 : 5,983	18.2	1 : 5,485	16.6	1 : 6,010	20.3	1 : 4,931	**16.9**	**1 : 5,918**
Acute hemolytic reaction (AHR)	1.2	1 : 81,218	1.4	1 : 69,181	1.3	1 : 78,979	1.1	1 : 89,726	1.4	1 : 70,480	**1.3**	**1 : 77,407**
Severe anaphylactic & anaphylactoid reactions (SAAR)	4.4	1 : 22,741	7.1	1 : 14,011	3.9	1 : 25,754	5.2	1 : 19,326	8.8	1 : 11,303	**5.9**	**1 : 17,003**
Hypotensive reaction (HR)	3.0	1 : 33,442	3.6	1 : 27,672	2.5	1 : 39,480	5.0	1 : 19,939	4.1	1 : 24,452	**3.7**	**1 : 27,236**
Delayed hemolytic reaction (DHR)	3.3	1 : 29,922	2.8	1 : 35,706	3.1	1 : 32,018	3.0	1 : 33,057	3.4	1 : 29,223	**3.1**	**1 : 31,800**
Transfusion-related acute lung injury (TRALI)	0.7	1 : 142,130	0.6	1 : 158,128	1.0	1 : 98,723	0.6	1 : 157,020	0.3	1 : 399,386	**0.6**	**1 : 154,814**
Possible TRALI	0.8	1 : 126,337	1.3	1 : 79,064	0.7	1 : 148,085	1.0	1 : 96,628	0.7	1 : 149,770	**0.9**	**1 : 113,133**
Transfusion-associated dyspnea (TAD)	1.4	1 : 71,065	3.1	1 : 32,556	1.5	1 : 65,185	1.6	1 : 62,808	3.9	1 : 25,493	**2.3**	**1 : 43,577**
Incompatible transfusion	0.6	1 : 162,434	0.5	1 : 184,483	0.7	1 : 148,085	0.8	1 : 125,616	0.3	1 : 399,386	**0.6**	**1 : 173,027**
Bacterial infection	0.4	1 : 284,259	0.6	1 : 158,128	0.8	1 : 131,631	0.2	1 : 418,720	0.0	--	**0.4**	**1 : 255,780**
Other	0.6	1 : 162,434	1.9	1 : 52,709	3.3	1 : 30,376	2.9	1 : 34,893	4.4	1 : 22,607	**2.6**	**1 : 37,711**
Unusual reactions	0.8	1 : 126,337	1.2	1 : 85,146	0.7	1 : 148,085	2.0	1 : 50,246	0.0	--	**0.9**	**1 : 106,962**
Total	**29.6**	**1 : 3,374**	**40.9**	**1 : 2,443**	**37.6**	**1 : 2,656**	**40.1**	**1 : 2,492**	**47.6**	**1 : 2,102**	**39.1**	**1 : 2,547**

Overall, the most common adverse transfusion reaction has consistently been transfusion-associated circulatory overload (TACO) which on average occurred once every 5,923 units of blood components transfused (Table 5). Moreover, from 2009 to 2013, there has been a significant 63% increase in its rate of occurrence (Figure 1). The least common was bacterial infection with just 22 cases in four years and no bacterial infection in 2013 (Table 5 & Figure 1).

[1] *UT = Units transfused*
[2] *X = Corresponding number (calculated) of units of blood components transfused*

5. OUTCOME OF ADVERSE TRANSFUSION-RELATED REACTIONS

Table 6A: Outcome of adverse reactions that resulted from transfusion of blood components, TTISS 2009-2013

Type of transfusion-related adverse reaction	Minor sequelae[1]		Major sequelae[2]		Death		Not determined[3]		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	913	44.3%	12	19.4%	14	35.0%	52	40.3%	**991**	**43.1%**
Acute hemolytic reaction (AHR)	59	2.9%	7	11.3%	1	2.5%	9	7.0%	**76**	**3.3%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	321	15.5%	8	12.9%	1	2.5%	14	10.9%	**344**	**15.0%**
Hypotensive reaction (HR)	205	9.9%	2	3.2%	0	0.0%	6	4.7%	**213**	**9.3%**
Delayed hemolytic reaction (DHR)	148	7.2%	19	30.6%	3	7.5%	15	10.9%	**185**	**8.0%**
Transfusion-related acute lung injury (TRALI)	32	1.6%	0	0.0%	3	7.5%	3	2.3%	**38**	**1.7%**
Possible TRALI	27	1.3%	6	9.7%	13	32.5%	6	4.7%	**52**	**2.3%**
Transfusion-associated dyspnea – TAD	121	5.8%	4	6.5%	1	2.5%	7	5.4%	**133**	**5.8%**
Incompatible transfusion	29	1.4%	0	0.0%	1	2.5%	4	3.1%	**34**	**1.5%**
Bacterial infection	18	0.8%	0	0.0%	1	2.5%	4	3.1%	**23**	**1.0%**
Other	146	7.0%	0	0.0%	2	5.0%	7	5.4%	**155**	**6.7%**
Unusual reactions	48	2.3%	4	6.5%	0	0.0%	3	2.3%	**55**	**2.4%**
Total	**2,067**	**100%**	**62**	**100%**	**40**	**100%**	**130**	**100%**	**2,299**	**100%**

N.B.: The sum total from Tables 6A & 6B does not match that of Table 1A because of missing outcome information on 19 cases.

More than two percent (2.3%, n=77) of the cases with outcome information developed either a serious infection or a transfusion reaction with major /long-term sequelae (Tables 6A & 6B). Approximately 64.3% of the 42 deaths recorded in the TTISS network

[1] **Minor sequelae** = Patient had no sequelae or permanent disability from the reaction or developed antibodies to low/medium frequency antigens (< 95%).
[2] **Major sequelae** = Patient developed either an infection with persistent infectious agent (HIV, Hepatitis C or B), or a transfusion reaction with major or long-term sequelae or the anticipation of difficulties with future transfusions (*e.g.* development of antibodies to antigens present in more than 95% of donations).
[3] **Not determined** = The outcome of the adverse reaction is not certain.

between 2009 and 2013 were determined to be either definitely (n=3), probably (n=9) or possibly (n=15) related to the adverse events that resulted from the transfusion of blood components (Table 7). Such linkage for the 15 other cases was either ruled out (n=6) or at best doubtful (n=9).

Table 6B: Outcome of adverse reactions that resulted from transfusion of blood products (plasma derivatives), TTISS 2009- 2013

Type of transfusion-related adverse reaction	Minor sequelae		Major sequelae		Death		Not determined		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Transfusion-associated circulatory overload (TACO)	41	4.1%	0	0.0%	1	50.0%	1	3.3%	**43**	**4.1%**
Acute hemolytic reaction (AHR)	77	7.7%	1	6.7%	0	0.0%	7	23.3%	**85**	**8.1%**
Severe anaphylactic & anaphylactoid reactions (SAAR)	79	7.9%	1	6.7%	0	0.0%	4	13.3%	**84**	**8.0%**
Hypotensive reaction (HR)	28	2.8%	0	0.0%	0	0.0%	1	3.3%	**29**	**2.8%**
Delayed hemolytic reaction (DHR)	165	16.5%	5	33.3%	0	0.0%	7	23.3%	**177**	**16.9%**
Transfusion-related acute lung injury (TRALI)	3	0.3%	0	0.0%	0	0.0%	1	3.3%	**4**	**0.4%**
Possible TRALI	1	0.1%	0	0.0%	0	0.0%	0	0.0%	**1**	**0.1%**
Transfusion-associated dyspnea – TAD	28	2.8%	1	6.7%	0	0.0%	0	0.0%	**29**	**2.8%**
IVIG-associated reaction	363	36.2%	1	6.7%	0	0.0%	2	6.7%	**366**	**34.9%**
Aseptic meningitis	39	3.9%	1	6.7%	0	0.0%	2	6.7%	**42**	**4.0%**
Incompatible transfusion	3	0.3%	0	0.0%	0	0.0%	0	0.0%	**3**	**0.3%**
Other	166	16.5%	5	33.3%	1	50.0%	5	16.7%	**177**	**16.9**
Unusual reactions	10	1.0%	0	0.0%	0	0.0%	0	0.0%	**10**	**1.0%**
Total	**1,003**	**100%**	**15**	**100%**	**2**	**100%**	**30**	**100%**	**1,050**	**100%**

The two cases of death registered among patients transfused with plasma derivatives (Table 6B) were determined not to be linked to transfusion. Fifteen (1.4%) of the recipients of plasma derivatives sustained major (or long-term) sequelae and of these, five had been diagnosed with transfusion-related delayed hemolytic reaction (Table 6B).

Table 7: Strength of the relationship between adverse transfusion reaction and death, TTISS 2009 – 2013

Transfusion-related death	Definite[1]	Probable[2]	Possible[3]	Doubtful[4]	Ruled out[5]	Total
Transfusion-associated circulatory overload (TACO)	0	2	5	5	3	**15**
Acute hemolytic reaction (AHR) - (incompatible transfusion)	1	0	0	0	0	**1**
Severe anaphylactic & anaphylactoid reactions (SAAR)	0	0	0	0	1	**1**
Delayed hemolytic reaction (DHR)	0	0	1	1	1	**3**
Transfusion-related acute lung injury (TRALI)	1	1	1	0	0	**3**
Possible TRALI	0	5	6	2	0	**13**
Transfusion-associated dyspnea – TAD	0	0	0	1	0	**1**
Incompatible transfusions	0	0	0	0	1	**1**
Bacterial infection	0	0	1	0	0	**1**
Other	1	1	1	0	0	**3**
Total	**3**	**9**	**15**	**9**	**6**	**42**

More than 81% of the cases of death were patients diagnosed either with TRALI and possible TRALI (51.9%) or TACO (29.5%) as per Table 8.

[1] **Definite** = The patient's death occurred within a time frame consistent with the administration of the blood, blood component, or blood product (plasma derivative) and was proven by investigation to have been caused by transfusion.

[2] **Probable** = The patient's death occurred within a time frame consistent with the administration of the blood, blood component, or blood product (plasma derivative) and did not seem to be explainable by any other cause.

[3] **Possible** = The patient's death occurred within a time frame consistent with the administration of the blood, blood component, or blood product (plasma derivative) but could be explained by concurrent disease(s) or by the administration of a drug or other agent.

[4] **Doubtful** = The patient's death occurred within a reasonable time frame in relation to the transfusion but the preponderance of data supports an alternative explanation.

[5] **Ruled out** = The patient's death occurred within a time frame inconsistent with the administration of the blood, blood component, or blood product (plasma derivative) or if it occurred within a consistent time period but was proven by investigation to have no relationship to the transfusion.

Table 8: Trend of definite, probable and possible transfusion-related deaths recorded in the TTISS network from 2009 to 2013

Transfusion-related death	2009	2010	2011	2012	2013	Total
Transfusion-associated circulatory overload (TACO)	1	1	1	2	1	**6**
Acute hemolytic reaction (AHR) - (incompatible transfusion)	0	0	0	0	1	**1**
Delayed hemolytic reaction (DHR)	0	0	0	0	1	**1**
Transfusion-related acute lung injury (TRALI)	0	1	1	1	0	**3**
Possible TRALI	2	3	2	2	2	**11**
Bacterial infection	0	0	1	0	1	**2**
Incompatible transfusion	0	0	0	0	1	**1**
Other	1	0	0	1	0	**3**
Total	**4**	**5**	**5**	**6**	**6**	**27**

Among the 2013 six transfusion-related deaths (Table 8), the relationship with transfusion was definite in two cases (incompatible transfusion and bacterial contamination), probable in one case (delayed hemolytic reaction), and possible in three cases (two cases of possible TRALI and one case of TACO). Definite transfusion-related cases occurred in males of 78 and 71 years of age unintentionally transfused respectively with blood of wrong type (B+ red blood cell to an A+ recipient) and apheresed platelets contaminated with alpha-hemolytic *streptococcus*. The first was admitted with community-acquired pneumonia and sepsis and as a result of incompatible transfusion developed a fatal acute hemolytic reaction, whereas the second who failed to recover from the transfusion of bacterially contaminated apheresed platelets was diagnosed with pancytopenia and had been hospitalized for over 30 days. The probable transfusion-related case was an 81 year old female victim of a motor vehicle accident with multiple injuries and significantly bleeding who expired on the same day following massive transfusion. Cases of death deemed to be possibly related to transfusion included: (i) a 56 year old female with relapsed acute myeloid leukemia on palliative chemotherapy who developed a possible TRALI following platelets transfusion, and (ii) a 75 year old diagnosed with idiopathic/ warm autoimmune hemolytic anemia who was transfused with red blood cells and IVIG and as a result developed a fatal hyper hemolysis coupled with severe multiple system dysfunction.