Public Health Agency of Canada
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Transfusion Transmitted Injuries Surveillance System

Program Report 2004-2005

Canada

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Transfusion Transmitted Injuries Section
Blood Safety Surveillance and Health Care Acquired Infections Division
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Transfusion Transmitted Injuries Surveillance System

Program Report
2004-2005

Transfusion Transmitted Injuries Section
Blood Safety Surveillance and
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List of Acronyms

AHTR	Acute hemolytic transfusion reaction
ATE	Adverse transfusion event
CBS	Canadian Blood Services
DHTR	Delayed hemolytic transfusion reaction
IVIg	Intravenous immune globulin
MHPD	Marketed Health Products Directorate
PHAC	Public Health Agency of Canada
PTP	Post-transfusion purpura
SPSS	Statistical Package for the Social Sciences
TACO	Transfusion associated circulatory overload
TAD	Transfusion associated dyspnea
TRAIN	Transfusion related alloimmune neutropenia
TRALI	Transfusion related acute lung injury
TTISS	Transfusion Transmitted Injuries Surveillance System
WBDP	Whole blood derived platelets

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Executive Summary

The Transfusion Transmitted Injuries Surveillance System (TTISS) evolved from a pilot project in 1999-2002 involving four provinces (British Columbia, Québec, Prince Edward Island, Nova Scotia) and has become the national surveillance system for capturing serious, moderate and selected minor adverse transfusion events reported in Canada. Adverse transfusion events that are captured through TTISS are compiled, analyzed and reported by the Public Health Agency of Canada (PHAC). In 2004-2005, nine Provinces and two Territories participated in the TTISS, which has expanded from 56 reporting hospitals in 2002 to 291 hospitals during 2004-2005. The hospitals reporting at the end of 2005 represented 70% of red blood cell transfusions occurring in Canada.

TTISS has continued to apply strict criteria for accepting cases and, overall, the quality of data has improved over previous years. The TTISS in its first two years had 244 adverse transfusion events reported compared to 569 in 2005 alone. In 2005, the top three reported adverse transfusion events were TACO, severe allergic (also called severe/anaphylactic/anaphylactoid) and TRALI.

The severity of reported cases in 2004-2005 has decreased compared to the period 2002-2003, which may be explained by a change in the reporting criteria for some adverse transfusion reactions. For example, in 2004-2005, all cases of TACO and delayed hemolytic transfusion reaction were to be reported while only the most severe cases of these two types of reactions were reportable in 2002-2003. There were 13 deaths possibly, probably or definitely related to transfusion, which represents 1.4% of all reported adverse transfusion reactions included in the analysis for the 2004-2005 period. Transfusion was only one of the contributing factors of death in more than half of these cases of adverse transfusion events; death was definitely related to transfusion in only 4 cases.

The incidence of bacterial contaminations has continued to decline and was ten-fold less in 2005 compared to 2002 (0.3 vs. 3.7 per 100,000 units, respectively). Implementation of diversion pouches at blood collection and tests for bacterial detection of platelets has likely contributed to the observed trend. There was also a two-fold decrease in the incidence of ABO incompatible transfusions between 2002 and 2005 (1.5 vs. 0.7 per 100,000 units).

In 2004-2005, TRALI occurred at a rate of approximately 2.5 per 100,000 blood units transfused. The reduction in the incidence of TRALI compared to 2002-2003 is likely explained by the use of a new and more restrictive definition of TRALI for inclusion of reported cases. The incidence of TRALI for the 2004-2005 period is probably an underestimation because many cases were reported to Canadian Blood Services by hospitals that were not participating in TTISS and were therefore not included in the calculation of incidence rates.

TACO occurred at a rate of 11.9 per 100,000 blood units transfused in 2004 and 13.5 per 100,000 units in 2005. The rise in incidence of TACO since 2002-2003 can be partly attributed to new reporting criteria for this reaction.

Severe allergic reaction occurred at a rate of 4.5 per 100,000 blood units transfused in 2004 and 5.5 per 100,000 units in 2005. This represented a two-fold decrease in incidence compared to the 2002-2003 period.

Future initiatives in the surveillance of adverse transfusion events include upgrading the TTISS database to a web-based system, which will also incorporate a module for reporting of transfusion-related errors. Also, PHAC, in collaboration with stakeholders, has developed guidelines for investigating bacterial contamination that were published in early 2008.

1 Introduction

The Transfusion Transmitted Injuries Surveillance System (TTISS) evolved from a pilot project in 1999-2002 (four provinces participated: British Columbia, Québec, Prince Edward Island, Nova Scotia) and has become the national surveillance system for capturing serious, moderate, and selected minor adverse transfusion events (ATEs) occurring in Canada. In 2004-2005, nine Provinces and two Territories participated in the TTISS expanding from 56 hospitals reporting in 2002 to 291 hospitals in 2004-2005. The hospitals reporting at the end of 2005 represented 70% of the transfusion activity in Canada. The TTISS in its first two years had 244 ATEs reported compared to 569 in 2005 alone. In 2005 the top three reported ATEs for all blood components were TACO, severe allergic, and TRALI.

Several improvements have been implemented in TTISS since the inaugural 2002-2003 Program Report. These improvements have all been as a direct result of input from the front line health care workers as well as the National TTISS Working Group and the National Working Party for Data Review which meet annually to discuss the TTISS data. The Public Health Agency of Canada (PHAC) supports an annual stakeholders meeting where suggestions are brought forward from the Provinces/Territories for discussion and consideration. The goal of this meeting is to improve and refine data definitions and quality of the data received. One of the improvements suggested was separating the severity of the event and the outcome of the patient. Severity of the actual event is graded as minor, severe, life-threatening, or causing death. Outcome of the patient now ranges from minor/no sequelae to death. The juncture has allowed for more consistent reporting and accurate analysis. Another important improvement was changing the TRALI definition to follow the Canadian Blood Services (CBS)/Héma-Québec (HQ) TRALI consensus conference definitions and the International Society for Blood Transfusion definitions. This improvement allows for a better case definition and comparison with international hemovigilance systems. The TTISS strives to produce quality data and strictly adheres to the definitions for the classifying of reactions.

TTISS collaborates with both CBS and HQ and also with the Marketed Health Products Directorate (MHPD) of Health Canada for reconciliation of all data collected to ensure that the Program Report is comprehensive with respect to ATEs reported in Canada. This is the first Program Report to contain all of the reconciled data. The TTISS is recognized internationally as one of the leading quality surveillance systems. PHAC is a member of the working group tasked with designing the American biovigilance system and also is a member of the European Hemovigilance Network. The TTISS data have been presented annually at the American and European meetings for discussion and comparison with all other recognized hemovigilance systems.

The system continues to evolve, change and improve. Future initiatives include upgrading the TTISS database to a web based technology which will incorporate a module for more in depth reporting of errors related to transfusion. Also, PHAC, in collaboration with stakeholders, has developed a standardized guideline for investigation of suspect transfusion

transmitted bacterial contamination that was published in early 2008. This guideline has been reviewed by experts in the fields of transfusion medicine and medical microbiology, as well as the Transfusion Safety Officers across Canada. It will prove to be useful to hospitals providing standardized investigation across Canada and will be practical in terms of implementation.

2 Methodology

Data on adverse transfusion events were collected and investigated at participating hospital sites. Data were usually reported based on standardized definitions to a provincial or territorial blood coordinating office on a standardized paper form or transferred electronically. Non-nominal data on moderate, severe, and selected minor adverse transfusion events were then transferred electronically as per provincial/territorial/federal agreement to the PHAC. ATEs were initially recorded on the Canadian Transfusion Adverse Events Report form using the guidelines in the TTISS User's Manual (version 2) and then entered into the TTISS database. Training on the use of the form, the definitions, and the database, supplied by PHAC, was provided to each participating province/territory. A data validation process was performed at the provincial level to ensure that the reported ATEs met the required standards.

Data on ATEs were exported to PHAC every quarter (for the 3-month period ending 6 months prior to the date of reporting) through an encrypted Microsoft Access data file. Participating provinces were also asked to provide the number of hospitals that had been participating in TTISS for each year and the proportion of total blood products transfused in the province attributed to the participating hospitals. They were also asked to provide the number of transfused units in the participating hospitals for each category of blood product. In some instances these non-nominal data were transferred electronically directly from the participating hospitals to the PHAC as per agreement with the provincial/territorial authority.

ATEs were categorized by hospital sites according to available clinical and laboratory data to one of the standard diagnoses provided in the TTISS User's Manual. Possible TRALI was not an available choice of reaction on the Canadian Transfusion Adverse Events Report form but was re-categorized at PHAC as per the consensus definition.

Relationship of ATEs to transfusion, severity of ATEs, and outcomes of adverse events were assigned by reporting hospitals. Outcome refers to the consequences of an ATE while severity refers to the degree of gravity of the ATE.

Relationship of ATEs to transfusion was defined as follows:

- **Definite**
  if a clinical and/or laboratory event occurred within a time period consistent with the administration of the blood product and was proven by investigation to have been caused by transfusion.
- **Probable**
  if a clinical and/or laboratory event occurred within a time period consistent with the administration of the blood product and did not seem to be explainable by any other cause.

- **Possible**
  if the clinical and/or laboratory event occurred within a time period consistent with the administration of the blood product but a concurrent disease or the administration of a drug or other agent could not be excluded as a possible cause of the event.

Severity of ATEs was graded as follows:

- **Death (Grade 4)**
  the recipient's death was, at least in part, the consequence of a transfusion.
- **Life-threatening (Grade 3)**
  the recipient required major life-saving intervention following the transfusion.
- **Severe (Grade 2)**
  the recipient required in-patient hospitalization or prolongation of hospitalization directly attributable to the event;

  or the adverse event resulted in persistent or significant disability or incapacity;

  or the adverse event necessitated medical or surgical intervention to preclude permanent damage or impairment of a body function.
- **Minor (Grade 1)**
  the recipient may have required medical intervention (e.g. symptomatic treatment) but lack of such would not result in permanent damage or impairment of a body function.
- **Not determined**
  the severity of the transfusion event could not be ascertained.

Outcome of ATEs was categorized as:

- **Death**
  if the recipient died, the relationship of the transfusion to the death was classified as Definite, Probable, Possible, Doubtful, Ruled Out, or Not Determined
- **Major or long-term sequelae**
  If the recipient developed either an infection with a persistent infectious agent, an ATE with major or long-term sequelae, or anticipated difficulties with future transfusions
- **Minor or no sequelae**
  If the recipient developed antibodies to low or medium frequency antigens or other minor reactions
- **Not determined**
  If the outcome was not certain

For the 2004-2005 report, TTISS cases were reconciled with cases of ATEs reported to CBS and separately with cases reported to MHPD. Cases that were reported only to CBS and/or MHPD were included in the analysis when they met TTISS reporting criteria and case definitions. Cases from the province of Quebec were reconciled between HQ and the Quebec hemovigilance system prior to aggregation with the TTISS dataset.

Data received at the PHAC were reviewed by the TTISS epidemiologist and medical advisor for completeness and validity. When required, additional information such as clinical signs and symptoms, and/or laboratory results were requested from the reporting hospitals. Cases were excluded if they were reported with insufficient information to enable analysis, did not meet TTISS standard definitions, or were not reportable. These cases were excluded only in the database used for analysis but were kept in the original data sets sent by the provinces. Data were then exported to the Statistical Package for the Social Sciences (SPSS v.12, Chicago, USA) for analysis. Only ATEs definitely, probably or possibly related to transfusion were considered for analysis.

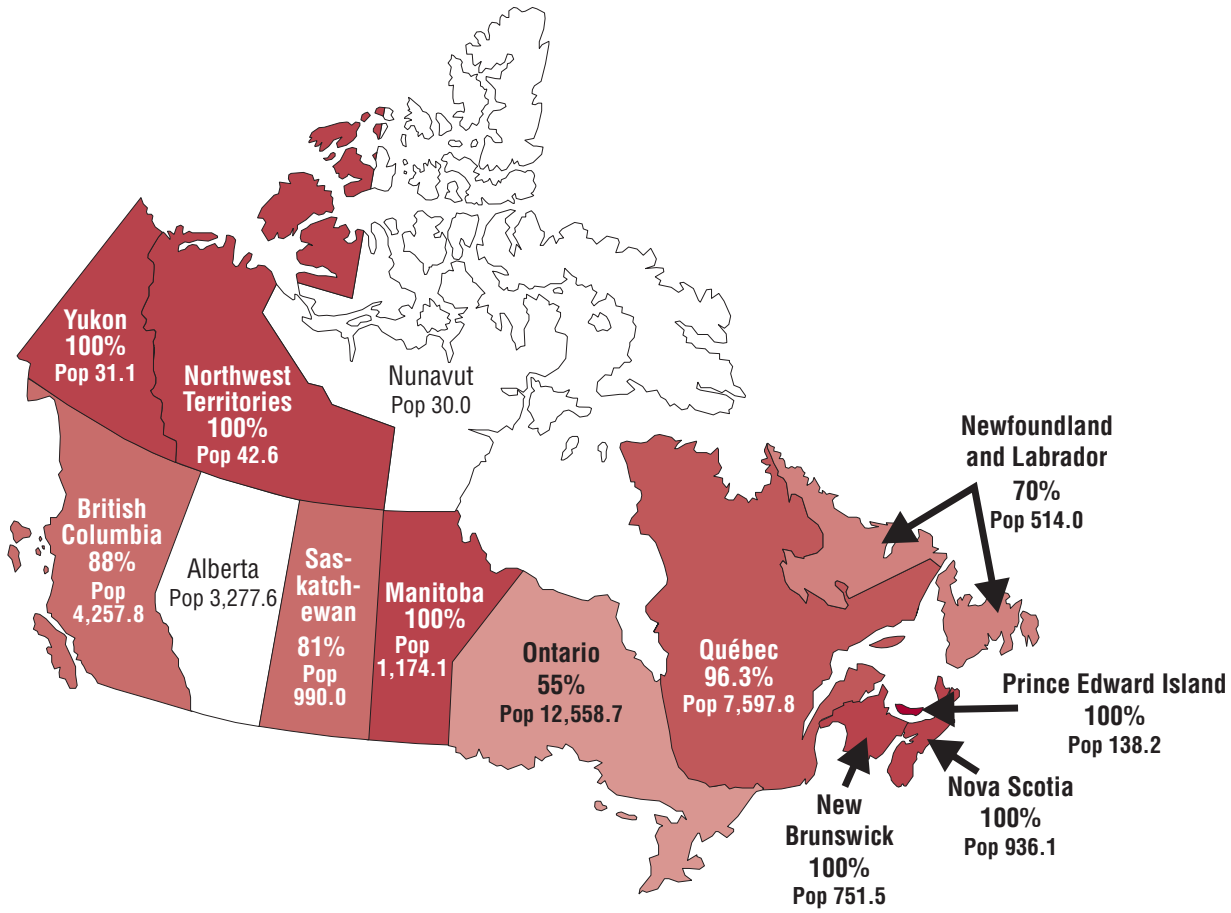
The incidence of ATEs was calculated using the number of units of blood products transfused in the participating hospitals as denominators. No denominator data were available for plasma derivatives therefore rates of ATEs were not calculated for this category of products.

3 Results

As of December 31, 2005, a total of nine provinces and two territories were participating in TTISS: Newfoundland, Prince Edward Island, Nova Scotia, New Brunswick, Québec, Ontario, Manitoba, Saskatchewan, British Columbia, Yukon and Northwest Territories. Figure 1 shows the proportion of the transfusion activity captured in each province and territory by hospitals participating in TTISS. Overall, hospitals participating in TTISS represented 70% of the transfusion activity in Canada.

Figure 1

Proportion of Canadian transfusion activity represented by hospitals participating in TTISS (as of 31 December, 2005)



NOTE : Population estimates (in thousands) from Statistics Canada. Canadian Population Census, 2005.

In 2004 and 2005, participating hospitals across these provinces transfused a total of 2,078,935 units of blood components, 56% being red blood cells (Table 1). The increase in apheresis platelet units is largely due to a massive transition from whole blood derived platelet to apheresis platelet production by Héma-Québec.

Table 1

Units of blood components transfused by hospital sites participating in TTISS, by year

	Year 2004		Year 2005		Total	
Blood components	**N**	**%**	**N**	**%**	**N**	**%**
Red blood cells	551,598	55.2	617,287	57.2	**1,168,885**	**56.2**
Apheresis platelets	22,708	2.3	46,996	4.4	**69,704**	**3.4**
Whole blood derived platelets (WBDP)	221,173	22.1	201,891	18.7	**423,064**	**20.4**
WBDP (Pools of 5 units)[1,2]	44,235		40,452		**84,687**	
Buffy Coat Platelets	–	–	74	0.01	**74**	**0.004**
Plasma	157,220	15.7	159,241	14.8	**316,461**	**15.2**
Cryoprecipitate	42,831	4.3	45,889	4.3	**88,720**	**4.3**
Whole blood	4,196	0.4	7,797	0.7	**11,993**	**0.6**
Granulocytes	25	0.003	9	0.001	**34**	**0.002**
Total	**999,751**	**100.0**	**1,079,184**	**100.0**	**2,078,935**	**100.0**

[1] WBDP divided by 5 and includes units of Buffy Coat Platelets

[2] Not included in total

3.1 Adverse Transfusion Events Included for Analysis

A total of 1058 ATEs were reported to the PHAC during the period 1 January 2004 to 31 December 2005. Of these, 405 (38.3%) were excluded from the data analysis. The reasons for exclusion are summarized in Table 2. The main reason for exclusion was that the event was minor and not to be reported to TTISS (69.6%). Cases reported only to MHPD (43) and/or CBS (66) were also added for analysis.

Table 2

Adverse transfusion events reported through TTISS and other sources, 2004-2005

	Reported ATEs	Included ATEs		Excluded adverse transfusion events and reasons for exclusion							
				Non reportable minor event		Incomplete/ missing information		Not meeting standard definitions		Total	
		N	%[1]	N	%[2]	N	%[2]	N	%[2]	N	%[1]
2004 TTISS	489	290	59.3	106	53.3	74	37.2	19	9.5	**199**	**40.7**
2005 TTISS	569	363	63.8	176	85.4	25	12.1	5	2.4	**206**	**36.2**
Total TTISS	**1,058**	**653**	**61.7**	**282**	**69.6**	**99**	**24.4**	**24**	**5.9**	**405**	**38.3**
MHPD cases[3]		**43**									
CBS cases[3]		**66**									
Total		**762**									

[1] Proportion of reported events per year
[2] Proportion within excluded events by year
[3] Cases not reported through TTISS but reported to MHPD and/or CBS through other sources

Thus, 762 ATEs were included in the analysis; 86% were related to blood components and 14% to plasma derivatives (Table 3).

Table 3

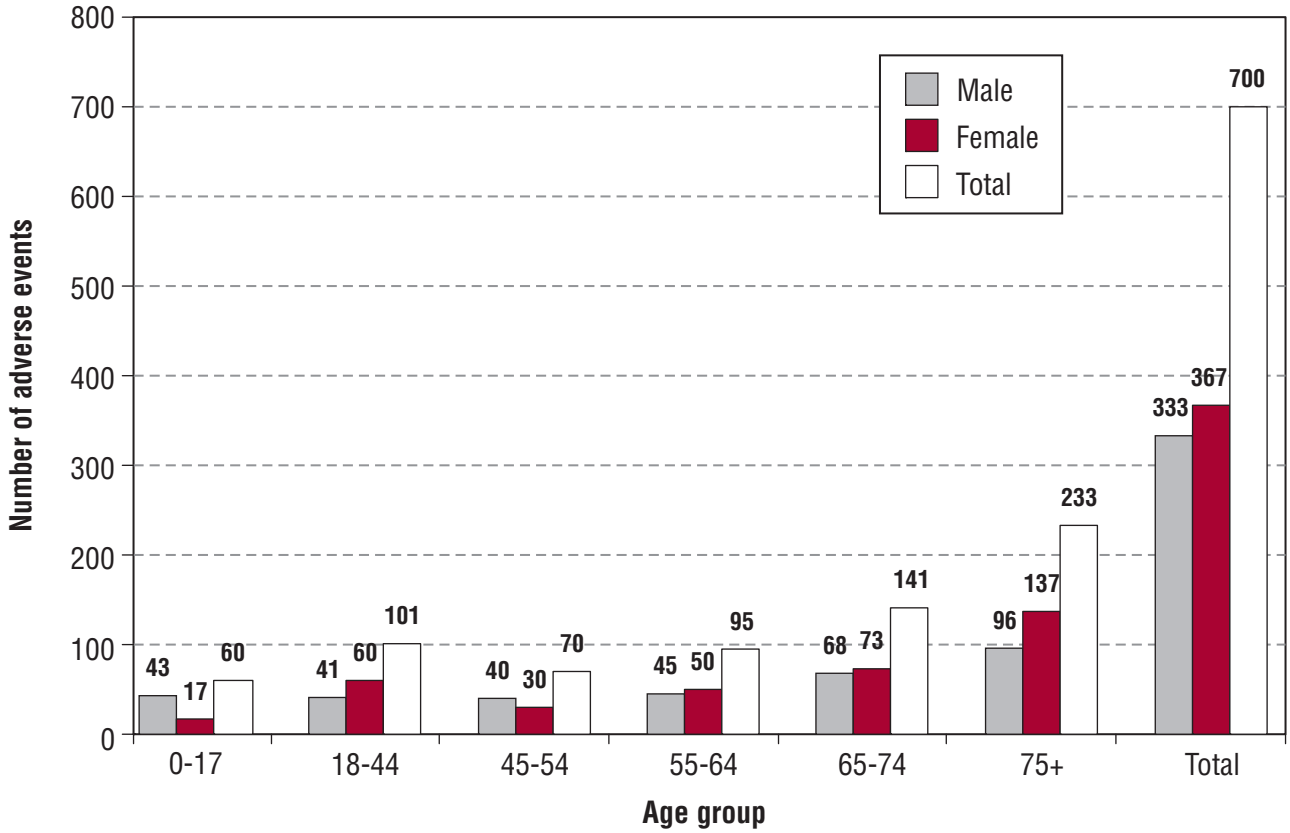
Adverse transfusion events by type of products and year of occurrence

	2 004		2 005		Total	
Type of products	N	%	N	%	N	%
Blood components	298	84.9	357	86.9	**655**	**86.0**
Plasma derivatives	53	15.1	54	13.1	**107**	**14.0**
Total	**351**	**100.0**	**411**	**100.0**	**762**	**100.0**

The distribution of ATEs by age and gender for 2004-2005 is shown in Figure 2. Adverse events were distributed quite evenly among males and females. Because no denominator data were available on the number of transfusions by age and gender, we could not report on the risk of ATEs related to those variables.

Figure 2

Distribution of adverse transfusion events by age and gender, 2004-2005



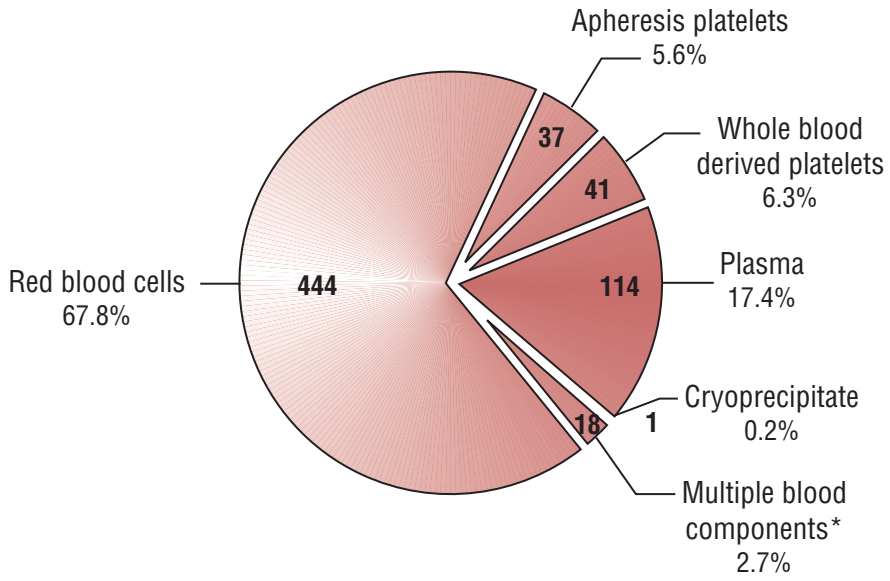
3.2 Adverse Transfusion Events Related to Blood Components

3.2.1 Type of Blood Components Implicated in Adverse Transfusion Events

More than two thirds of ATEs related to blood components involved red blood cells (Figure 3).

Figure 3

Blood components involved in adverse transfusion events (N = 655), 2004-2005



* refers to ATEs that could not be attributed to a single blood component

There was no significant difference in the type of component implicated between 2004 and 2005 as shown in Table 4.

Table 4

Type of blood components implicated in ATEs by year

	2004		2005		Total	
Blood component	**N**	**%**	**N**	**%**	**N**	**%**
Red blood cells	203	68.1	241	67.5	**444**	**67.8**
Apheresis platelets	20	6.7	17	4.8	**37**	**5.6**
WBDP	19	6.4	22	6.2	**41**	**6.3**
Plasma	44	14.8	70	19.6	**114**	**17.4**
Cryoprecipitate	1	0.3	0	0.0	**1**	**0.2**
Multiple blood components[1]	11	3.7	7	2.0	**18**	**2.7**
Total	**298**	**100.0**	**357**	**100.0**	**655**	**100.0**

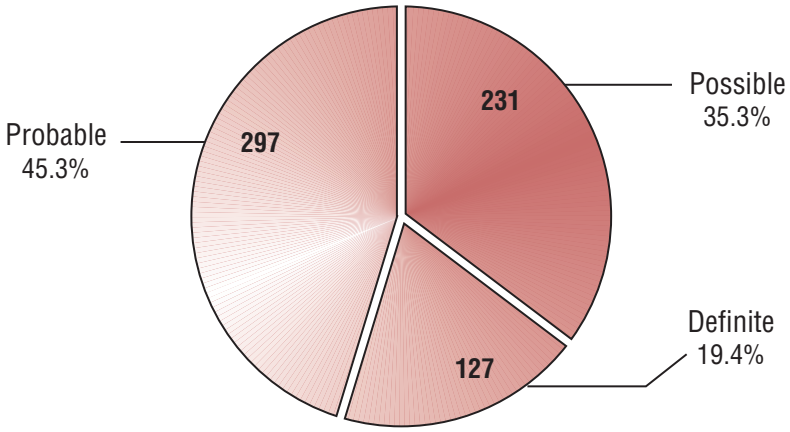
[1] refers to ATEs that could not be attributed to a single blood component (e.g. granulocytes, buffy coat platelets)

3.2.2 Relationship of Adverse Transfusion Events to Transfusion

Two thirds of ATEs were assessed to be definitely or probably related to transfusion, while a third of cases were possibly related to transfusion (Figure 4).

Figure 4

Relationship of adverse transfusion events with transfusion of blood components (N = 655), 2004-2005



Compared to 2005, relationship to transfusion was stronger in 2004 and appeared to be stronger for apheresis platelets than for other types of blood components (Table 5).

Table 5

Relationship of adverse transfusion events to transfusion by type of blood component and year

	2004						2005					
	Definite		Probable		Possible		Definite		Probable		Possible	
	N	%	N	%	N	%	N	%	N	%	N	%
Red blood cells	54	26.6	58	28.6	91	44.8	33	13.7	117	48.5	91	37.8
Apheresis platelets	5	25.0	9	45.0	6	30.0	5	29.4	8	47.1	4	23.5
WBDP	4	21.1	11	57.9	4	21.1	3	13.6	6	27.3	13	59.1
Plasma	8	18.2	22	50.0	14	31.8	9	12.9	28	40.0	33	47.1
Other[1]	4	33.3	4	33.3	4	33.3	2	28.6	1	14.3	4	57.1
Total	**75**	**25.3**	**104**	**35.0**	**119**	**40.1**	**52**	**14.6**	**160**	**44.8**	**145**	**40.6**

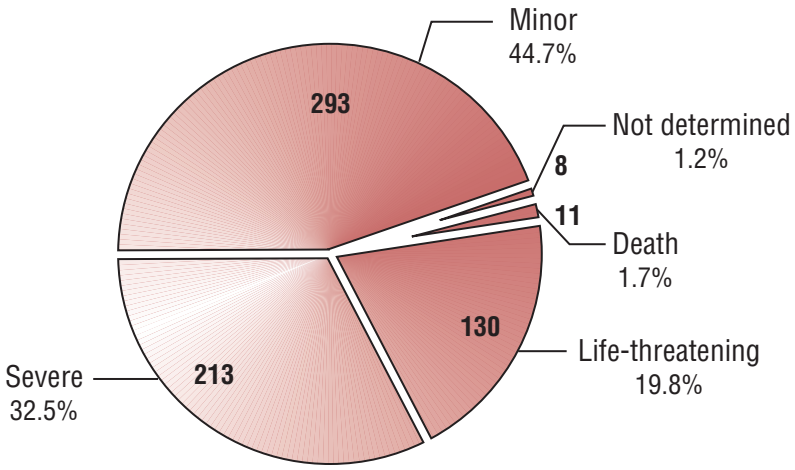
[1] includes whole blood, granulocytes, cryoprecipitate

3.2.3 Severity and Outcome of Adverse Transfusion Events

Severity was graded as life-threatening in close to 20% of the reported ATEs related to blood components. Nearly 2% of ATEs resulted in death of the recipient. Forty-five percent (45%) of ATEs were graded as minor and 32% as severe (Figure 5).

Figure 5

Severity of adverse transfusion events related to blood components (N = 655), 2004-2005



There were more severe cases reported in 2005 than in 2004 (Table 6).

Table 6

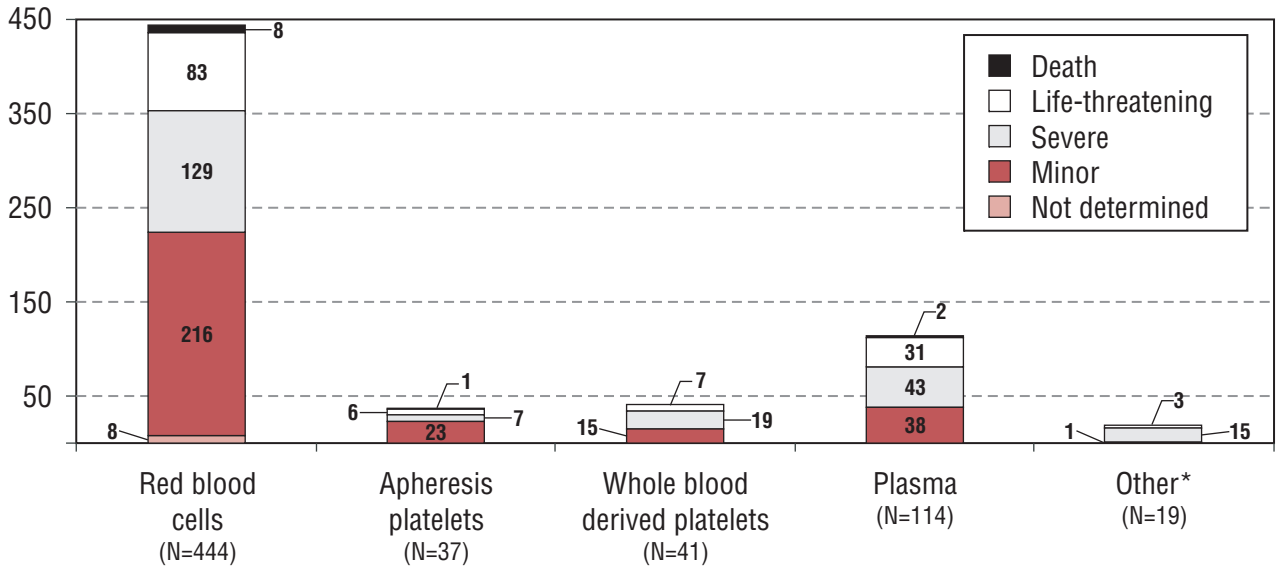
Severity of adverse transfusion events related to blood components by year

	2004		2005		Total	
Severity	**N**	**%**	**N**	**%**	**N**	**%**
Death	6	2.0	5	1.4	**11**	**1.7**
Life threatening	65	21.8	65	18.2	**130**	**19.8**
Severe	70	23.5	143	40.1	**213**	**32.5**
Minor	155	52.0	138	38.7	**293**	**44.7**
Not determined	2	0.7	6	1.7	**8**	**1.2**
Total	**298**	**100.0**	**357**	**100.0**	**655**	**100.0**

The proportion of minor cases was greater with apheresis platelets and red blood cells than with other components (Figure 6).

Figure 6

Severity of adverse transfusion events by type of blood component, 2004-2005

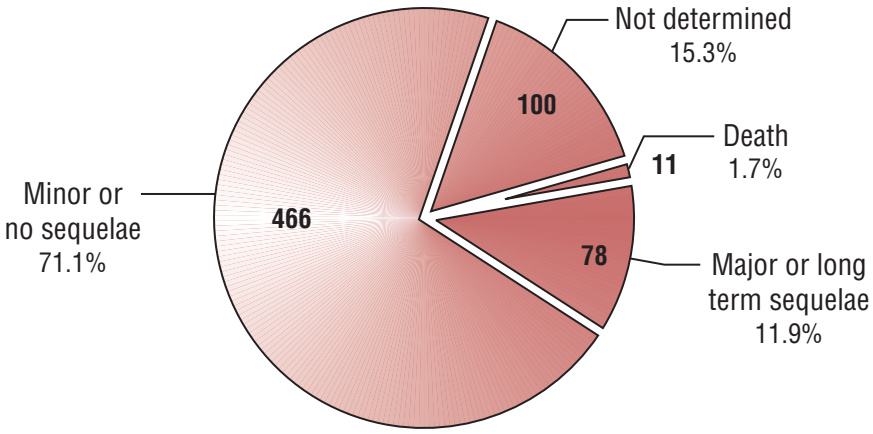


* Includes granulocytes, buffy coat platelets, and cryoprecipitate.

As previously noted, 11 cases of ATEs resulted in death of the recipient while for the majority of cases (71.1%) there were minor or no sequelae for the recipients (Figure 7).

Figure 7

Outcome of adverse transfusion events related to blood components (N = 655), 2004-2005



There was no difference between 2004 and 2005 in the reported outcome of ATEs. There was, however, a much higher proportion of cases in 2005 for which outcome information was available (Table 7). The majority of cases coded as major or long term sequelae were cases that developed new alloantibodies that put them at risk for future transfusions.

Table 7

Outcome of adverse transfusion events related to blood components by year

	2004		2005		Total	
Outcome	**N**	**%**	**N**	**%**	**N**	**%**
Death	6	2.0	5	1.4	**11**	**1.7**
Major or long-term sequelae	35	11.7	43	12.0	**78**	**11.9**
Minor or no sequelae	192	64.4	274	76.8	**466**	**71.1**
Not determined	65	21.8	35	9.8	**100**	**15.3**
Total	**298**	**100.0**	**357**	**100.0**	**655**	**100.0**

3.2.4 Type of Adverse Transfusion Events Related to Blood Components

ATEs related to each type of blood component transfused are shown in Table 8. For the period 2004-2005, the largest proportion of ATEs reported was transfusion associated circulatory overload (TACO) at 39.2%, followed by severe allergic reactions at 16.6% and transfusion related acute lung injury (TRALI) at 16.0%. For red blood cells, the three most frequently reported ATEs were TACO at 44.8%, TRALI at 13.5% and delayed hemolytic reaction at 9.5%. For platelets, severe allergic reactions were reported most frequently, followed by TACO and TRALI. As for plasma, severe allergic reactions and TACO were the two most frequently reported adverse reactions, followed by TRALI.

Table 8

Type of adverse transfusion events related to blood components by year

Type of adverse transfusion event	Red blood cells			Apheresis platelets			Whole blood derived platelets			Plasma			Other[1]			Total		
	2004	2005	Total	2004	2005	Total	2004	2005	Total	2004	2005	Total	2004	2005	Total	2004	2005	Total
Severe/Allergic/ Anaphylactoid	11 (5.4)	25 (10.4)	**36 (8.1)**	10 (50.0)	8 (47.1)	**18 (48.6)**	9 (47.4)	5 (22.7)	**14 (34.1)**	17 (35.6)	21 (30.0)	**38 (33.3)**	2 (16.7)	1 (14.3)	**3 (15.8)**	**49 (16.4)**	**60 (16.8)**	**109 (16.6)**
ABO Incompatibility	7 (3.4)	4 (1.7)	**11 (2.5)**	-	1 (5.9)	**1 (2.7)**	-	-	**-**	2 (4.5)	3 (4.3)	**5 (4.4)**	-	-	**-**	**9 (3.0)**	**8 (2.2)**	**17 (2.6)**
Hemolytic reaction: acute	15 (7.4)	13 (5.4)	**28 (6.3)**	-	-	**-**	-	3 (13.6)	**3 (7.3)**	-	1 (1.4)	**1 (0.9)**	-	-	**-**	**15 (5.0)**	**17 (4.8)**	**32 (4.9)**
Hemolytic reaction: delayed	24 (11.8)	18 (7.5)	**42 (9.5)**	1 (5.0)	1 (5.9)	**2 (5.4)**	-	-	**-**	-	1 (1.4)	**1 (0.9)**	-	-	**-**	**25 (8.4)**	**20 (5.6)**	**45 (6.9)**
TACO	88 (43.3)	111 (46.1)	**199 (44.8)**	5 (25.0)	3 (17.6)	**8 (21.6)**	3 (15.8)	8 (36.4)	**11 (26.8)**	14 (31.8)	24 (34.3)	**38 (33.3)**	-	1 (14.3)	**1 (5.3)**	**110 (36.9)**	**147 (41.2)**	**257 (39.2)**
TRALI	32 (15.8)	28 (11.6)	**60 (13.5)**	2 (10.0)	2 (11.8)	**4 (10.8)**	6 (31.6)	2 (9.1)	**8 (19.5)**	8 (18.2)	14 (20.0)	**22 (19.3)**	7 (58.3)	4 (57.1)	**11 (57.9)**	**55 (18.5)**	**50 (14.0)**	**105 (16.0)**
Possible TRALI	-	-	**-**	-	-	**-**	-	-	**-**	1 (2.3)	1 (1.4)	**2 (1.8)**	-	-	**-**	**1 (0.3)**	**1 (0.3)**	**2 (0.3)**
TAD	1 (0.5)	5 (2.1)	**6 (1.4)**	-	-	**-**	-	-	**-**	1 (2.3)	-	**1 (0.9)**	-	1 (14.3)	**1 (5.3)**	**2 (0.7)**	**6 (1.7)**	**8 (1.2)**
Bacterial Contamination	5 (2.5)	3 (1.2)	**8 (1.8)**	1 (5.0)	1 (5.9)	**2 (5.4)**	1 (5.3)	1 (4.5)	**2 (4.9)**	-	-	**-**	-	-	**-**	**7 (2.3)**	**5 (1.4)**	**12 (1.8)**
TRAIN	-	2 (0.8)	**2 (0.5)**	-	-	**-**	-	-	**-**	-	-	**-**	-	-	**-**	**-**	**2 (0.6)**	**2 (0.3)**
Hypotensive reaction	15 (7.4)	26 (10.8)	**41 (9.2)**	1 (5.0)	1 (5.9)	**2 (5.4)**	-	2 (9.1)	**2 (4.9)**	1 (2.3)	4 (5.7)	**5 (4.4)**	-	-	**-**	**17 (5.7)**	**33 (9.2)**	**50 (7.6)**
Post-transfusion purpura	-	1 (0.4)	**1 (0.2)**	-	-	**-**	-	1 (4.5)	**1 (2.4)**	-	-	**-**	2 (16.7)	-	**2 (10.5)**	**2 (0.7)**	**2 (0.6)**	**4 (0.6)**

Table 8 *(continued)*

Diagnosis of adverse transfusion events related to blood components by year

Type of adverse transfusion event	Red blood cells			Apheresis platelets			Whole blood derived platelets			Plasma			Other[1]			Total		
	2004	2005	Total	2004	2005	Total	2004	2005	Total	2004	2005	Total	2004	2005	Total	2004	2005	Total
Other[2]	3 (1.5)	-	**3 (0.6)**	-	-	**-**	-	-	**-**	-	-	**-**	1 (8.3)	-	**1 (5.3)**	**4 (1.3)**	**-**	**4 (0.7)**
Unknown	2 (1.0)	5 (2.1)	**7 (1.6)**	-	-	**-**	-	-	**-**	-	1 (1.4)	**1 (0.9)**	-	-	**-**	**2 (0.7)**	**6 (1.7)**	**8 (1.2)**
Total	**203**	**241**	**444**	**20**	**17**	**37**	**19**	**22**	**41**	**44**	**70**	**114**	**12**	**7**	**19**	**298**	**357**	**655**

[1] includes multiple blood components, cryoprecipitates, whole blood, granulocytes

[2] includes hemochromatosis, hypocalcemia

3.2.5 Type of Adverse Transfusion Event by Relationship to Transfusion

Relationship to transfusion was the strongest for ABO incompatibilities, acute and delayed haemolytic reactions and the weakest for transfusion associated dyspnea (TAD) and hypotensive reactions (Table 9).

Table 9

Type of adverse transfusion events by relationship to transfusion, 2004-2005

Type of adverse transfusion event	Relationship to transfusion							
	Definite		Probable		Possible		Total	
	N	%[1]	N	%[1]	N	%[1]	N	%
Severe/Allergic/Anaphylactoid	16	14.7	68	62.4	25	22.9	**109**	**16.6**
ABO incompatibility	17	100.0	-	-	-	-	**17**	**2.6**
Hemolytic reaction: acute	13	40.6	14	43.8	5	15.6	**32**	**4.9**
Hemolytic reaction: delayed	28	62.2	13	28.9	4	8.9	**45**	**6.9**
TACO	36	14.0	128	49.8	93	36.2	**257**	**39.2**
TRALI	10	9.5	37	35.2	58	55.2	**105**	**16.0**
Possible TRALI	-	-	1	50.0	1	50.0	**2**	**0.3**
TAD	-	-	1	12.5	7	87.5	**8**	**1.2**
Bacterial contamination	3	25.0	7	58.3	2	16.7	**12**	**1.8**
TRAIN	1	50.0	1	50.0	-	-	**2**	**0.3**
Hypotensive reaction	-	-	20	40.0	30	60.0	**50**	**7.6**
Post-transfusion purpura	2	50.0	1	25.0	1	25.0	**4**	**0.6**
Other[2]	1	25.0	2	50.0	1	25.0	**4**	**0.6**
Unknown	-	-	4	50.0	4	50.0	**8**	**1.2**
Total	**127**	**19.4**	**297**	**45.3**	**231**	**35.3**	**655**	**100.0**

[1] percentage within row

[2] includes hemochromatosis, hypocalcemia

3.2.6 Type of Adverse Transfusion Events by Severity

Nearly 45% of the reported ATEs were graded as minor. As would be expected, TRALI and severe allergic reactions had the highest proportion of cases that were graded as severe or life-threatening (Table 10). ABO incompatibility, hypotensive reactions and delayed hemolytic reactions represented the largest proportion of cases that were graded as minor.

Transfusion was the likely or possible cause of death in five TRALI cases, three TACO cases and one case each of bacterial contamination, delayed hemolytic reaction and hemochromatosis (included in Other).

Table 10

Type of adverse transfusion events by severity, 2004-2005

Type of adverse transfusion event	Severity of events											
	Death		Life threatening		Severe		Minor or no sequelae		Not determined		Total	
	N	%[1]	N	%[1]	N	%[1]	N	%[1]	N	%[1]	N	%
Severe/Allergic/Anaphylactoid	-	-	28	25.7	42	38.5	39	35.8	-	-	**109**	**16.6**
ABO incompatibility	-	-	4	23.5	-	-	13	76.5	-	-	**17**	**2.6**
Hemolytic reaction: acute	-	-	3	9.4	10	32.0	16	50.0	3	9.4	**32**	**4.9**
Hemolytic reaction: delayed	1	2.2	3	6.7	10	22.2	30	66.7	1	2.2	**45**	**6.9**
TACO	3	1.2	40	15.6	59	23.0	154	59.9	1	0.4	**257**	**39.2**
TRALI	5	4.8	37	35.2	62	59.0	-	-	1	1.0	**105**	**16.0**
Possible TRALI	-	-	1	50.0	1	50.0	-	-	-	-	**2**	**0.3**
TAD	-	-	3	37.5	5	62.5	-	-	-	-	**8**	**1.2**
Bacterial contamination	1	8.3	2	16.7	1	8.3	6	50.0	2	16.7	**12**	**1.8**
TRAIN	-	-	-	-	2	100.0	-	-	-	-	**2**	**0.3**
Hypotensive reaction	-	-	4	8.0	11	22.0	35	70.0	-	-	**50**	**7.6**
Post-transfusion purpura	-	-	-	-	4	100.0	-	-	-	-	**4**	**0.6**
Other[2]	1	25.0	2	50.0	1	25.0	-	-	-	-	**4**	**0.6**
Unknown	-	-	3	37.5	5	62.5	-	-	-	-	**8**	**1.2**
Total	**11**	**1.7**	**130**	**19.8**	**213**	**32.5**	**293**	**44.7**	**8**	**1.2**	**655**	**100.0**

[1] percentage within row
[2] includes hemochromatosis, hypocalcemia

3.2.7 Analysis by Specific Type of Adverse Transfusion Event: ABO incompatibility, AHTR, DHTR, TRALI and bacterial contamination

3.2.7.1 ABO Incompatibility

Seventeen cases of unintended ABO incompatible transfusions were reported, nine in 2004 and eight in 2005; nearly two thirds were with red blood cells (Table 11).

Table 11

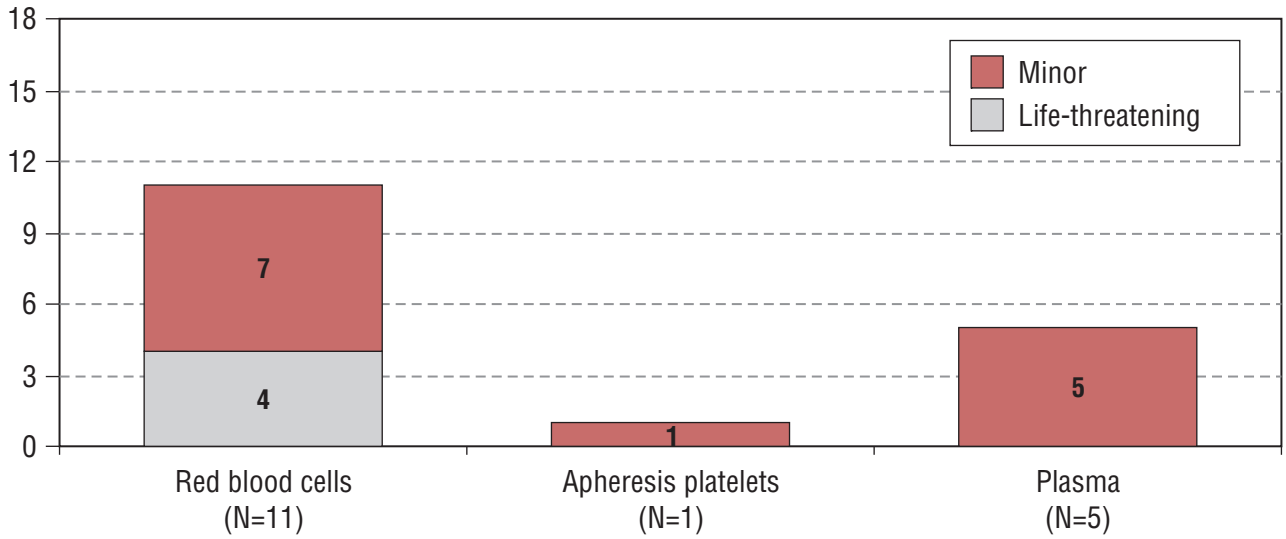
Adverse transfusion events involving ABO incompatibility, by type of blood component

	2004		2005		Total	
Blood components	**N**	**%**	**N**	**%**	**N**	**%**
Red blood cells	7	77.8	4	50.0	**11**	**64.7**
Apheresis platelets	-	-	1	12.5	**1**	**5.9**
Plasma	2	22.2	3	37.5	**5**	**29.4**
Total	**9**	**100.0**	**8**	**100.0**	**17**	**100.0**

All cases of ABO incompatibility related to plasma and platelets were minor; in fact these cases were asymptomatic. More than a third of cases related to red blood cells were life-threatening (Figure 8).

Figure 8

Severity of ABO incompatibility by type of blood component, 2004-2005*



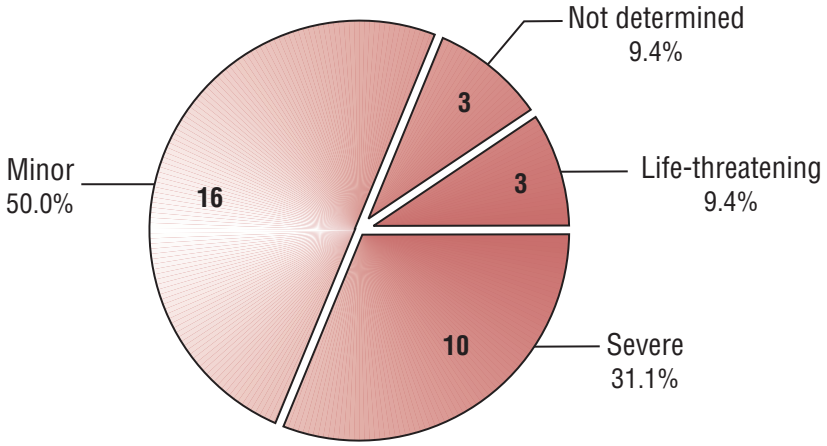
* no deaths or severe adverse transfusion events reported

3.2.7.2 Acute Hemolytic Transfusion Reactions (AHTR)

There were 32 cases of AHTR reported, accounting for nearly 5% of cases reported in 2004-2005. Twenty-eight (87.5%) cases were with red blood cells, three (9.4%) with whole blood-derived platelets and one (3.1%) with plasma. Half of the cases were minor ones and more than 40% of cases were graded as severe or life-threatening (Figure 9).

Figure 9

Severity of acute hemolytic transfusion reactions (N = 32), 2004-2005*

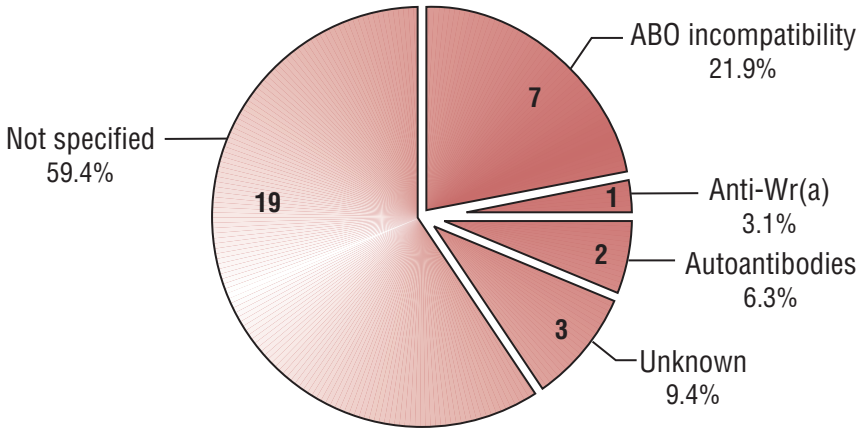


* no deaths were reported

The cause of AHTR was not provided in nearly 60% of cases. ABO-incompatible transfusion was the cause in 18.8% of cases (Figure 10). The large proportion of unspecified AHTR causes is attributed to missing data.

Figure 10

Causes of acute hemolytic transfusion reactions (N = 32), 2004-2005

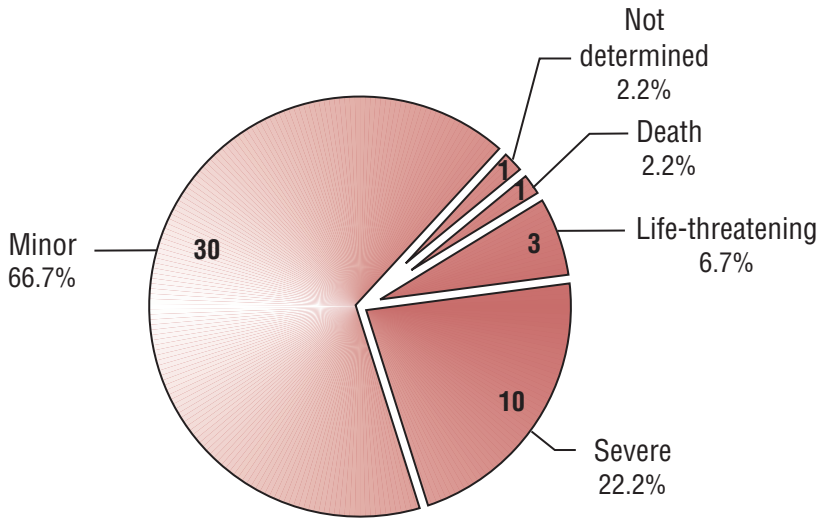


3.2.7.3 Delayed Hemolytic Transfusion Reactions (DHTR)

There were a total of 45 cases of DHTR reported in 2004-5 compared to three cases in 2002-2003. This difference is due to the fact that all cases were to be reported irrespective of severity in 2004-2005 and not just the severe ones as was previously the case. Almost all cases of DHTR were related to red blood cells (93.3%), two cases were associated with whole blood-derived platelets and one with plasma. Two thirds of cases were minor ones and one case resulted in death of the recipient (Figure 11).

Figure 11

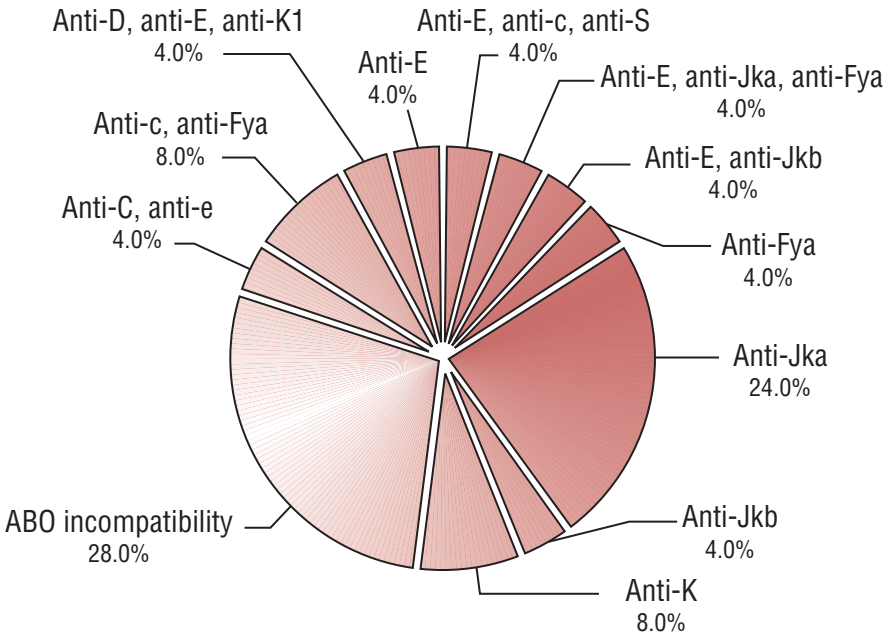
Severity of delayed hemolytic transfusion reactions (N = 45), 2004-2005



In a quarter of cases, anti-Jka was the responsible antibody for hemolysis. A variety of antibodies were involved in the other cases (Figure 12).

Figure 12

Antibodies implicated in delayed hemolytic transfusion reactions (N = 45), 2004-2005



3.2.7.4 Bacterial Contamination

A total of 12 cases of bacterial contamination definitely, probably or possibly related to transfusion were reported, 58% of those having been reported in 2004.

In the *Canadian Adverse Event Reporting Form User's Manual*, bacterial contamination is defined as follows:

Bacterial contamination is considered **Definite** if it meets ALL of the following criteria:

- The same bacteria are found in the recipient and the blood product.
- Contamination of the blood sample or the laboratory is not suspected.

Bacterial contamination is considered **Probable** if it meets the following criteria:

- Positive blood product culture.
- Contamination of the blood sample or the laboratory is not suspected.
- The recipient is symptomatic (nothing else explains it).
- The recipient blood culture was not done.
  - No specimen was available.
  - A blood culture was not ordered.

- The recipient's blood culture is negative.
  - The recipient is already taking antibiotics.
  - There were problems with the recipient's blood culture.

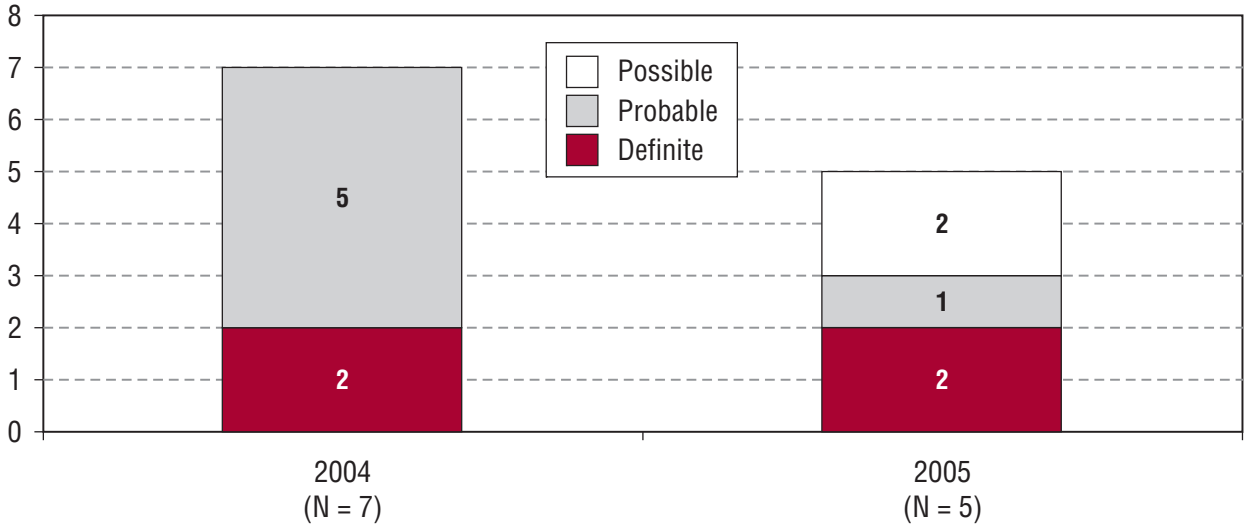
Bacterial Contamination is considered **Possible** if it meets the following criteria:

- The recipient's blood culture is positive.
- Contamination of the blood sample and the laboratory is not suspected.
- The recipient is symptomatic (nothing else explains it).
- A blood product culture was not done.
  - No specimen was available.
- The blood product culture is negative.
  - There were problems with the culture of the blood product.

For both years, 8 cases (66.7%) of bacterial contamination were related to red blood cells, two (16.7%) to apheresis platelets, and two (16.7%) to whole blood-derived platelets. Distribution of relationship to transfusion by year is presented in Figure 13.

Figure 13

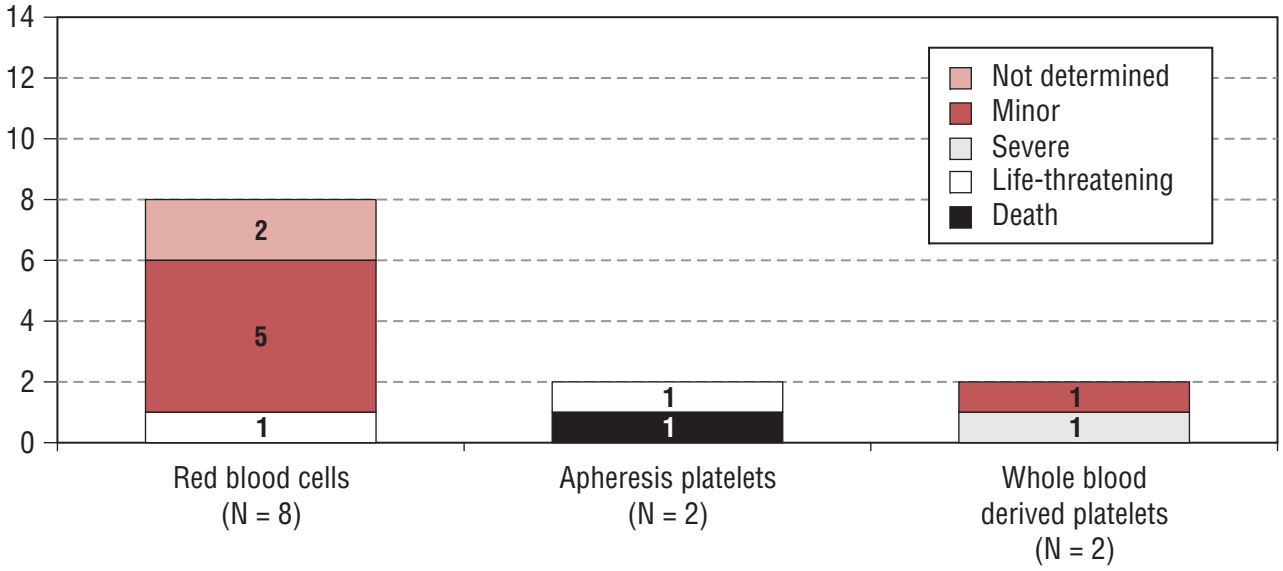
Adverse transfusion events involving Bacterial contamination, by relationship to transfusion, 2004-2005



Cases related to red blood cells were less severe than those associated with platelets (Figure 14).

Figure 14

Severity of bacterial contamination by type of blood component, 2004-2005



Ten of the 12 bacteria implicated in bacterial contamination cases were gram positive. All bacterial contaminations related to red blood cells and whole blood-derived platelets were with gram-positive bacteria while the two cases related to apheresis platelets were with gram-negative bacteria. Among the reported cases of bacterial contamination, ten were definitely or probably related to transfusion, that is, with a positive blood product culture. A variety of organisms were identified in these cases, with a predominance of gram-positive cocci such as *Staphylococcus* and *Streptococcus* species (Table 12).

One case resulted in death after transfusion of an apheresis platelet unit contaminated with *Serratia marcesens*. The platelet unit was screened for bacteria and none was detected. After reviewing the case, no failure was identified in the culture technique. The life-threatening case associated with the transfusion of a *Salmonella typhimurium* contaminated apheresis platelet unit was similar with a failure to detect the presence of bacteria by the culture system at the blood supplier. Again the culture method was according to the manufacturer specifications. These two cases probably represent failures of the culture system to detect a very low level of bacteria at an early stage.

Table 12

Severity of bacterial contaminations by type of organism and blood component*

Severity	Red Blood Cells (N=6)	Apheresis PLT (N=2)	WBDP (N=2)
Death	-	*Serratia marcescens* (1)	-
Life threatening	Alpha hemolytic *Streptococcus* (1)	*Salmonella typhimurium* (1)	-
Severe	-	-	*Staphylococcus aureus* (1)
Minor	*Staphylococcus epidermidis* (2) *Propionibacterium spp* (1) Coagulase negative *Staphylococcus* (1)	-	Coagulase negative *Staphylococcus* (1)
Not determined	*Streptococcus viridans* (1)	-	-

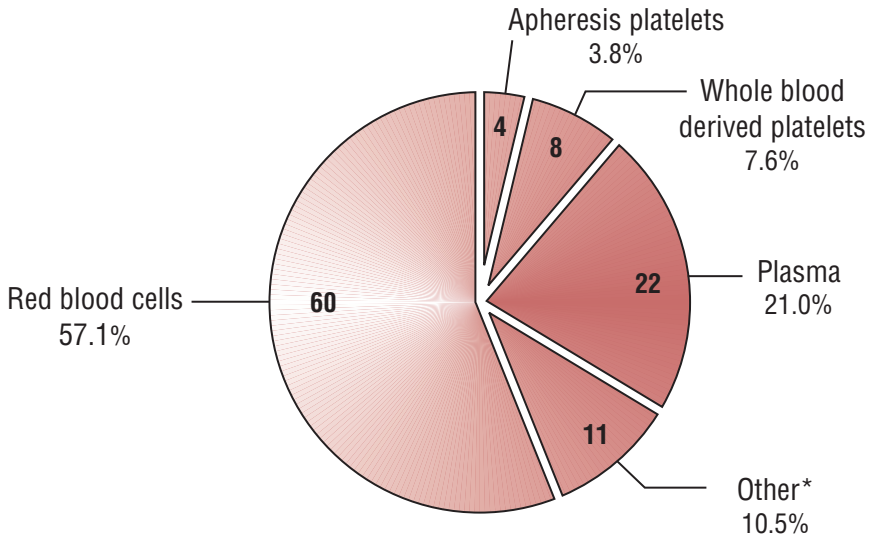
* organism was not reported in two cases of bacterial contamination

3.2.7.5 TRALI and possible TRALI

For TRALI, almost half of cases (51 out of 105) were reported only to CBS by hospitals not participating in TTISS. The 105 TRALI cases represent all cases reported in Canada in 2004-2005, either to TTISS or to CBS and follow the definition as per the Toronto Consensus Conference. The two cases of possible TRALI were with plasma and were reported to TTISS only. The distribution of TRALI cases by type of blood component is shown in Figure 15.

Figure 15

Type of blood component implicated in TRALI (N = 105), 2004-2005



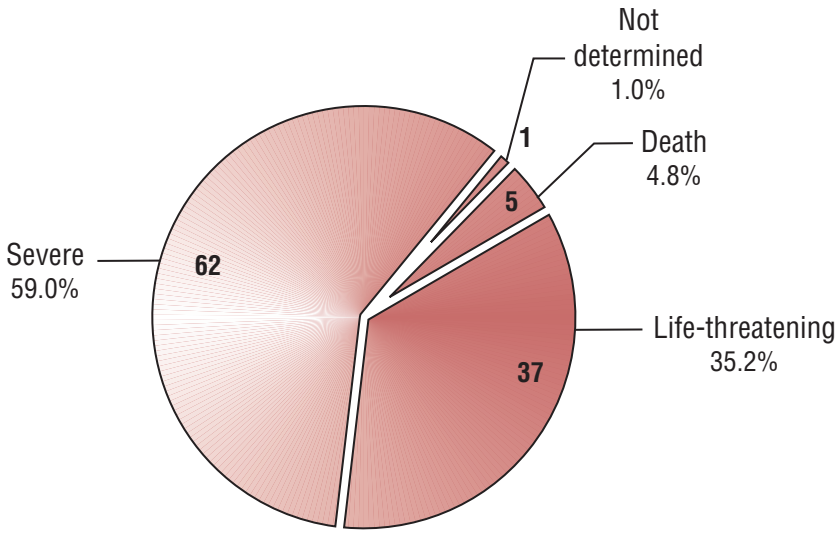
*refers to multiple blood components

The majority (57.1%) of TRALI cases were related to the transfusion of red blood cells. The category other refers mainly to multiple blood components where no single type of component could be implicated in the reaction.

One case of possible TRALI was graded as severe and one as life-threatening. The severity of TRALI cases is shown in Figure 16. Five cases resulted in death for a fatality rate of 4.8%.

Figure 16

Severity of TRALI related to blood components (N = 105), 2004-2005



Cases related to red blood cells were as severe as those related to higher plasma-containing products (Table 13).

Table 13

Severity by type of blood component implicated in TRALI cases

	RBCs		Apheresis platelets		WBDP		Plasma		Other[1]		Total	
Severity	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Death	4	6.7	-	-	-	-	1	4.5	-	-	**5**	**4.8**
Life-threatening	21	35.0	3	75.0	2	25.0	9	40.9	2	18.2	**37**	**35.2**
Severe	34	56.7	1	25.0	6	75.0	12	54.5	9	81.8	**62**	**59.0**
Minor	-	-	-	-	-	-	-	-	-	-	**-**	**-**
Not determined	1	1.7	-	-	-	-	-	-	-	-	**1**	**1.0**
Total	**60**	**100.0**	**4**	**100.0**	**8**	**100.0**	**22**	**100.0**	**11**	**100.0**	**105**	**100.0**

[1] Multiple components and whole blood

3.2.8 Incidence of Adverse Transfusion Events

The incidence of each type of ATE for 2004 and 2005 is presented in Tables 14 and 15 respectively. Data for ratio calculations include only cases reported to TTISS because we did not have denominator data for hospitals that reported cases to CBS only and not participating in TTISS. Thus, of the 655 ATEs related to blood components, only 589 cases were used to calculate incidence. The 66 excluded cases were: TRALI (51), severe allergic (5), acute hemolytic reaction (3), bacterial contamination (3), post-transfusion purpura (2), TACO (1) and hypotensive reaction (1).

Overall incidence ratios were similar in 2004 and 2005 at 1:3860 and 1:3270 units transfused respectively. It is important to note the incidence of ABO-incompatible transfusions related to red blood cells decreased by half in 2005 compared to 2004 and that incidence of bacterial contaminations also decreased by half.

The comparative ratios of ATEs expressed per 100,000 units of blood components transfused from 2002 to 2005 are presented in Figure 17. The observed downward trend in incidence of bacterial contaminations and ABO-incompatible transfusions in 2002-2003 continued in the period 2004-2005. Incidence of AHTR decreased by 50% in 2004-2005 compared to 2003. There was a sharp increase in incidence of TACO in 2004 and 2005 compared to the previous period. This is due to the fact that all cases of TACO were reportable in the last two years whereas only the most serious cases were to be reported previously. The situation is the same for DHTR.

The incidence of TRALI was quite stable but the situation was much different for severe allergic reactions where the incidence has decreased by half in the last two years.

Table 14

Incidence of adverse transfusion events by blood component, 2004[1]

	Red blood cells (551,598)		Apheresis platelets (22,708)		Whole blood derived platelets				Plasma (157,220)		Other[3] (47,052)		All components (999,751)	
					Units (221,173)		Pools(5)[2] (44,235)							
Diagnosis	N	Incidence	N	Incidence	N	Incidence	N	Incidence	N	Incidence	N	Incidence	N	Incidence
Severe/Allergic/Anaphylactoid	11	1:50,145	8	1:2,839	9	1:24,575	9	1:4,915	16	1:9,826	1	1:47,052	**45**	**1:22,217**
ABO incompatibility	7	1:78,800	-	-	-	-	-	-	2	1:78,610	-	-	**9**	**1:111,083**
Hemolytic reaction: acute	13	1:42,431	-	-	-	-	-	-	-	-	-	-	**13**	**1:76,904**
Hemolytic reaction: delayed	24	1:22,983	1	1:22,708	-	-	-	-	-	-	-	-	**25**	**1:39,990**
TACO	88	1:6,268	5	1:4,542	3	1:73,724	3	1:14,745	14	1:11,230	-	-	**110**	**1:9,089**
TRALI	16	1:34,475	2	1:11,354	5	1:44,235	5	1:8,847	2	1:78,610	-	-	**25**	**1:39,990**
Possible TRALI	-	-	-	-	-	-	-	-	1	1:157,220	-	-	**1**	**1:999,751**
TAD	1	1:551,598	-	-	-	-	-	-	1	1:157,220	-	-	**2**	**1:499,876**
Bacterial contamination	4	1:137,900	1	1:22,708	1	1:221,173	1	1:44,235	-	-	-	-	**6**	**1:166,625**
Hypotensive reaction	15	1:36,773	1	1:22,708	-	-	-	-	1	1:157,220	-	-	**17**	**1:58,809**
Other[4]	3	1:183,866	-	-	-	-	-	-	-	-	1	1:47,052	**4**	**1:249,938**
Unknown	2	1:275,799	-	-	-	-	-	-	-	-	-	-	**2**	**1:499,876**
Total	**184**	**1:2,998**	**18**	**1:1,262**	**18**	**1:12,287**	**18**	**1:2,458**	**37**	**1:4,249**	**2**	**1:23,526**	**259**	**1:3,860**

[1] includes only cases reported by hospitals participating in TTISS

[2] not included in total for "All components"

[3] includes cryoprecipitate, granulocytes and whole blood

[4] includes hemochromatosis, hypocalcemia, acquired anti-GP, ischemic event

Table 15

Incidence of adverse transfusion events by blood component, 2005[1]

Diagnosis	Red blood cells (617,287)		Apheresis platelets (46,996)		Whole blood derived platelets				Plasma (159,241)		Other[3] (53,695)		All components[4] (1,079,110)	
					Units (201,891)		Pools(5)[2] (40,452)							
	N	Incidence	N	Incidence	N	Incidence	N	Incidence	N	Incidence	N	Incidence	N	Incidence
Severe/Allergic/Anaphylactoid	25	1:24,691	8	1:5,875	5	1:40,378	5	1:8,090	20	1:7,962	1	1:53,695	**59**	**1:18,290**
ABO incompatibility	4	1:154,322	1	1:46,996	-	-	-	-	3	1:53,080	-	-	**8**	**1:134,889**
Hemolytic reaction: acute	13	1:47,484	-	-	2	1:100,946	2	1:20,226	1	1:159,241	-	-	**16**	**1:67,444**
Hemolytic reaction: delayed	18	1:34,294	1	1:46,996	-	-	-	-	1	1:159,241	-	-	**20**	**1:53,956**
TACO	111	1:5,561	3	1:15,665	8	1:25,236	8	1:5,057	23	1:6,924	1	1:53,695	**146**	**1:7,391**
TRALI[5]	14	1:44,092	1	1:46,996	1	1:201,891	1	1:40,452	10	1:15,924	1	1:53,695	**29**	**1:37,211**
Possible TRALI	-	-	-	-	-	-	-	-	1	1:159,241	-	-	**1**	**1:1,079,110**
TAD	5	1:123,457	-	-	-	-	-	-	-	-	1	1:53,695	**6**	**1:179,852**
Bacterial contamination	2	1:308,644	1	1:46,996	-	-	-	-	-	-	-	-	**3**	**1:359,703**
TRAIN	2	1:308,644	-	-	-	-	-	-	-	-	-	-	**2**	**1:539,555**
Hypotensive reaction	26	1:23,742	1	1:46,996	1	1:201,891	1	1:40,452	4	1:39,810	-	-	**32**	**1:33,722**
Post-transfusion purpura	1	1:617,287	-	-	1	1:201,891	1	1:40,452	-	-	-	-	**2**	**1:539,555**
Unknown	5	1:123,457	-	-	-	-	-	-	1	1:159,241	-	-	**6**	**1:179,852**
Total	**226**	**1:2,731**	**16**	**1:2,937**	**18**	**1:11,216**	**18**	**1:2,247**	**64**	**1:2,488**	**4**	**1:13,421**	**330**	**1:3,270**

[1] includes only cases reported by hospitals participating in TTISS

[2] not included in total for "All components"

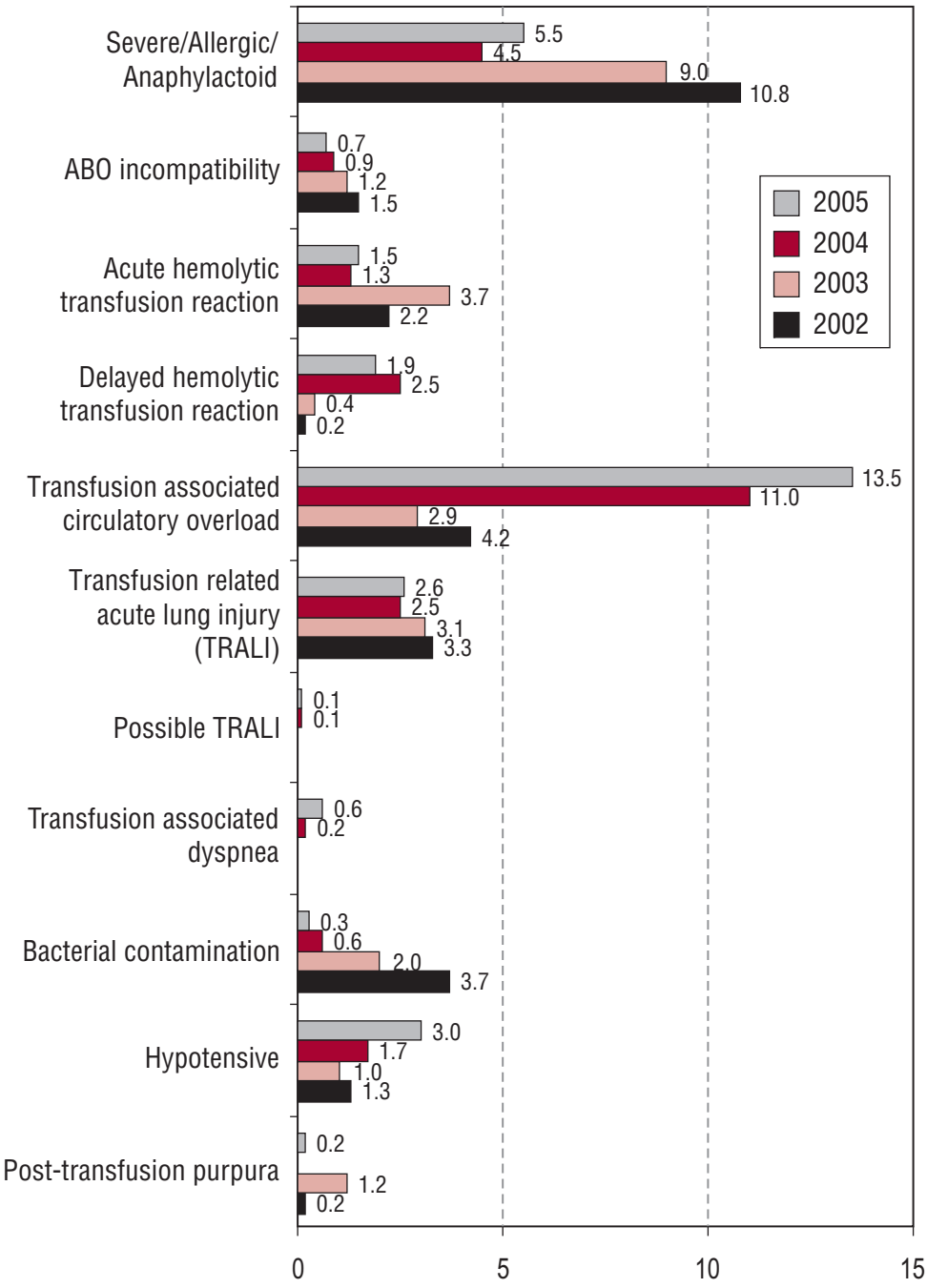
[3] includes cryoprecipitate, granulocytes, whole blood

[4] includes two cases where the implicated product could not be ascertained

[5] TRALI incidence includes two cases for which the implicated blood component could not be ascertained

Figure 17

Rates of adverse transfusion events per 100 000 units of blood components transfused by year, 2002-2005

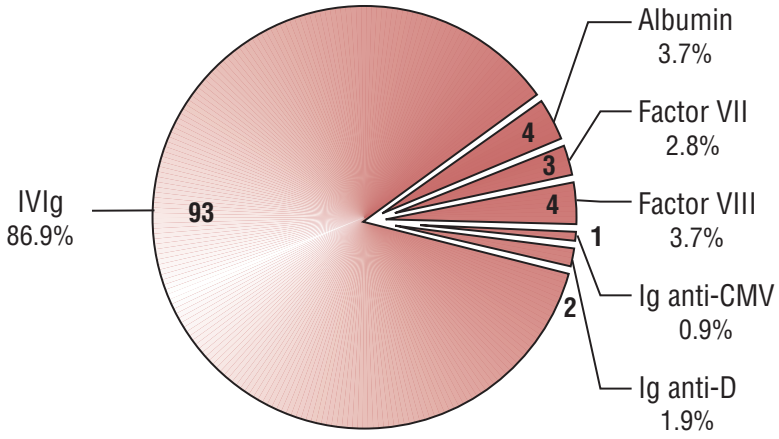


3.3 Adverse Transfusion Events Related to Plasma Derivatives and Recombinant Products

A total of 107 ATEs were related to plasma derivatives and recombinant blood products (53 in 2004 and 54 in 2005). Nearly 87% of these reactions were related to the administration of intravenous immune globulin (IVIg) (Figure 18).

Figure 18

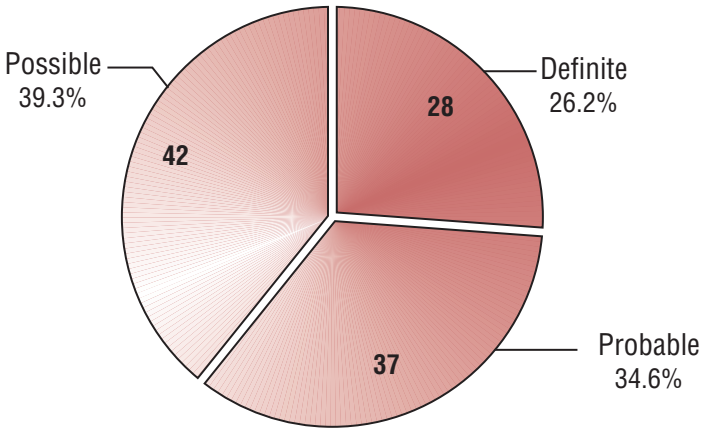
Plasma derivatives and recombinant products related to adverse transfusion events (N = 107), 2004-2005



The relationship to transfusion of ATEs related to plasma derivatives and recombinant products was similar to that of ATEs related to blood components except for a slightly higher proportion of definite cases (Figures 19 and 4).

Figure 19

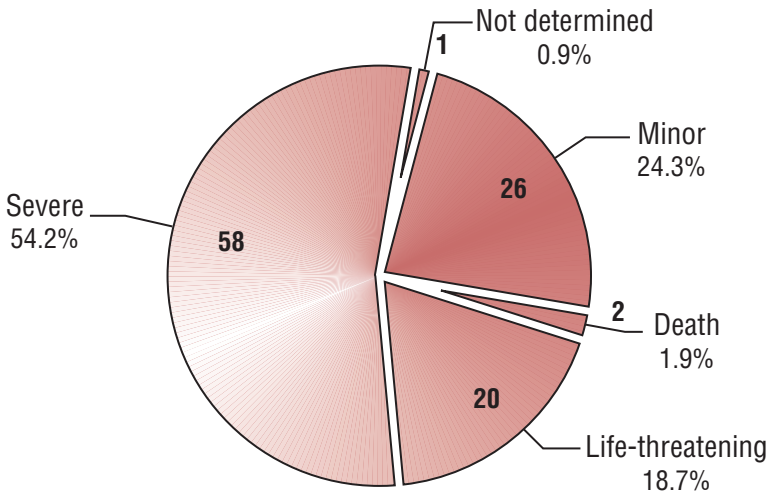
Relationship to transfusion of adverse transfusion events related to plasma derivatives and recombinant products (N = 107), 2004-2005



There were two deaths related to the administration of plasma derivatives, one was related to IVIg and one to anti-D. They are described in section 3.4. A quarter of cases were minor ones (Figure 20).

Figure 20

Severity of adverse transfusion events related to plasma derivatives and recombinant products (N = 107), 2004-2005



The types of ATEs related to each category of plasma derivatives and recombinant products are shown in Table 16.

Severe allergic reactions were the most frequently reported adverse events (38.3%), followed by delayed hemolytic reactions (13.1%) and acute hemolytic reactions (10.3%), and TACO (9.3%). These four diagnoses represented 70% of ATEs related to IVIg. There was a total of 25 cases of hemolytic reactions of which 24 were related to IVIg. Such cases were not reported to TTISS in the 2002-2003 period. The vast majority of these cases were associated with a new IVIg brand. There were also six cases of thrombotic events related to the administration of IVIg including one case possibly causing death of the recipient.

Table 16

Type of adverse transfusion event related to plasma derivatives and recombinant products, 2004-2005

Type of adverse transfusion event	IVIg			Albumin			Anti-D			Other*			All products		
	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)
Severe/Allergic/Anaphylactoid	23 (50.0)	14 (29.8)	37 (39.8)	-	1 (33.3)	1 (25.0)	-	1 (100.0)	1 (50.0)	1 (50.0)	1 (16.7)	2 (25.0)	**24 (48.0)**	**17 (29.8)**	**41 (38.3)**
ABO incompatibility	-	1 (2.1)	1 (1.1)	-	-	-	-	-	-	-	-	-	**-**	**1 (1.8)**	**1 (0.9)**
Hemolytic reaction: acute	3 (6.5)	7 (14.9)	10 (10.8)	-	-	-	1 (100.0)	-	1 (50.0)	-	-	-	**4 (8.0)**	**7 (12.3)**	**11 (10.3)**
Hemolytic reaction: delayed	3 (6.5)	11 (23.4)	14 (15.1)	-	-	-	-	-	-	-	-	-	**3 (6.0)**	**11 (19.3)**	**14 (13.1)**
TACO	3 (6.5)	5 (10.6)	8 (8.6)	1 (100.0)	1 (33.3)	2 (50.0)	-	-	-	-	-	-	**4 (8.0)**	**6 (10.5)**	**10 (9.3)**
Hypotensive reaction	4 (8.7)	1 (2.1)	5 (5.4)	-	1 (33.3)	1 (25.0)	-	-	-	-	-	-	**4 (8.0)**	**2 (3.5)**	**6 (5.6)**
Hypertensive reaction	-	1 (2.1)	1 (1.1)	-	-	-	-	-	-	-	-	-	**-**	**1 (1.8)**	**1 (0.9)**
Aseptic meningitis	6 (13.0)	2 (4.3)	8 (8.6)	-	-	-	-	-	-	-	-	-	**6 (12.0)**	**2 (3.5)**	**8 (7.5)**
Atypical pain	-	1 (2.1)	1 (1.1)	-	-	-	-	-	-	-	-	-	**-**	**1 (1.8)**	**1 (0.9)**
Development of factor VIII inhibitors	-	-	-	-	-	-	-	-	-	-	4 (66.7)	4 (50.0)	**-**	**4 (7.0)**	**4 (3.7)**
Neutropenia	1 (2.2)	1 (2.1)	2 (2.2)	-	-	-	-	-	-	-	-	-	**1 (2.0)**	**1 (1.8)**	**2 (1.9)**
Thrombotic event	2 (4.3)	2 (4.3)	4 (4.3)	-	-	-	-	-	-	1 (50.0)	1 (16.7)	2 (25.0)	**3 (6.0)**	**3 (5.3)**	**6 (5.6)**

Table 16 *(continued)*

Diagnosis of ATEs related to plasma derivatives and recombinant products in 2004 and 2005

Type of adverse transfusion event	IVIg			Albumin			Anti-D			Other*			All products		
	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)	2004 N (%)	2005 N (%)	Total N (%)
Unknown	1 (2.2)	1 (2.1)	2 (2.2)	-	-	-	-	-	-	-	-	-	**1 (2.0)**	**1 (1.8)**	**2 (1.9)**
Total	**46**	**47**	**93**	**1**	**3**	**4**	**1**	**1**	**2**	**2**	**6**	**8**	**50**	**57**	**107**

*Includes events related to Factor VII (1), anti- CMV Ig (1), Factor VIII (4)

3.4 Deaths

The 13 deaths associated with transfusion are described in Table 17. Eleven (84.6%) were related to the transfusion of blood components and two (15.4%) to plasma derivatives. TRALI was the leading cause of death, representing 45.5% of deaths related to blood components and 38.5% of all transfusion-related deaths. Red blood cells were implicated in four TRALI deaths and plasma in the other one. TACO was the second cause of transfusion-associated deaths. There was one death due to bacterial contamination of a platelet product with *Serratia Marcesens*. It is important to note that there were no deaths associated with incompatible transfusions.

One death was attributed to hemochromatosis. It is not possible to attribute this death to a specific product transfused in the 2004-2005 period because this complication arises from multiple red cell transfusions over a prolonged period of time.

A death related to the administration of anti-D was the result of acute hemolysis secondary to an overdose. The overdose was due to the incorrect calculation of the dosage to be administered. The other death associated with plasma derivative was a case of a thrombotic event related to the administration of recombinant factor VIIa.

Table 17

Relationship of transfusion to deaths by blood product and type of adverse transfusion reaction, 2004-2005

	Possible		Probable		Definite		Total	
	N	%[1]	N	%[1]	N	%[1]	N	%
Blood components								
Bacterial contamination	-	-	-	-	1	100.0	**1**	**7.7**
TACO	3	100.0	-	-	-	-	**3**	**23.1**
Hemolytic reaction: delayed	1	100.0	-	-	-	-	**1**	**7.7**
TRALI	2	40.0	1	20.0	2	40.0	**5**	**38.5**
Plasma derivatives and recombinant products								
Hemolytic reaction: acute	-	-	-	-	1	100.0	**1**	**7.7**
Thrombotic event	1	100.0	-	-	-	-	**1**	**7.7**
Total	**7**	**53.8**	**2**[2]	**15.4**	**4**	**30.8**	**13**[2]	**100.0**

[1] percentage within row

[2] includes the hemochromatosis case mentioned above

The overall incidence of death for blood components was roughly one in 200,000 units transfused (Table 18). Incidence for apheresis platelets was higher at approximately one in 70,000 units. The case of hemochromatosis was removed from incidence calculations because it was the consequence of transfusions having occurred throughout the life of the recipient.

Table 18

Incidence of deaths by type of adverse transfusion event, 2004-2005

Type of adverse transfusion event	Red blood cells (1,168,885)		Apheresis platelets (69,704)		Plasma (316,461)		All components[1] (2,078,935)	
	N	Incidence	N	Incidence	N	Incidence	N	Incidence
Bacterial contamination	-	-	1	1:69,704	-	-	**1**	**1:2,078,935**
TACO	2	1:584,442	-	-	1	1:316,461	**3**	**1:692,978**
Hemolytic reaction: delayed	1	1:1,168,885	-	-	-	-	**1**	**1:2,078,935**
TRALI	4	1:292,221	-	-	1	1:316,461	**5**	**1:415,787**
Total	**7**	**1:166,984**	**1**	**1:69,704**	**2**	**1:158,230**	**10[2]**	**1:207,894**

[1] includes WBDP, buffy coat, cryoprecipitate, whole blood, granulocytes in addition to red blood cells, apheresis platelets, and plasma
[2] does not include hemochromatosis case

4 Discussion

TTISS is now well implemented in Canada, covering 70% of the transfusion activity in the country. The 2004-2005 TTISS Program Report is a better reflection of the adverse transfusion events reported in Canada than the previous report of 2002-2003. This can be partly attributed to increased participation in TTISS and because the analysis has included cases that were reported to CBS and MHPD by hospitals not participating in TTISS.

4.1 Data quality

TTISS has continued to apply strict criteria for accepting cases and therefore 405 cases were excluded from analysis. These events were mainly cases that were not to be reported to TTISS because they were minor events such as delayed serological reactions, febrile reactions or minor allergic reactions. There were also some cases not meeting standard definitions or cases that were transferred to PHAC with a substantial amount of missing information.

Overall, the quality of data has improved. There was a slight reduction in the proportion of excluded cases, from 42.2% in 2002-2003 to 38.3% in 2004-2005. For some variables such as the outcome of reaction, there was a two-fold reduction in the proportion of missing information. However, there is continued need for improvement. For example, the cause of AHTR was missing in more than half of the cases reported. Timeliness of data reporting continues to be a limitation of the current system. The delay between completion of an ATE investigation at a hospital site, data entry, and subsequent reporting of the event to PHAC often requires at least 6 months. This issue will be partly addressed with the movement of TTISS to a secure web-based reporting system in 2008.

4.2 Severity of adverse transfusion events and deaths

The severity of cases reported to TTISS in 2004-2005 has decreased compared to the period 2002-2003, which can be explained by a change in the reporting criteria for some ATEs. Now all cases of TACO and DHTR are to be reported, but for the 2002-2003 period, only the most severe cases of these two types of reactions were to be reported. There were 13 deaths possibly, probably or definitely associated with transfusion of blood components as well as plasma derivatives, representing 1.4% of all reported ATEs included in the analysis for the 2004-2005 period. Transfusion was only one of the contributing factors to the death of recipients in more than half of these cases. Death was classified as “Definitely” related to transfusion in only 4 of the 13 cases.

4.3 Bacterial contamination, ABO incompatibilities, and other reactions

The incidence of bacterial contaminations has continued to decline being ten-fold less in 2005 compared to 2002 (0.3 vs. 3.7 per 100,000 units respectively). Implementation of preventive measures by blood manufacturers such as diversion pouches at blood collection and bacterial detection tests for platelet products has contributed to this encouraging result.

There was also two-fold decrease in incidence of ABO mistransfusions from 2002 to 2005 (1.5 vs. 0.7 per 100,000 units). This also represents a significant improvement in transfusion safety in Canada. It has been demonstrated in the province of Quebec that computerization of blood banks together with inter-hospital consultation of patient transfusion history was in part responsible for this reduction in the incidence of ABO mistransfusions. The increase in incidence of hypotensive reactions, especially in 2005, might be due to an increase awareness of this type of reaction by the transfusion community.

4.4 TRALI

The apparent reduction in the incidence of TRALI in 2004-2005 compared with 2002-2003 period is probably explained by the use of a new and more restrictive definition of TRALI (the Canadian TRALI consensus definition) for validating the cases. The incidence figures for the 2004-2005 period represents probably an underestimation of TRALI incidence because many cases were reported to CBS by hospitals not participating in TTISS, as was the case for the previous period, therefore they were not included in incidence calculations.

4.5 TACO, DHTR, and PTP

The impressive rise in incidence of TACO is attributable to new reporting criteria for this reaction. As previously mentioned, all cases, irrespective of severity, are now to be reported compared to only the most severe cases reported previously. The same applies to explain the rise in incidence of DHTR. The high incidence of PTP seen in 2003 (1.2 per 100,000 units) was only due to random fluctuations in rates of rare events since no cases were reported in 2004 and incidence was back to 0.2 per 100,000 units in 2005, the same as in 2002.

4.6 Severe/anaphylactic/anaphylactoid reaction

The two-fold decrease in incidence of severe allergic reactions in 2004-2005 compared to 2002-2003 period is lacking a definitive explanation. There was no change in reporting criteria nor in definition of this reaction. The modification of the manufacturing process of platelets by CBS, from platelet-rich plasma to buffy coat process, could not explain this reduction. The buffy coat process was applied in only one of the 13 CBS centres as a pilot project during that period and the reduction in incidence was across all types of components.

Rates of severe allergic reactions were calculated using only reports from three provinces in 2002-2003 since very few cases of allergic reactions were reported by the other provinces. In contrast, all cases from participating provinces and territories were used for the calculation for the 2004-2005 period. Thus, the observed decreased rate may be due to a bigger denominator being used in the calculation.

4.7 Plasma derivatives

Data for plasma derivatives was enriched by consolidating TTISS cases with ATEs reported to MHPD of Health Canada. Forty-two percent of cases in 2004 and 39% in 2005 were reported to MHPD by sources that are not part of TTISS. Nearly 90% of ATEs were related to the administration of IVIg. It is important to note that 24 hemolytic reactions were associated with that product for the two-year period. This represents a major increase of that type of reaction that was only rarely reported before and almost all occurred in patients of blood group A. It has been mostly associated with one type of IVIg product (Gamunex), which was authorized for marketing in Canada at the end of 2003.

4.8 Conclusion

In summary, TTISS has continued to be implemented across Canada in 2004-2005 with an increase in hospital participation. This additional participation has resulted in an increase in the number of reported cases. The analysis of the TTISS data has allowed invaluable information to be gathered on trends of blood transfusion associated adverse events in Canada.