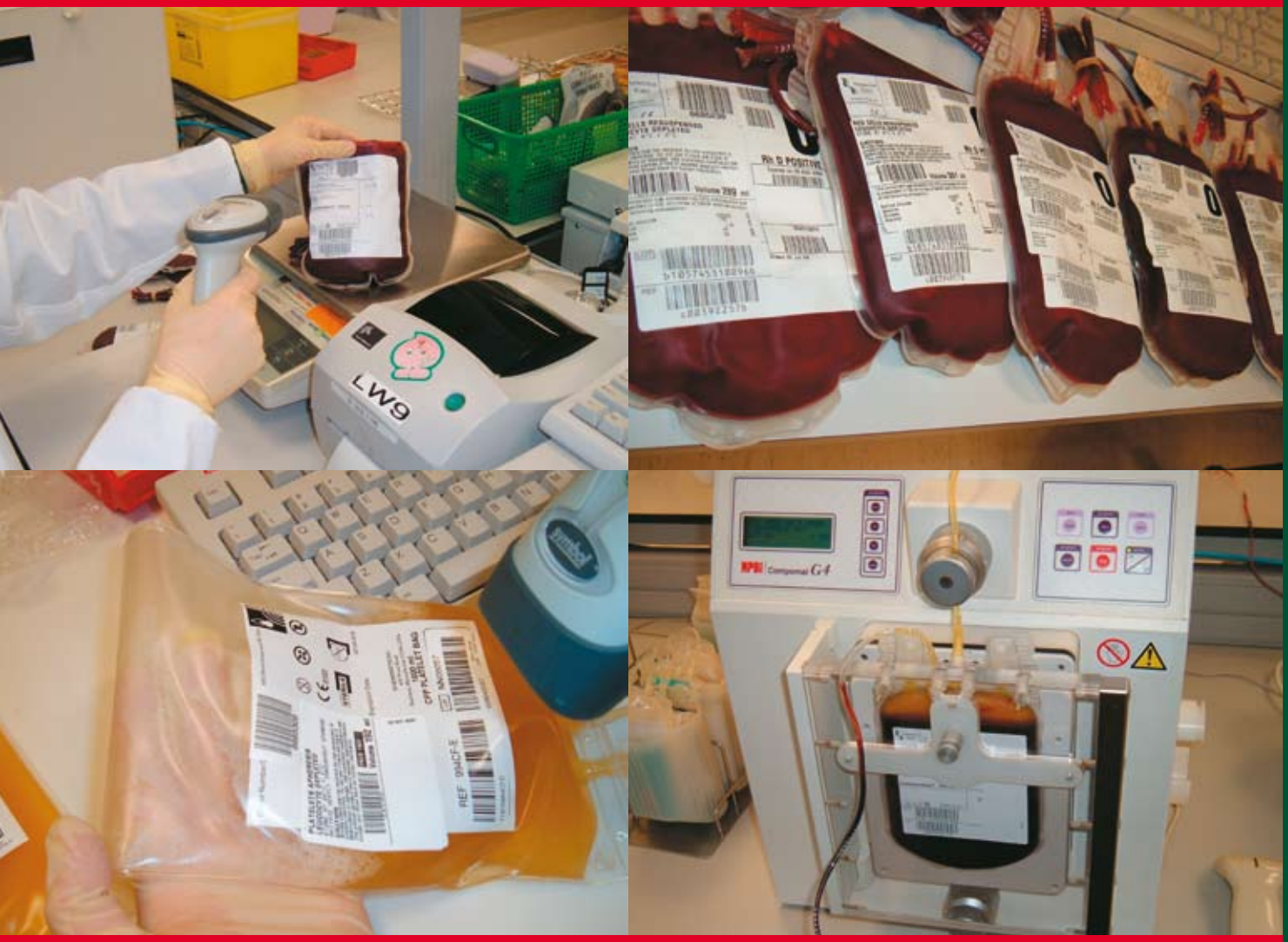
NZBLOOD
Te Ratonga Toto O Aotearoa

National Haemovigilance Programme



Annual Report 2007

Produced June 2008

By

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Abbreviations

BNP	Brain Natriuretic Peptide
CAG	Clinical Advisory Group
DAT	Direct Antiglobulin Test
DHB	District Health Board
DHTR	Delayed Haemolytic Transfusion Reaction
FFP	Fresh Frozen Plasma
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HLA	Human Leucocyte Antigen
HNA	Human Neutrophil Antigen
HTLV	Human T Cell Lymphotrophic Virus
IBCT	Incorrect Blood Component Transfused
LDH	Lactate Dehydrogenase
NAT	Nucleic Acid Amplification Test
NHFTR	Non-Haemolytic Febrile Transfusion Reaction
NZBS	New Zealand Blood Service
PTP	Post-Transfusion Purpura
TACO	Transfusion Associated Circulatory Overload
TA-GVHD	Transfusion Associated Graft Versus Host Disease
TRALI	Transfusion-Related Acute Lung Injury
TTI	Transfusion Transmitted Infection

Foreword

This is the third annual Haemovigilance report for New Zealand. The system continues to work well with all major District Health Boards and private hospitals reporting adverse events and reactions. The ability to produce a report of this type requires the support of many individuals, including doctors, nurses and laboratory staff involved in the delivery of transfusion to patients. NZBS is very appreciative of the time and effort that these individuals have given to ensure the success of the scheme.

Management of the scheme was transferred from Auckland to Wellington at the end of 2007. The decision to change arose from the resignation of Simon Benson who was responsible for the set up and initial management of the Haemovigilance Programme. Dr Dorothy Dinesh and John Dagger have taken over the reins successfully in Wellington and were responsible for the production of the current report. The indications are that the change has been successful and this bodes well for the future development of the scheme.

Data obtained from haemovigilance activities should be used to further improve the overall safety of transfusion and to monitor the impact of changes as they are implemented. Transfusion Related Acute Lung Injury (TRALI) has been identified as a significant cause of transfusion related morbidity and mortality with 9-10 cases reported in New Zealand each year. Early in 2008, NZBS introduced a programme of 'male only' Fresh Frozen Plasma. A similar initiative in the United Kingdom lead to a significant reduction in both the frequency and severity of TRALI reports. The Haemovigilance Programme provides a mechanism to monitor the impact of the intervention here in New Zealand and is a good example of the benefits of this type of activity.

I hope that you will find the report informative and look forward to your ongoing support of the National Haemovigilance Programme.

Dr Peter Flanagan
NZBS National Medical Director

Introduction

Blood transfusion therapy is a well-established component of modern medicine. Health care workers have a professional responsibility to report any adverse events related to transfusion, as they can impact on the safety and well-being of blood product recipients.

The New Zealand Blood Service (NZBS) has adopted the Council of Europe definition of haemovigilance: *"the organised surveillance procedures related to serious or unexpected events or reactions in donors or recipients and the epidemiological follow up of donors".*[1]

The National Haemovigilance Programme was established in New Zealand in May 2005. NZBS is obliged to monitor the occurrence of adverse events at all stages of the vein-to-vein transfusion process.

Figure 1.1 > The Transfusion Chain

Any failure in the chain of events has the potential to cause significant harm to donors or patients. Such events include donor incidents, specimen labelling errors, blood bank errors, bedside checking errors and transfusion reactions. All New Zealand blood banks participate in the programme, reporting any transfusion-related adverse events experienced by patients in the hospitals they serve. Appendix 1 shows the flowchart for reporting transfusion related adverse events.

The NZBS complies with national privacy legislation. No patient or clinician names are entered into the haemovigilance database and all haemovigilance reports are stored in a secure location. This is important in promoting a no-blame culture for reporting adverse events related to transfusion.

The purpose of this report is to provide information that will help health professionals to better understand the current risks associated with transfusion and thus assist to communicate these to potential recipients of blood products. The Haemovigilance Programme also provides a means for identifying emerging trends in hazards of blood transfusion.

Haemovigilance is a quality assurance activity that will allow us to identify where errors occur in the chain of transfusion events so that we can focus on strategies to improve the overall safety of the transfusion process.

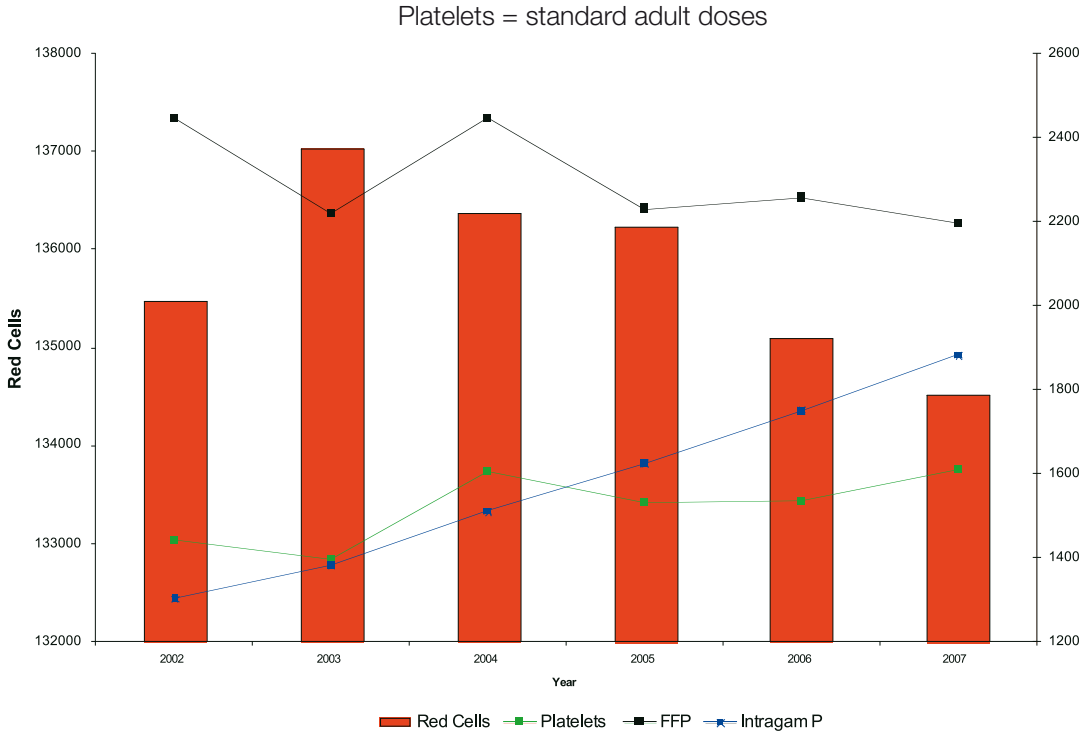
2 Trends in Blood Product use in New Zealand

Blood components are produced from individual donations by voluntary blood donors and include red cells, platelet concentrates, fresh frozen plasma (FFP) and cryoprecipitate. Plasma derivatives are manufactured from large pools of New Zealand plasma by CSL Bioplasma in Melbourne, Australia. Plasma is derived from whole blood donations or plasmapheresis, an automated procedure where plasma is collected from a donor using an apheresis machine. Platelet concentrates are produced by pooling buffy coats from four whole blood donations or collected by apheresis (plateletpheresis), which can yield up to two adult doses per procedure. Cryoprecipitate is produced from apheresis plasma from donors with suitable fibrinogen levels. Pre-storage leucodepletion of all blood components was implemented in July 2001 in New Zealand. White blood cells are removed by a filtration process. This reduces the frequency of febrile transfusion reactions. Other benefits of leucodepletion include reduction in the risk of transmission of cytomegalovirus, less HLA alloimmunisation and possible reduction in the risk of transmission of variant Creutzfeld-Jakob disease.

The NZBS utilises a national blood management system, Progesa. All blood donations in New Zealand are managed through Progesa and most blood banks also use this system. We can extract data from Progesa to provide information on blood product usage.

The overall demand for blood components remains stable, as shown in Figure 2.1. However, Intragam P use continues to rise with a 7% increase compared to 2006.

Figure 2.1 > Total Annual Blood Component & Intragam P Issues



Intragam P = 12g/200ml units

2 Trends in Blood Product use in New Zealand continued

Table 2.1 shows the total numbers of units of individual blood components transfused in 2006 and 2007.

Table 2.1 > Transfused Blood Components for 2007 and 2006

Component	Number Transfused in 2007	Number Transfused in 2006	% increase
Red cells	118,751	117,688	0.9
Platelets - apheresis	6,762	6,758	0.1
Platelets - pooled	4,749	4,657	2.0
Fresh frozen plasma	19,956	20,619	-3.2
Cryoprecipitate	1,991	1,847	7.8
Cryodepleted plasma	927	690	34.3
Total	153,136	152,259	0.6

Overall, the number of red cell units transfused to patients in 2007 was slightly higher than 2006. It is interesting to note that this has occurred in a period when overall issues of red cell components to DHBs has reduced (Fig 2.1). This reflects the considerable efforts by both NZBS and the DHBs during the year to improve the overall efficiency of the supply chain.

The number of patients receiving blood components during 2007 is shown in Table 2.2. In 2007, 27,028 patients were transfused with red cells, 3,245 received platelets and 4,686 patients received FFP. Overall 38,392 individuals received a blood product (includes blood components and plasma derivatives) in 2007; this represents approximately 1% of the New Zealand population. The demographic profile of transfusion recipients is similar to that in the previous year with a slight preponderance of females and includes recipients of all ages.

Table 2.2 > Blood Component Recipients 2007

		Red cells	Platelets	FFP
Gender of recipients	Female	15,332	1,251	1,890
	Male	11,622	1,993	2,788
	Unknown	74	1	8
	Total	**27,028**	**3,245**	**4,686**
Age of recipients (years)	Mean	61	45	55
	Median	68	51	65
	Minimum	0	0	0
	Maximum	108	99	98
Units transfused per recipent	Mean	5.4	3.7	4.5
	Median	3	2	2
	Minimum	1	1	1
	Maximum	106	87	267

3 Overview of Notifications for 2007

Adverse transfusion reactions are notified to hospital blood banks using the NZBS Notification and Investigation of Adverse Transfusion Reaction form which was developed in 2001 (Appendix 2). The form provides guidelines on the management of adverse transfusion reactions. Some hospitals use locally-developed forms. A Transfusion-Related Adverse Event Notification Form (Appendix 3) is completed and sent to the National Haemovigilance Office. Further specific information may be requested from the blood bank where indicated. Late in 2007 imputability assessment was incorporated into the notification form (Appendix 3). The imputability assessment (0 - 3) rates how likely it is that the event was caused by the transfusion. A score of 0 is given when the evidence is in favour of attributing the event to cause(s) other than blood transfusion; a score of 3 is given when there is conclusive evidence beyond reasonable doubt for attributing the event to blood transfusion.

Adverse events relating to plasma derivatives are reported on a separate form and reviewed separately. Report summaries are sent to the manufacturer and also periodically to the regulator Medsafe (New Zealand Medicines and Safety Devices Authority).

A total of 455 events involving 419 patients were reported to the National Haemovigilance Programme in 2007. This is an 8% increase from 2006 where a total of 420 events involving 385 recipients were reported. This may reflect improved reporting rather than a true increase in the rate of adverse events. One patient had five events reported during 2007. Table 3.1 shows the number of reported events per patient.

Table 3.1 > Number of Reported Events per Patient 2007

	1 report	2 reports	3 reports	5 reports	Total
Number of Patients	391	21	6	1*	419

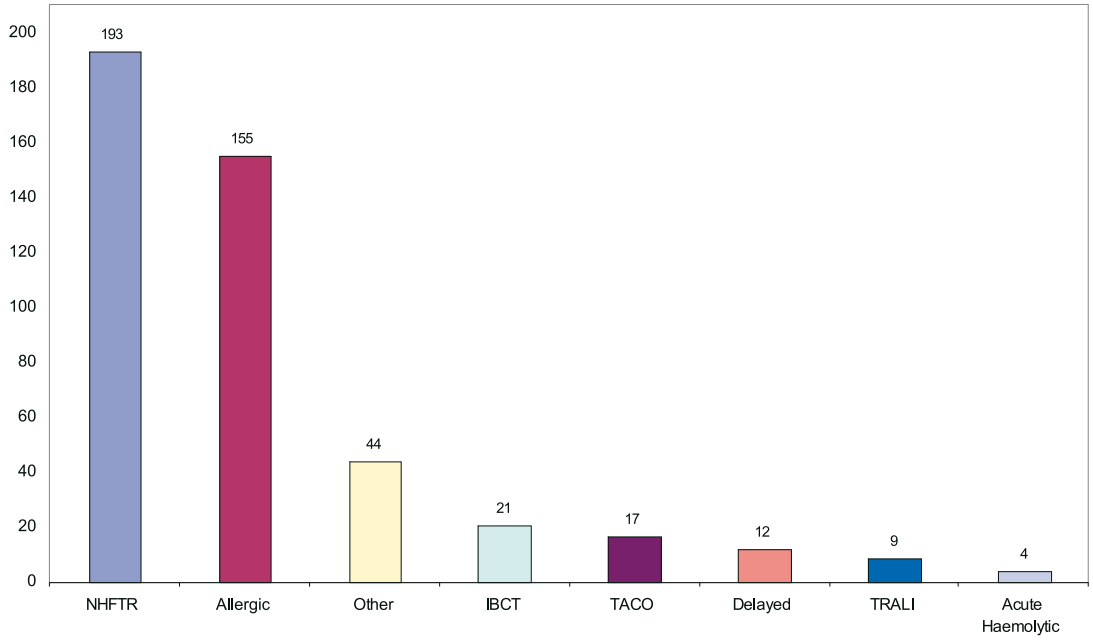
**incorrect blood component transfused, same error occurred on 5 occasions*

Breakdown of 2007 Reported Events

Figure 3.1 shows the types of events reported for 2007. The most frequently reported event was non-haemolytic febrile transfusion reaction (NHFTR) followed by allergic reactions. There were no reports of transfusion-transmitted infection (TTI), transfusion-associated graft versus host disease (TA-GVHD) or post-transfusion purpura (PTP) in 2007.

3 Overview of Notifications for 2007 continued

Figure 3.1 > Events Reported in 2007 by type (n=455)

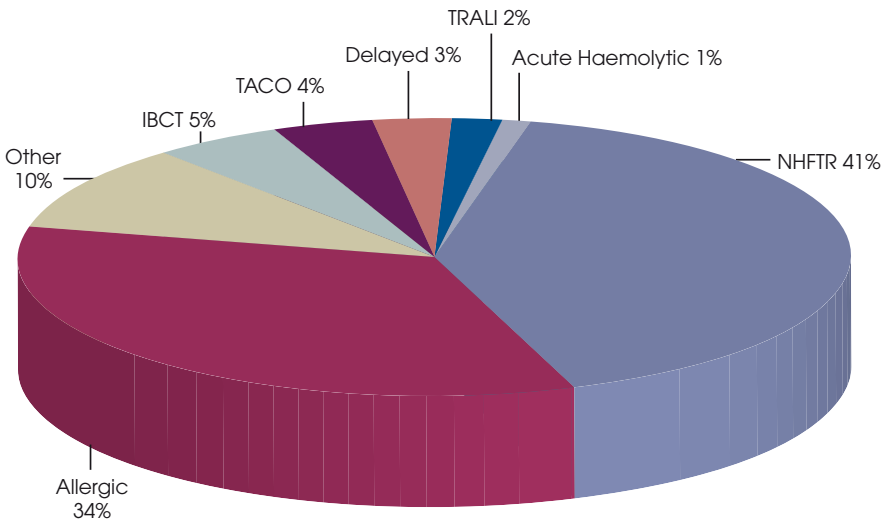


Key:

NHFTR:	*Non-haemolytic febrile transfusion reactions*
Allergic:	*Allergic reactions*
IBCT:	*Incorrect blood component transfused*
TACO:	*Transfusion-associated circulatory overload*
Delayed:	*Delayed haemolytic transfusion reactions*
TRALI:	*Transfusion-related acute lung injury*
Acute Haemolytic:	*Acute haemolytic and other severe acute reactions*

Figure 3.2 shows the type of event as a percentage of all reported events. The breakdown of event type by percentage is very similar to that from 2006.

Figure 3.2 > Type of Event as Percentage of Events for 2007 (n=455)



Reported Events by Region

There are 21 District Health Boards (DHBs) in New Zealand that are responsible for providing health care services for specific geographical areas (Figure 3.3). Some DHBs have several hospitals in their region.

Figure 3.3 > Map of New Zealand showing DHB Regions

Table 3.2 shows the origin of reports for 2007 by DHB and the rate of events per 10,000 components transfused, in descending order of frequency. Three DHBs did not report any events in 2007. This may reflect variation in the reporting rates or simply be a consequence of the low level of blood component transfusion in some DHBs.

Table 3.2 > Origin of Reports for 2007

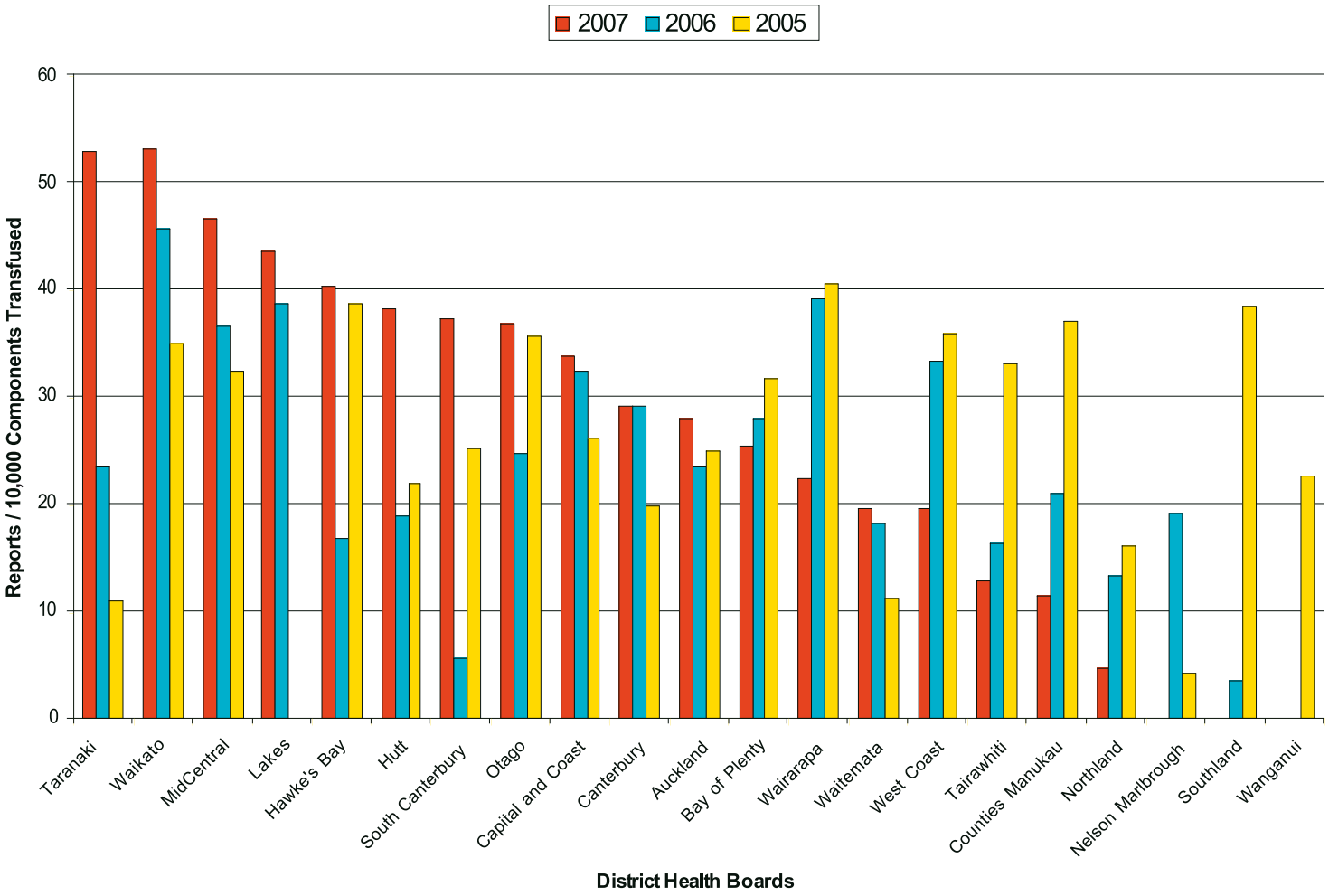
District Health Board	Reported Adverse Events 2007 (n=455)	Components Transfused *	Events/10,000 Components Transfused
Taranaki	17	3,211	53
Waikato	88	16,547	53
MidCentral	32	6,866	47
Lakes	10	2,288	44
Hawke's Bay	18	4,441	41
Hutt	14	3,653	38
South Canterbury	4	1,068	37
Otago	25	6,751	37
Capital and Coast	54	15,958	34
Canterbury	46	15,711	29
Auckland	88	31,286	28
Bay of Plenty	17	6,678	25
Wairarapa	3	1,336	22
Waitemata	20	10,171	20
West Coast	1	511	20
Tairawhiti	2	1,552	13
Counties Manukau	14	12,224	11
Northland	2	4,220	5
Nelson Marlborough	0	3,922	0
Southland	0	2,519	0
Wanganui	0	1,327	0

** Red cells, Platelets, FFP, Cryodepleted plasma, Cryoprecipitate*

3 Overview of Notifications for 2007 continued

Figure 3.4 shows the annual rate of reported events per 10,000 components transfused for each DHB since the Haemovigilance Programme commenced in May 2005. The 2005 data spans an 8 month period. The graph shows that the reporting rate has increased in some DHBs and decreased in others.

Figure 3.4 > Reported Events per 10,000 Transfusions 2005 - 2007



Type of Blood Component Associated with Adverse Events

Transfusion related adverse events are more frequently reported with platelet and plasma transfusions than red cell transfusions. Table 3.4 shows the rate of reported events by component type. The overall rate of an adverse event related to transfusion of a blood component is 1 in 317 units transfused.

Table 3.4 > Reported Events by Component Type

Component	Number Transfused	No. Events*	Frequency	Per 10,000 units Transfused
Red Cells	118,751	308	1:386	26
Platelets - apheresis	6,762	55	1:123	81
Platelets - pooled	4,749	25	1:190	53
FFP	19,956	85	1:235	43
Cryoprecipitate	1,991	5	1:398	25
Cryodepleted plasma	927	5	1:185	54

** Includes events where multiple component types transfused*

Of the 455 events reported, 425 involved the transfusion of one type of blood component. Table 3.5 provides information on the nature of event by blood component type for 2007.

Table 3.5 > Nature of Event by Blood Component Type 2007

	Red Cells	Platelets Apheresis	Platelets Pooled	FFP	Cryoprecipitate	Cryodepleted Plasma	Other	Multiple Components*
Acute Haemolytic	3	1						
Allergic	53	24	12	46		5	1	13
Delayed Reaction	10							2
IBCT	6	4		1			9	
NHFTR	160	13	3	10	1		1	8
Other	34	4		1	1			3
TACO	13			1				3
TRALI	3			5				1
All (n = 455)	**282**	**46**	**15**	**64**	**2**	**5**	**11**	**30**

**Events may include transfusions of both blood components and plasma derivatives*

Overview of Notifications for 2007 continued

Profile of Recipients with Reported Adverse Events

246 of the 455 reported events involved female recipients and 209 involved males. Figure 3.5 demonstrates the age distribution and gender of the recipients as a percentage of total reported events for 2007. This probably represents the overall profile of transfusion recipients, with a peak in the 61 - 80 year old group and a substantially higher number of females in the 21 - 40 year age band, due to the obstetric-related transfusions.

Figure 3.5 > Age and Sex of Recipients with Adverse Events

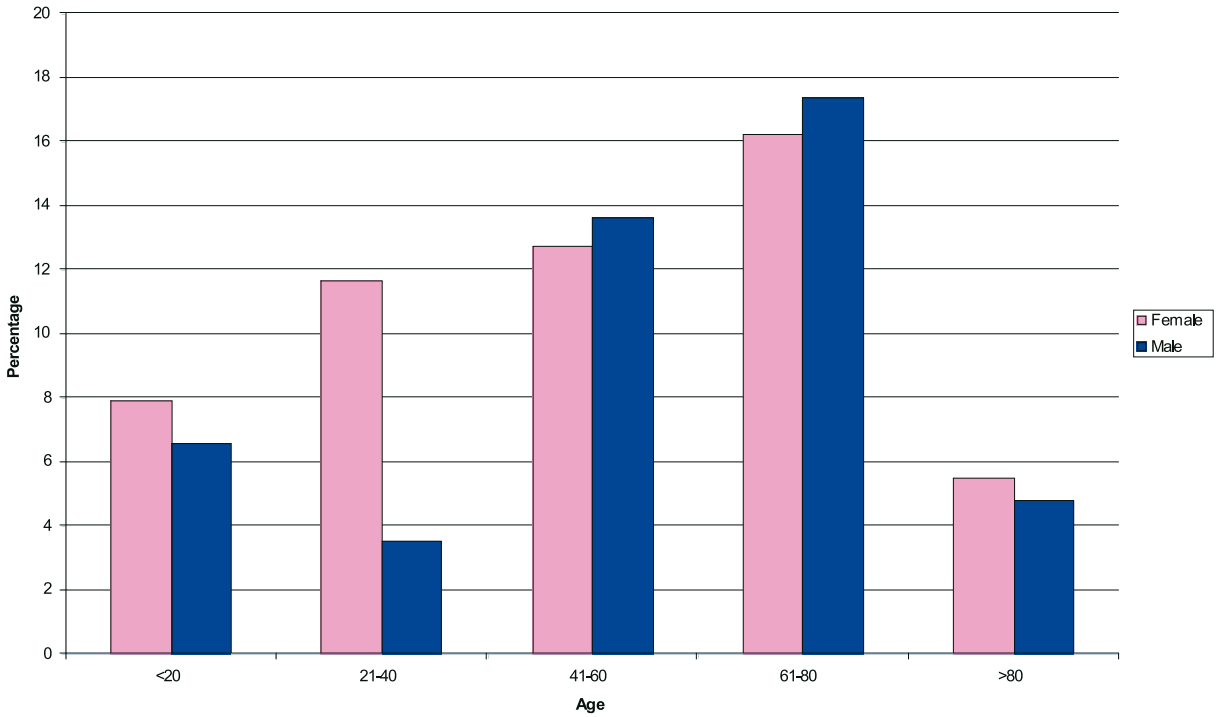


Table 3.6 shows that platelet transfusion recipients have the highest rate of reported adverse events, followed by plasma transfusion, then red cells.

Table 3.6 > Adverse Events per Recipient for Various Blood Components

Component	Recipients	No. Events	Frequency	Per 1,000 Recipients
Red Cells	27,028	308	1:88	11
Platelets	3,245	80	1:41	25
FFP	4,686	85	1:55	18

Overall 1 in 78 recipients (of red cells, platelets or plasma) in 2007 had an adverse event reported. Table 3.7 shows the frequency of the specific types of adverse events reported in recipients for 2007.

Table 3.7 > Adverse Events in Transfusion Recipients 2007

Event	Number	Frequency 2007
Acute Haemolytic	4	1:8,740
Allergic	155	1:226
Delayed transfusion reaction	12	1:2,913
IBCT *	15	1:2,330
NHFTR	193	1:181
TACO	17	1:2,056
TRALI	9	1:3,884
Other	44	1:795
All	449	1:78

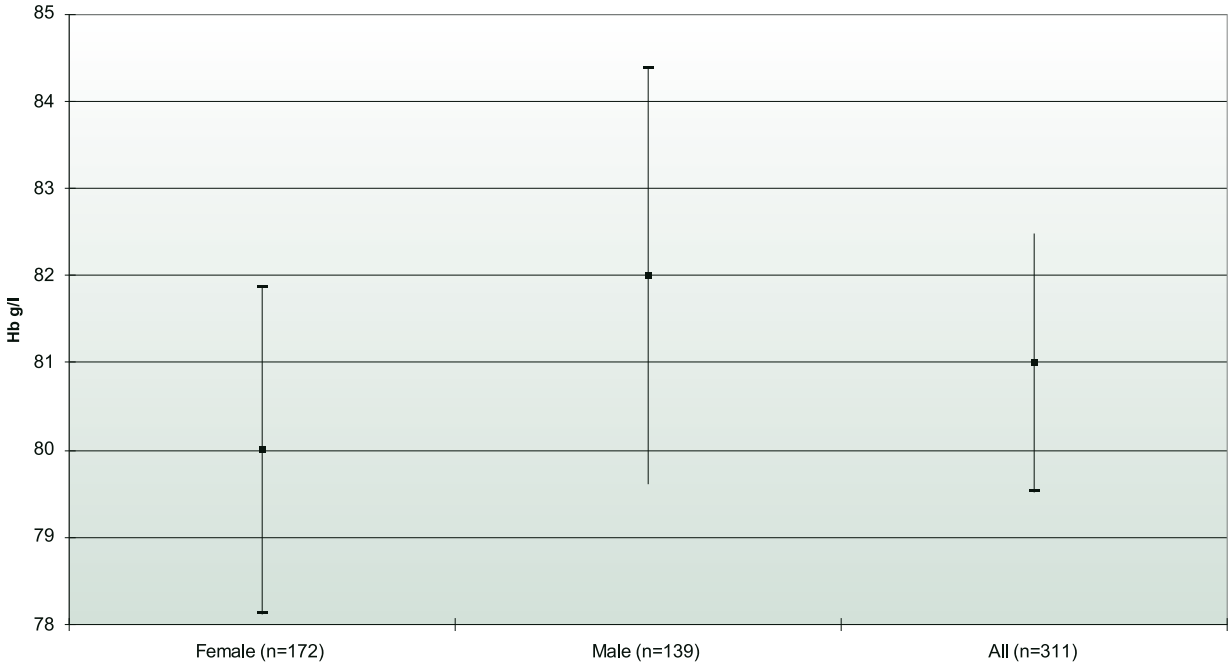
**excludes 6 IBCTs relating to Rh D Immunoglobulin*

Pre-transfusion Haemoglobin Levels

Haemoglobin values were provided in 311 of the reports in 2007. Figure 3.6 shows the mean pre-transfusion haemoglobin was 81g/L with a slightly lower mean in female transfusion recipients. The minimum pre-transfusion haemoglobin level was 35g/L and the maximum 143g/L. The data includes pre-operative haemoglobin values in the setting of elective surgery in some patients (i.e. not used in decision to transfuse). Improvements in data entry will enable a more meaningful assessment of pre-transfusion haemoglobin levels in the future. The haemoglobin provides a crude indicator of the appropriateness of red cell transfusion. The data suggests that most transfusions were appropriate.

Figure 3.6 > Mean Pre-transfusion Haemoglobin Values

(95% confidence intervals)



4 Non-Haemolytic Febrile Transfusion Reactions (NHFTRs)

- **Mild NHFTR:** fever < 38.5°C or an increase of < 1.5°C from pre-transfusion value without any symptoms
- **Moderate/severe NHFTR:** fever ⩾ 38.5°C or an increase of ⩾ 1.5°C from the pre-transfusion value plus one or more of the following: chills, cold, rigor, headache, nausea/vomiting
- Within 4 hours of completing transfusion
- Reaction not due to a haemolytic transfusion reaction or bacterial infection

NHFTRs are thought to be mediated by cytokines in blood components or HLA antibodies in the recipient. Although not life-threatening, reactions can be dramatic and create considerable apprehension in patients. Symptoms are non-specific and can also be caused by underlying comorbidity such as sepsis or malignancy. Units associated with febrile reactions should be returned to the blood bank and sent for microbiological testing.

In 2007 there were 193 (79 mild and 114 moderate/severe) reports of NHFTR. It is the most frequently reported type of transfusion-related adverse event with similar rates for males and females (98 & 95 respectively), with a mean recipient age of 59 years (range 1 month - 94 years).

Table 4.1 shows the imputability scores for NHFTRs in 2007. Ideally imputability scores should be completed by the treating clinician as they will be aware of pre-existing underlying conditions that may cause fever and thus exclude the diagnosis of a NHFTR.

Table 4.1 > Imputability Scores for NHFTRs 2007

		Number of Events	
	Imputability Scale	Mild	Moderate / Severe
	Not Reported / Unknown	30	38
0	Excluded/Unlikely	6	3
1	Possible	21	30
2	Likely, probable	21	38
3	Certain	1	5
	Total	**79**	**114**

Hypertension (a rise in the systolic blood pressure by > 30mmHg from the baseline recording) has been observed to occur concurrently with a number of NHFTRs. In 2007 26 (13%) of the 193 NHFTRs were associated with hypertension, with a higher frequency in females. Table 4.2 shows the mean and median blood pressure and temperature increments in these patients.

Table 4.2 > NHFTR and Hypertension

		Systolic Blood Pressure increase (mmHg)		Temperature Increase (°C)	
	Number	Mean	Median	Mean	Median
Female	18	52	52	1.8	1.7
Male	8	76	58	2.0	1.9
All	26	63	54	1.9	1.8

Further investigation of the association of hypertension and febrile transfusion reactions is planned.

5 Allergic Reactions

- **Allergic Reaction:** rash, urticaria, generalised pruritus, dyspnoea, stridor, wheeze, cyanosis or angioedema during or within 4 hours of transfusion
- **Anaphylactoid/Anaphylactic Reaction:** allergic reaction with hypotension (drop in systolic blood pressure by ⩾ 30mmHg)

Allergic reactions are the second most frequently reported type of adverse event after NHFTR, accounting for 155 (34%) of reports in 2007. There were 133 allergic reactions and 22 anaphylactoid/anaphylactic reactions.

The number of allergic reactions reported was higher in female recipients (90) than in male recipients (65). The youngest patient reported to have an allergic reaction was 2 years old and the oldest, was 91 years.

Adverse events associated with transfusion do not always fit neatly within single categories in the current classification scheme. Nine patients in whom allergic reactions were reported in 2007 also had an increase in temperature and two patients had an increase in their blood pressure. Table 5.1 shows the imputability scores for allergic reactions reported in 2007.

Table 5.1 > Imputability Scores for Allergic Reactions 2007

	Imputability Scale	Number of Events	
		Allergic	Anaphylactic/ Anaphylactoid
	Not Reported/Unknown	51	2
NA	Not Assessable	1	1
0	Excluded/Unlikely	1	
1	Possible	12	7
2	Likely, probable	56	11
3	Certain	12	1

Case

Patient A had major abdominal surgery one week ago. She was on a heparin infusion. Coagulation test results were normal (APTT 24 seconds, INR 1.1). She developed peritonitis from a bowel perforation and urgent laparotomy was planned. 2 units of FFP were prescribed. Urticaria was reported after infusion of the first unit, at 15 minutes.

Learning point: the patient suffered a minor allergic reaction with FFP that was inappropriately prescribed; if the APTT had been prolonged and reversal of unfractionated heparin was indicated, protamine would be the appropriate reversing agent.

6 Transfusion Associated Circulatory Overload (TACO)

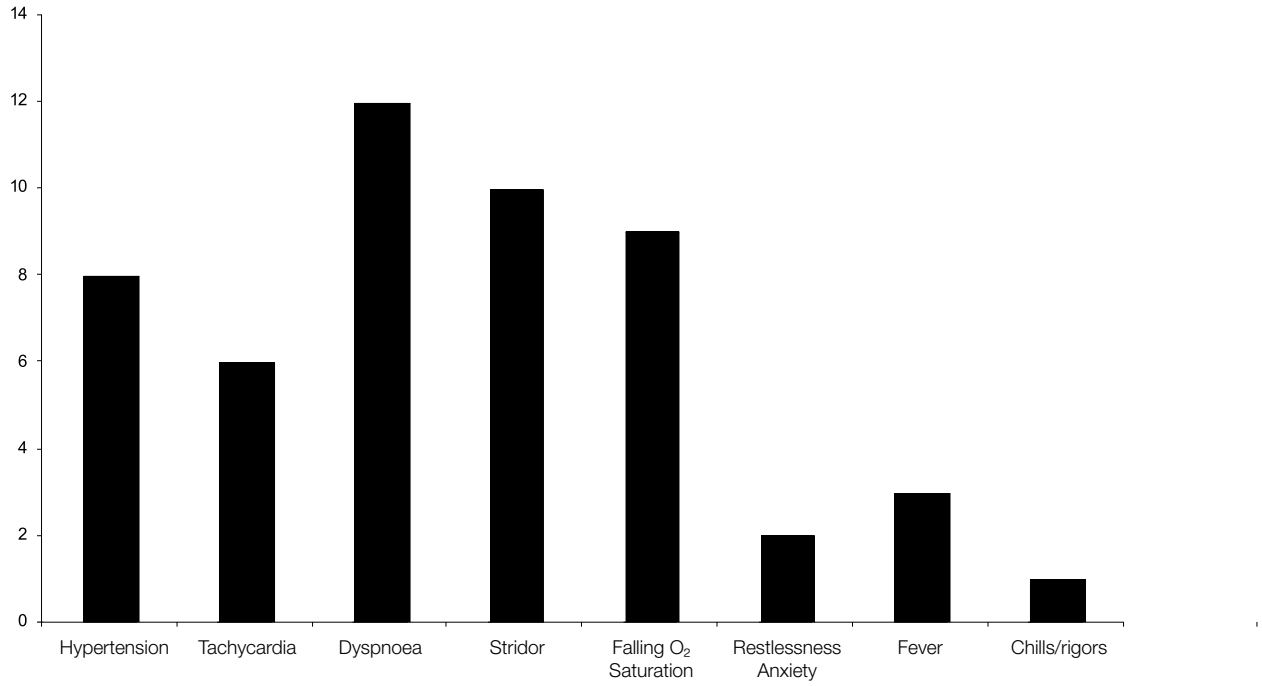
- TACO is characterised by respiratory distress, tachycardia and increased blood pressure within 12 hours of completion of the transfusion
- The diagnosis of TACO is supported by radiological signs of cardiogenic pulmonary oedema, a positive fluid balance and pre-existing cardiac dysfunction

There were 17 reports (4% of total events) of TACO in 2007, a greater than two-fold increase from the 7 cases reported in 2006. The cases involved 16 patients, 8 female and 8 male. All were adults and 14 were over the age of 60 years (range 33 - 95 years). Most cases were associated with red cell transfusion (Table 3.5). Seven patients had pre-existing cardiorespiratory disease, two had renal failure and two, cirrhosis.

Imputability scores were completed in 13 reports, 6 had a score of 1 (possible), 6 had a score of 2 (probable) and in one case the patient's symptoms were attributed to asthma and was scored 0 (unlikely). Outcome was reported in 14 cases: twelve patients recovered and two died although both deaths were unrelated to the transfusions.

Dyspnoea, stridor, falling O_2 saturation and hypertension were the most frequent clinical features observed (Figure 6.1)

Figure 6.1 > Clinical Features of TACO



Respiratory symptoms in the context of a transfusion may also be seen in TRALI and allergic reactions. Pulmonary oedema is a feature of both TACO and TRALI. Although reports did not include plasma BNP (brain natriuretic peptide) levels, this may be a useful marker to distinguish between these two syndromes.[2]

Transfusion-Related Acute Lung Injury (TRALI)

TRALI is non-cardiogenic pulmonary oedema that occurs within 6 six hours of a transfusion and is essentially a diagnosis of exclusion. The diagnostic criteria are based on clinical and radiological features rather than laboratory tests. The following criteria[3] are used to diagnose TRALI:

- Hypoxaemia: PaO_2/FiO_2 < 300 mmHg, or oxygen saturation <90% on room air
- bilateral infiltrates on frontal chest radiograph
- no evidence of left atrial hypertension (i.e. circulatory overload)
- no pre-existing acute lung injury before transfusion
- onset during or within 6 hours of transfusion
- no temporal relationship to an alternative risk factor for acute lung injury

Where there is an underlying risk factor for acute lung injury the diagnosis of TRALI is **possible** rather than **probable**. Risk factors for acute lung injury include aspiration, pneumonia, toxic inhalation, lung contusion, near drowning, severe sepsis, shock, multiple trauma, burn injury, acute pancreatitis, cardiopulmonary bypass and drug overdose.[3]

In 2007 there were nine reports of TRALI, compared with 10 in 2006. The patients were between 15 and 84 years of age and comprised 5 males and 4 females. Six patients were given an imputability score of 2 (probable) and the remaining three patients did not have imputability assessments completed.

Five patients were transfused FFP, three received red cell transfusions and one patient received both FFP and platelets (Table 3.5). Outcomes were reported in four cases; one patient recovered after six hours, two patients recovered after nine days and one patient died after five days.

The pathogenesis of TRALI in many cases can be explained by white cell antibodies in donor plasma causing leukoagglutination and capillary leak in the recipient's pulmonary microvasculature (immune TRALI). White cell antibodies are found more frequently in multiparous females. Using FFP from male donors only has led to a dramatic reduction of immune TRALI in the United Kingdom. A non-immune "two-hit" hypothesis for TRALI has also been proposed where the patient's underlying condition causes neutrophil priming (first hit) and substances in stored red cells or platelets lead to activation of pulmonary capillary endothelium (second hit).

Confirmed cases of TRALI are investigated by testing the donor for HLA (human leucocyte antigen) and HNA (human neutrophil antigen) antibodies. A donor is implicated if a positive white cell crossmatch between donor serum and recipient white blood cells is demonstrated or the donor antibody is specific to a recipient antigen.

7 Transfusion-Related Acute Lung Injury (TRALI) continued

Table 7.1 shows the results of investigations in six of the reported cases of TRALI. Investigations in some cases are incomplete as it can take months to complete following the event because donors have to be contacted and tested. In addition, some donors may not respond to requests for further testing.

Table 7.1 > TRALI Investigations (n = 6)

Case	Component (units transfused & donor gender)	Donor result	Donor outcome
1	FFP (7 female)	3 : class I HLA antibody positive	All 3 have history of pregnancy; retired from donating
		1: class II IgM reactive, significance uncertain	No history of transfusion or pregnancy; retired as precautionary measure
		3: negative HLA antibody	Reinstated
		All 7 negative for HNA antibody	
2	FFP (2 female, 1 male)	1 female tested: Class I HLA antibody positive	In progress
	Platelets apheresis (1 female)	Untested	
3	RBC (3 female, 1 male)	2: class I HLA antibody with specificity against recipient antigen	Both retired from donating
		1: negative HLA antibody	Reinstated
		Male donor untested	No action
4	FFP (1*)	positive class I & II HLA antibody	Retired
5	RBC (1*)	negative HLA & HNA antibody	Reinstated
6	FFP (5 female, 1 male)	3: negative HLA antibody (includes male)	In progress
		2: positive HLA antibody	
		1: untested	

**donor gender not provided*

The National Tissue Typing Laboratory investigated 10 cases of TRALI in 2007. One of these cases was not reported to the Haemovigilance Programme and occurred in a smaller hospital. One case was classified as an allergic reaction, one as TACO and one patient had pneunomia. This shows that TRALI may not always be easily recognised.

A review of TRALI investigations in New Zealand showed that 88% of cases involved donors with detectable HLA antibodies, of which 86% were female and FFP was the most frequent blood component implicated.[4]

Early in 2008 NZBS introduced the provision of male donor plasma only for transfusion of FFP. Although numbers are small it will be interesting to see if this reduces the number of TRALI reports.

8 Acute Haemolytic & Other Severe Acute Transfusion Reactions

Acute reactions occur within 24 hours following a transfusion. Features of a haemolytic transfusion reaction include:

- Fever, tachycardia, change in blood pressure, flank or back pain
- Inadequate rise in haemoglobin after transfusion or a drop in haemoglobin
- Rise in LDH, bilirubin
- Haemoglobinuria
- Decrease in haptoglobin

A haemolytic transfusion reaction is confirmed by a positive direct antiglobulin test (DAT) and a positive red cell crossmatch.

There were 4 reports of acute haemolytic or other severe acute reaction in 2007. No major ABO incompatible red cell transfusions were reported.

Patient B:

A 66 year old woman had lethargy and dyspnoea associated with a haemoglobin of 72g/L. Several minutes after starting a red cell transfusion she became clammy, nauseous and reported pain along the infusion site and in her abdomen. Temperature remained stable. However she became hypotensive (blood pressure fell from 140/80 to 74/44mmHg). Repeat haemoglobin post-reaction was 62g/L. Bilirubin increased to 65 µmol/L (ref range 4-22) 2 days later. DAT was negative on pre- and post-transfusion samples. Microbiological testing on the unit was negative. A further 4 units of red cells were transfused over the next 2 days with no reported reactions.

Comment: the clinical picture is highly suggestive of an acute haemolytic episode however no serological explanation for this was identified. It is important that all adverse events are reported.

Patient C:

A 3 year old patient with ALL (acute lymphocytic leukaemia) required frequent red cell and platelet transfusions for pancytopenia induced by chemotherapy. Her haemoglobin was 52g/L and she received one unit (355mL) of red cells uneventfully. She returned to hospital after 21 hours with jaundice and dark urine. Her haemoglobin was 86g/L, bilirubin 55 µmol/L and urine showed a large amount of blood with no growth on culture. DAT was strongly positive for complement only, on both pre- and post-transfusion samples and a blood film showed RBC agglutination. The event occurred in winter.

Comment: the patient may have a cold reacting antibody with a haemolytic episode. It is uncertain whether the transfusion was causative in this case. No further investigations were undertaken.

8 Acute Haemolytic & Other Severe Acute Transfusion Reactions continued

Patient D:

An 18 month old Group B oncology patient with pancytopenia had a platelet count of 20 x 10^9/L. 100mL of a Group O unit of apheresis platelets was transfused over 40 minutes. He developed respiratory distress and decreased consciousness. His temperature rose by 2.8°C, heart rate increased by 25 beats per minute and the systolic blood pressure fell by 45 mmHg. He was treated with adrenaline, hydrocortisone, phenergan and a fluid bolus. His perfusion improved after intubation and ventilation. Laboratory investigation showed haemoglobin 26g/L, pH 7.06, elevated lactate and a large amount of blood (haemoglobin) in the urine. DAT was positive and anti-B was eluted from the patient's red cells. He was transfused Group O red cells and improved quickly.

Comment: all donations are tested for the presence of haemolysin and the provision of group O platelets that are haemolysin (IgG anti-A/anti-B) negative is consistent with NZBS' issuing policy. Occasionally haemolysin negative platelets can cause haemolysis. Transfusion of platelets suspended in plasma ABO-incompatible with the recipient's ABO blood group should be avoided in children below 25kg body weight. Subsequently this patient was transfused with Group B platelets.

Patient E:

A 59 year old woman was dialysed for acute renal failure from a drug overdose. Haemoglobin was 86g/L and red cells were transfused. After 90minutes (146mL) she developed dyspnoea, tachycardia (heart rate increased to 132 from baseline 90bpm), hypertension 216/106mmHg (baseline 162/94), falling O_2 saturation, haemoglobinuria and restlessness. A chest xray showed "extreme pulmonary oedema".

Comment: her reaction could represent TACO however haemoglobinuria suggests that intravascular haemolysis may have occurred. No follow-up information was received. Reported events do not always fit within one category type.

9 Delayed Haemolytic Transfusion Reactions (DHTRs)

DHTRs occur after 24 hours, typically at 7 - 10 days following transfusion. They are due to red cell antibodies and confirmed by a positive direct antiglobulin test (DAT) or evidence of haemolysis (drop in haemoglobin and haptoglobin; rise in bilirubin or LDH and reticulocytosis). Free haemoglobin may be detected in the urine if intravascular haemolysis has occurred.

There were 12 DHTRs reported in 2007, compared with 10 in 2006. These are often detected by blood bank when requests for further red cells are made. Ten of the 12 patients had a negative pre-transfusion red cell antibody screen. One patient with pre-existing Rh and Fy antibodies developed anti-Jkb and anti-s following transfusion, a further patient with an antibody of undetermined specificity developed anti-Jka. All 12 patients had a positive DAT and follow-up information for 5 patients confirmed haemolysis. One patient also had a febrile transfusion reaction reported (temperature increase of 1.6°C).

Three patients developed more than one red cell antibody. A total of 16 new allo-antibodies were identified amongst the 12 patients. The most frequent specificity was Kidd, followed by Rh and Duffy (Table 9.1). Anti-Jka was also the most frequent antibody implicated in DHTRs in 2006.

Table 9.1 > Specificity of Red Cell Antibodies Involved in DHTRs

Specificity of Antibody	Number
C	1
c	1
E	1
e	1
K	1
Fya	3
Jka	4
Jkb	2
S	1
s	1
Total	16

Delayed haemolytic transfusion reactions generally result from an anamestic response to an antigen to which the recipient has previously been exposed to and the antibody has diminished to undetectable levels. The usual modes of immunisation are by previous transfusion or pregnancy. Antibodies of the Kidd system (anti-Jka and anti-Jkb) often cause this type of reaction. Milder cases of haemolysis may not be identified.

Delayed Haemolytic Transfusion Reactions (DHTRs) continued

Patient F:

A 53 year old female with a history of rheumatic heart disease underwent elective aortic and mitral valve replacement with tricuspid annuloplasty. Red cell antibody screen on a pre-operative sample was negative. Peri-operative transfusion included 16 units red cells, 4 units platelets, 12 units FFP and 2 units of cryoprecipitate. All units were ABO matched with the patient. On Day 8 post-surgery her haemoglobin was 75g/L and a sample was sent to the blood bank with a request for red cells. The sample had a positive red cell antibody screen and anti-Fya was identified. The direct antiglobulin test was positive (IgG 3+, C3b,C3d 1+) and anti-Fya was eluted off her red cells. Further investigations confirmed haemolysis: total bilirubin 209µmol/L (ref range 4-22), LDH 1135U/L (ref range 240-480), haptoglobin 0.03g/L (ref range 0.34-2.0), reticulocytes 4.84% (normal <2%) and urine dipstick showed haemoglobinuria.

Learning points: delayed haemolytic transfusion reactions may be missed and are often identified by blood bank when a further request for red cells is submitted with a new sample. In general, intravascular haemolysis occurs in acute haemolytic reactions and is characterised by haemoglobinuria, while extravascular haemolysis is seen in delayed reactions and characterised by accumulation of heme breakdown products e.g. bilirubin. However the features of acute and delayed haemolysis do overlap. Patient F had prosthetic heart valves, which can also cause haemolysis.

10 Incorrect Blood Component Transfused (IBCT)

Incorrect blood component transfused is defined as a transfusion with a blood product that did not meet the appropriate requirements or which was intended for another patient.

21 IBCT were reported in 2007 compared to 22 in 2006. However 5 reports involved recurrence of the same error in one patient so overall the reports involved a total of 17 patients. Table 10.1 summarises the events.

Table 10.1 > Summary of IBCT in 2007

Type of event	Number	Description
Request form and dispensing errors	2	• Tetanus immunoglobulin issued when tetanus toxoid requested • Biostate issued to a paediatric patient instead of Kogenate when the request for factor VIII did not identify a specific product
Rh D Immunoglobulin	6	• 3 patients with confirmed allo-anti-D were given Rh D Ig • 2 patients with an Rh D negative infant were given Rh D Ig • 1 patient's record showed an incorrect blood group so Rh D Ig was not administered within 72 hours of delivery
Failure to follow protocol	9	• blood warmer not used although instructed by Transfusion Specialist • HLA matched platelets not irradiated (error occurred 5 times in same patient) • Zoster immunoglobulin not approved by Transfusion Medicine Specialist • One unit of uncrossmatched O negative red cells transfused to 2 paediatric trauma patients in the emergency department (2 events)
Inappropriate transfusion	3	• A paediatric oncology patient requiring a surgical procedure refused a blood sample. 1 unit of FFP was transfused to prevent bleeding. Three weeks earlier the child had an INR of 1.0. • Expired unit of red cells transfused (Patient G) • 2 units of uncrossmatched red cells transfused to a head injury patient in the emergency department, with no signs of shock or external haemorrhage. The post-transfusion haemoglobin was 165g/L
Incompatible red cell transfusion	1	• A patient with known anti-Fya was transfused with an Fya positive unit of red cells (Patient H)

There were twice as many reported Rh D Immunoglobulin errors compared with 2006. In one case the blood bank staff member misread the date of when Rh D Ig was administered as 2007 instead of 2006, hence Rh D Ig was administered in a recipient with allo-anti-D; in two other cases the product was issued without checking the infant's Rh D type (infants were Rh D negative); in a further case the cord blood result was incorrectly recorded.

Errors can occur at any point in the transfusion chain. Table 10.2 shows the site of primary error for these events. Half occurred in the blood bank. This is higher than the proportion of laboratory errors reported in other schemes such as the UK SHOT programme where approximately one third occurred in the laboratory.[5]

10 Incorrect Blood Component Transfused (IBCT) continued

Table 10.2 > Site of Error of IBCT 2007

Site of error	Number
Prescription of blood product	5
Laboratory	11
Administration of blood product	5

Important learning points to be noted from these events:

- Be specific on the blood prescription and request form. Multiple products may be available for the same purpose e.g. plasma derived and recombinant factor FVIII products are available.
- Once a transfusion has commenced, never share the same unit between recipients. The sterility of the unit may be compromised and traceability of the blood product cannot be maintained.
- Errors can be propagated, always check results when prescribing blood products.

Case:

Patient G with metastatic renal cell carcinoma and a haemoglobin of 78g/L was prescribed 2 units of red cells in the evening during a weekend. One unit was transfused and the 2nd unit was placed in a blood fridge. At 4.15 am the next day the 2nd unit was removed and transfused. Later that day blood bank staff identified that the unit had expired at midnight despite being checked by 2 people.

Learning point: ensure adequate lighting when checking transfusions, check units carefully before administering.

Case:

Patient H, an 83 year old female with a non-ST elevation myocardial infarction (NSTEMI) and a haemoglobin of 96g/L was transfused red cells. After 150mL had been transfused her temperature rose by 1.9°C, she became tachycardic (130 from baseline of 56 bpm) and hypertensive (160/110 from baseline of 134/62 mmHg). She suffered an inferior myocardial infarction and had a cardiac arrest. She was known to have anti-Fya however subsequent investigations revealed the unit transfused was Fya positive and incompatible. The pre-transfusion sample had a negative DAT and the post-transfusion sample had a positive DAT, with anti-Fya eluted. The error was attributed to possibly using the incorrect sample for crossmatching and/or error in antigen typing. Although the features are consistent with an acute haemolytic transfusion reaction, it was concluded that her death was due to myocardial infarction.

Learning point: transfusion errors can occur in the blood bank. Laboratory staff must constantly be vigilant and not rush procedures that impact on compatibility testing.

11 Other Types of Reactions

These reports (Table 11.1) do not clearly fit into any of the existing categories already described. The numbers of such reports appear to be increasing as evidenced by 44 reports for 2007, compared to 27 in 2006. There were 25 females and 19 males, with an age range of 1 month to 91 years.

Table 11.1 > Other Types of Reactions

Event Type	Number
Abdominal pain	1
Anxiety	7
Chest pain	1
Chest pain, lightheaded, sweating	1
Chills/rigors/nausea	7
Dyspnoea	1
Dyspnoea/chest pain	1
Hyperkalaemia	1
Hypertension/chest pain	1
Hypertension	3
Hypertension/anxiety	2
Hypertension/pain at infusion site	1
Hypertension/tachycardia	1
Hypotension	7
Hypotension/chest pain	1
Hypotension/rigor/dyspnoea	1
Pain	3
Rigor/tachycardia/dyspnoea	1
Tachycardia	1
Tachypnoea	1
Polycythaemia*	1

**patient received granulocyte transfusions*

Pain syndromes and anxiety are events that have not been reported previously. Chills and rigors related to transfusion probably have a similar mechanism to non-haemolytic febrile transfusion reactions.

Other Types of Reactions continued

Case:

Patient J, an 86 year old male with Parkinsons disease, thalassaemia trait, peptic ulcer disease and history of transient ischaemia attack, had three reported events related to red cell transfusion in 2007:

1. One hour 15 minutes (130mL) after start of transfusion he became agitated (but remained oriented) and reported dyspnoea, back pain and rigors. His temperature remained stable however the respiratory rate, heart rate and blood pressure all increased. The transfusion was stopped.

2. Pre-medicated with hydrocortisone and paracetamol. One hour after start of transfusion (135mL) he developed facial flushing, agitation, dyspnoea and pain in the sacral region. No change in his recordings apart from a drop in blood pressure from 162/82 to 132/70mmHg. The transfusion was stopped.

3. Pre-medicated with phenergan, hydrocortisone and paracetamol. 90 minutes (185mL) after start of transfusion he developed back pain (mainly left loin), dyspnoea and wheeze. Respiratory rate increased from 24 to 32/minute. No change in temperature, oxygen saturation, pulse, blood pressure. The transfusion was stopped.

Learning point: Patient J had the same reaction on three occasions and was unable to complete transfusion of a whole unit of red cells. The nature of his symptoms is uncertain however is suggestive of a transfusion associated acute pain syndrome. All adverse events should be reported as this will improve our understanding of how and when they occur.

Case:

Patient K is a 9 year old with osteogenesis imperfecta. The child weighed 10kg and was taken to the operating theatre following trauma. Massive blood loss ensued. Whilst under anaesthesia, 3 units of red cells, 1 platelet dose and 1 unit of cryoprecipitate were transfused. The patient's potassium increased after the 2nd unit of red cells (from 4.4 up to 8.3mmol/L). The patient had a cardiac arrest and attempts to resuscitate the child were unsuccessful. The anaesthetist tested the 2nd unit of red cells for potassium which was elevated at 34mmol/L. The units were 22 days old.

Learning point: hyperkalaemia can occur after large volume transfusion. Recipients with smaller blood volumes have a higher risk and fresher red cell units should be considered.

12 Adverse Reactions to Plasma Derivatives

CSL Bioplasma manufactures the following products for NZBS using plasma from New Zealand donors:

- Albumex (4% & 20%)
- Intragam P (IVIg)
- Biostate (FVIII)
- MonoFIX (FIX)
- Prothrombinex (II, IX, X)
- Thrombotrol (ATIII)
- Rh D Immunoglobulin*
- Hepatitis B Immunoglobulin
- Zoster Immunoglobulin
- Normal Immunoglobulin
- Tetanus Immunoglobulin

**also manufactured from plasma collected in the United States of America*

WinRho-SDF is produced in Canada and supplied by NZBS to meet the demand for Rh D immunoglobulin. Adverse reactions to plasma derivatives are reported by NZBS to the manufacturer and to the regulator, Medsafe.

In 2007 there were 29 reports of adverse reactions to plasma derivatives, compared to 20 in 2006. The blood product most frequently implicated was Intragam P (Table 12.1). Patient ages ranged from 1 - 80 years and involved 19 males and 10 females.

Table 12.1 > Plasma Derivatives Implicated in Adverse Reactions 2007

Implicated Product	Number
Albumex®4	1
Intragam®P	24
Rh(D) Immunoglobulin-VF	2
WinRho SDF™	2

Reactions include fever, myalgia and allergic symptoms. There were 2 reports of chest pain and one report of aseptic meningitis associated with Intragam P. Table 12.2 shows the adverse events reported with Intragam P.

Table 12.2 > Adverse Events Reported with Intragam P (n=24)

Type of Reaction	Number
Pyrexia	4
Myalgia/arthalgia/rash	1
Myalgia/arthalgia	1
Allergic/inflammatory	10
Aseptic meningitis	1
Chest pain	2
Atrial fibrillation	1
Hypothermia & hypertension	1
Hepatitis B*	1
Hypotension	1
Weakness	1

**same batch transfused to many recipients, HBV infection is likely to be unrelated to Intragam P administration.*

13 Adverse Reactions in Donors

NZBS monitors adverse reactions that occur during the donation process. These events can occur at the collection venue or are reported later.

There were 797 adverse reactions reported in donors from a total of 177,843 donations collected (includes whole blood and apheresis donations), representing an overall rate of 1 in 223 donations in 2007. This is an increase from 2006 where 651 adverse reactions were reported with a rate of 1 in 261 donations.

Vasovagal reactions, haematoma and bruising are the most frequently reported donor events (Table 13.1). There was an increase in the number of nerve injuries and arterial puncture, compared to 2006 events (12 and 5 respectively).

Table 13.1 > Donor Adverse Events 2007

Nature of Reaction	Number	Frequency	Per 100,000 Donations
Vasovagal	465	1:382	261
Haematoma/bruise	208	1:855	117
Automated procedures	34	1:5,231	19
Nerve injury	31	1:5,737	17
Arterial puncture	13	1:13,680	7
Soft tissue/tendon	4	1:44,461	2
Cardiovascular	3	1:59,281	2
Infection/inflammation	2	1:89,922	1
Other	37	1:4,807	21
TOTAL	**797**	**1:223**	**448**

The reporting categories have changed since 2006; haematoma/bruise has been separated from soft tissue injury and events associated with automated procedures (apheresis) now have a separate category. Increased efforts are also being devoted to improve reporting incidents related to apheresis procedures. Preliminary results are shown in Table 13.2. “Red cells not returned” occurs where there is cessation of blood flow during the procedure with an extracorporeal volume of donor blood in the apheresis machine that cannot be returned to the donor. The donor cannot donate for 1 month following this type of event.

Table 13.2 > Events Associated with Automated Procedures (n=34)

Type of Event	Number
Red cells not returned	29
Diffuse allergic reaction	3
Citrate toxicity	1
Other	1

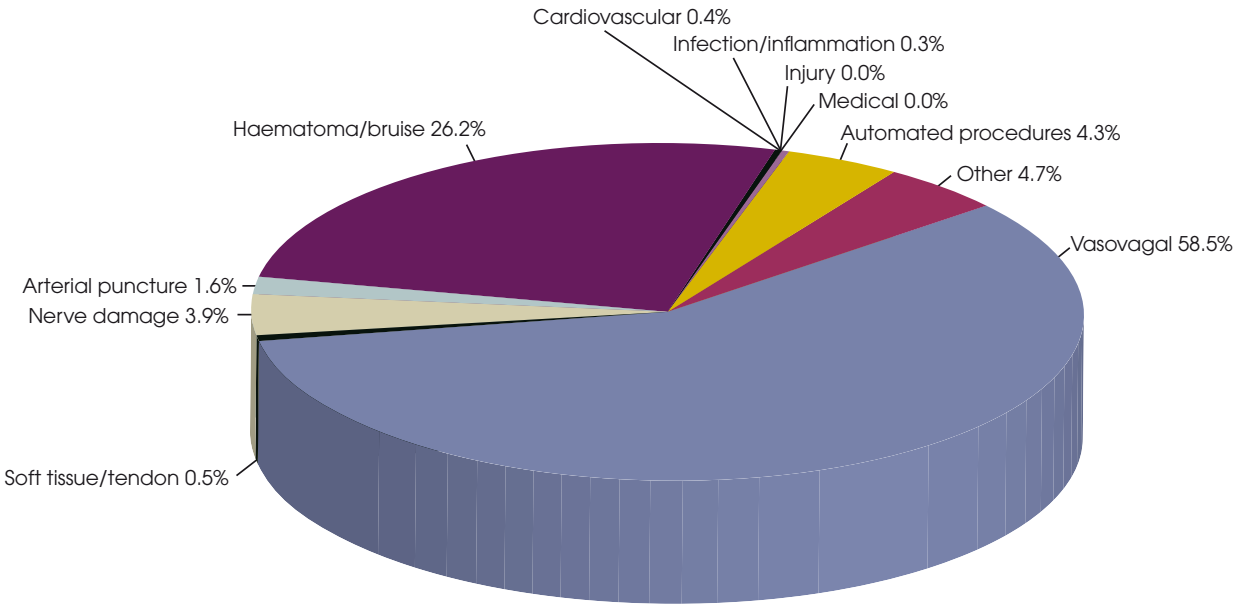
Vasovagal reactions represent a spectrum of events ranging from the donor feeling lightheaded and dizzy to complete loss of consciousness (Table 13.3). Faints can occur after the donor has left the venue and although uncommon, injuries can also occur. Donors are encouraged to be well-hydrated prior to donating. Donor staff are trained to recognise and manage complications of donation.

Table 13.3 > Vasovagal Reactions in Donors

Reaction	Number
Without faint	172
Immediate faint	142
Delayed faint	151
TOTAL	**465**

Figure 13.1 shows the adverse donor events as a percentage of all events.

Figure 13.1 > Donor Adverse Events 2007 (n=797)



14 Donor Infectious Disease Screening

All donations are screened for infectious diseases that may be transmitted by transfusion. The mandatory tests include:

- HBsAg, HBV DNA
- Anti-HCV, HCV RNA
- Anti-HIV I & II, HIV RNA
- Syphilis EIA
- Anti-HTLV (all new donors)

Nucleic acid amplification tests performed on single donor samples were introduced in September 2007. This includes an ability to detect HBV DNA, HCV RNA and HIV RNA. Testing was previously undertaken in minipools for HCV and HIV RNA.

Selected donations are screened for:

- CMV IgG
- Malaria antibody
- *Trypanosoma cruzi* test

A total of 177,843 donations were tested in 2007. Table 14.1 shows the breakdown of the 51 confirmed Hepatitis B, Hepatitis C and HIV positive donations in 2007. The rates were lower for all 3 infectious markers than in 2006. Only 4 of the donations came from regular donors (those who had previously undergone serological testing with a negative result). In these circumstances an extensive look-back is undertaken.

Table 14.1 > Donations with Confirmed Positive Serology 2007

		Hepatitis B	Hepatitis C	HIV
Number of positive donations		33 (31 = new donors)	17 (15 = new donors)	1 (new donor)
% positive donations		0.019%	0.010%	0.001%
Frequency of positive donation	New donor	1:677	1:1,400	1:21,001
	Regular donor	1:7,841	1:7,841	0
Overall frequency		1:5,389	1:10,461	1:177,843

15 Other Haemovigilance Associated Activities

DHB Clinical Oversight Programme

The NZBS DHB Clinical Oversight Programme, introduced in January 2005, provides DHBs with specialist transfusion medicine support (both clinical and technical) in line with the requirements of NZS/ISO 15189:2007 *'Medical Laboratories - Particular Requirements for quality and competence'*.[6]

The programme's key activities also provide assistance in implementing strategies to enhance transfusion medicine knowledge, best practice and efficient utilisation of blood products. The four elements of the programme are as follows:

- **Clinical Audit Of DHB Transfusion Policies And Procedures**

One clinical audit every two years of hospitals where transfusions are carried out. These audits include the blood product storage conditions of fresh, frozen and manufactured products, informed consent, dispensing systems and the clinical records documenting transfusions and traceability.

- **Site Visits**

One formal site visit per year to non-NZBS blood banks or laboratories where pretransfusion testing is performed. These site visits are intended as a collaborative review of systems and processes to promote best practice. A report of each site visit is prepared that may include corrective action requests and recommendations, these reports are available to International Accreditation New Zealand (IANZ), the national authority for the accreditation of laboratories. Where possible, an NZBS Transfusion Medicine Specialist will also attend the DHB Hospital Transfusion Committee meeting. Access to clinical advice from a Transfusion Medicine Specialist is available at all times, via an on-call rota which is distributed weekly to blood banks.

- **Regional Meetings/Seminars**

Three meetings are held annually by each of the four main NZBS centres (Auckland, Waikato, Wellington and Christchurch). These regional meetings and/or seminars are intended to supplement the site visit programme. The meetings are attended by scientists from DHB and NZBS blood banks, NZBS logistics, IT and processing staff, Transfusion Medicine Specialists and Transfusion Nurse Specialists. The meetings provide a forum for scientific presentations, discussion of problems and NZBS initiatives.

- **Education**

Developing and maintaining appropriate educational and training resources. The Transfusion Nurse Specialists have a major role in education within the larger hospitals.

A Transfusion Medicine Handbook produced by NZBS is available to those involved with transfusion.

15 Other Haemovigilance Associated Activities continued

Clinical Audits

Adverse transfusion-related events can be minimised by ensuring that blood products are prescribed appropriately. Audit of clinical transfusion practice provides useful data on usage of blood products. In addition, DHBs are motivated to understand their demand of blood products because they are charged for them, on a cost-recovery basis.

NZBS conducts multi-centre audits, co-ordinated by a NZBS Transfusion Medicine Specialist, at eight DHBs, six of which have NZBS-operated blood banks and employ Transfusion Nurse Specialists, and two where the DHB employs a Transfusion Nurse Specialist. In addition local audits are undertaken, some of which act as pilots for the larger collective audits. These audits take place as part of a more general service of demand management, including monthly blood utilisation reports and retrospective data analyses.

Since 2004, eight audits have been undertaken. In 2007 audits of platelet and FFP use were completed and an audit on perioperative red cell use for specific elective procedures was commenced.

Four key findings came out of the FFP audit: a high proportion (79%) of transfusions were considered clinically indicated. This compares well with other countries. However, dosing was poorly managed with 50% of transfusions underdosed, even allowing for those transfusions split over time for patients with congestive heart failure. Thirdly, warfarin reversal continues to use a large volume of FFP, although a better alternative product, Prothrombinex®-VF, is widely available. Lastly, some patients received FFP for mildly abnormal non-warfarin-induced INR values, despite good evidence in the literature, and from the audit, that this does not change the INR or the outcome for the patient.

Interestingly, the audits conducted thus far have demonstrated good compliance with clinical guidelines regarding when to transfuse. Table 15.1 shows the proportion of appropriate and correctly dosed transfusions reported from NZBS audits and indicates lower compliance with correct dosing for components where more than 1 unit may be required for a single therapeutic dose i.e. FFP and cryoprecipitate.

Table 15.1 > Proportion of Appropriate and Correctly Dosed Transfusions

	Platelets	Fresh Frozen Plasma (FFP)	Cryoprecipitate
Standard therapeutic dose	1 bag	12-15mL/kg	1 bag/30kg
Transfusion clinically indicated	87%	79%	82%
Correct dose of component given	89%	50%	68%

The partnership between NZBS and DHBs has enabled the audit process to provide useful insights into where blood component use in New Zealand can be improved, while reassuring that, for the most part, clinicians are using blood appropriately.

16 Bacterial Monitoring of Platelet Concentrates

Bacterial transmission remains one of the major causes of morbidity and mortality associated with transfusion-transmitted infection. Cumulative data from SHOT, the United Kingdom Haemovigilance system, published in 2002 identified 21 reported cases over a 6 year period, 6 of which were fatal. 17 of the cases related to bacterial contamination of platelets with 5 of the deaths occurring in this group. Similar data has been reported from the French Haemovigilance system and from the USFDA (United States Food and Drug Administration).

Increasing concern relating to bacterial transmission of platelet concentrates has led a number of Blood Services to investigate possible methods to reduce the risk. Canada, The Netherlands and Hong Kong have already introduced pre-release bacterial detection systems for platelet concentrates, a number of other countries are also actively investigating this. There is however no clear consensus on the definition of an optimal system for bacterial culture. A number of variables can significantly impact on overall system sensitivity. These include the volume of initial inoculum, the timing of culture (day one or two post-collection) and whether only a single aerobic bottle or both aerobic and anaerobic bottles are used.

A number of systems are currently available to support bacterial detection in platelet concentrates. These can either be used to monitor the level of contamination, as required by the Council of Europe Guide, or to support release of platelets on a 'negative at release' basis. NZBS commenced a pilot study to assess the frequency of bacterial contamination during October 2003. The scheme has been progressively rolled out such that by the end of 2007 all sites within NZBS that manufacture platelets were participating.

The NZBS protocol for bacterial monitoring involves testing of platelets on day 2 of storage. A 6ml sample of the concentrate is used to inoculate the BacTalert aerobic culture bottle. The bottles are cultured until a positive signal is obtained or until the platelet concentrate has expired. Currently approximately 50% of all platelet concentrates manufactured by NZBS will be tested. Results of testing undertaken during 2007 are shown in Table 16.1.

Data from the scheme indicate that NZBS systems compare well with published data. The Council of Europe Guide to the preparation, use and quality assurance of blood components (13th edition) identifies a contamination rate of 0.2 to 0.4%. No clinical reports of septic reactions to platelet transfusions have yet been reported through the national haemovigilance system in the three years that this has been in place.

Platelets are also sampled at expiry. This data will potentially be of value if NZBS were to consider extension of the shelf life of platelets beyond the current 5 days.
2007 data for testing product at expiry is shown in table 16.2.

16 Bacterial Monitoring of Platelet Concentrates continued

Table 16.1 > Results of Day 2 Testing of Platelet Concentrates

Site	Total Doses Collected	Total Components Sampled	Total Number Reactive	%	Number Confirmed Positives	%
Auckland	5,509	3,563	7	0.20	3	0.08
Hamilton	2,476	2,001	0	0.00	0	0
Palmerston North	311	223	1	0.45	0	0
Wellington	2,241	1,452	0	0.00	0	0
Christchurch	2,044	1,663	0	0.00	0	0
Dunedin	230	217	1	0.46	0	0
NATIONAL	12,811*	9,119	9	0.10	3	0.03

**a single plateletpheresis collection procedure can yield up to 2 therapeutic doses*

Table 16.2 > Results of Testing of Expired Platelet Concentrates

Site	Total Components Sampled	Number Reactive	% Reactive	Frequency of Reactives
National: total reactive	1,696	6	0.4	1:283
National: confirmed reactive	1,696	1	0.06	1:1,696

The confirmed positive rate of 1 in 1,696 suggests that the current system for detecting platelet contamination is only partially effective. This is consistent with international data. Most contamination arises during the collection process. The number of bacteria entering during collection is typically low. Sampling of platelet concentrates may therefore fail to identify the contamination. The bacteria will proliferate during storage and potentially lead to septic transfusion reactions.

Data from Ireland and the American Red Cross published during 2007 indicates that this testing might only detect 50% of contaminated platelet concentrates (these studies tested on day 1 whereas NZBS tests on day 2). There is however considerable debate on the clinical significance of this. The majority, though not all, of organisms that are not detected by current strategies are slow growing anaerobic species. These have not been shown to be associated with septic transfusion reactions. Some experts argue that detection of these organisms is not required and that bacterial culture should be optimised to detect only clinically significant bacteria. Others argue that blood services should aim to provide sterile platelet concentrates and that any risk that can be avoided should be avoided. In doing so they believe that bacterial culture is an imperfect solution to the problem and that pathogen inactivation systems may be the only method to achieve sterility. In considering this issue it is important to bear in mind that current bacterial strategies have the ability to significantly reduce risk when compared to no intervention. In the context of five day storage of platelet concentrates current systems reduce the risk of bacterial septic events considerably. The debate becomes more problematic when the role of bacterial culture is considered in the context of an extended seven day shelf life for platelet concentrates.

NZBS continues to utilise bacterial testing as a monitoring scheme. The Australian Red Cross Blood Service introduced testing of all platelet concentrates in early 2008 with the intention of moving progressively to a 'culture negative at release' strategy.

At this stage NZBS plans to continue utilising the bacterial monitoring programme as a quality assurance tool. This is consistent with recommendations contained in the Council of Europe Guide.[1] During 2007 Australian authorities announced a decision to move to 100% pre release testing by the end of 2008. This will be a significant logistical challenge. NZBS will closely monitor progress with this initiative. The current NZBS policy position will be reviewed in the light of the Australian experience and if sufficient data emerges to indicate that bacterial detection systems can be used to extend the shelf life of platelets to seven days.

17 Request Form and Sample Labelling Errors

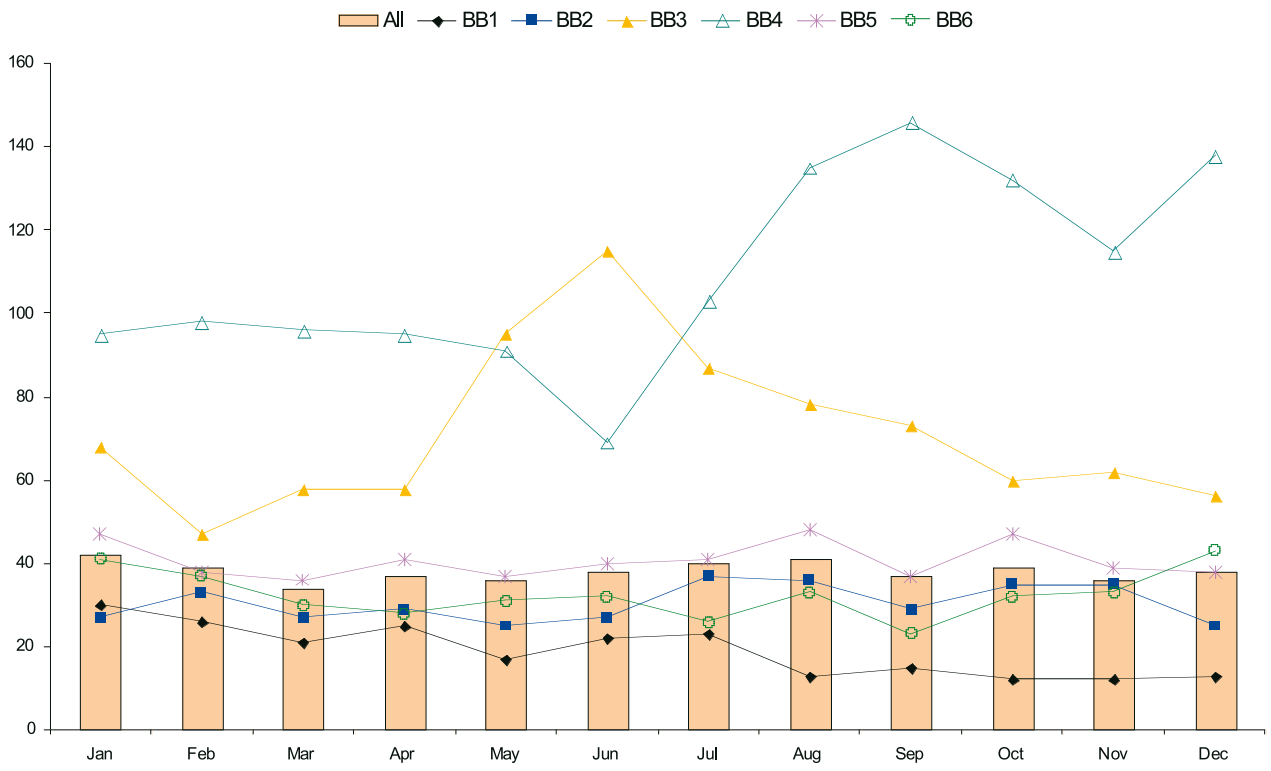
On 1 May 2006 NZBS began collecting standardised national data regarding sample and request form labelling errors at the six NZBS blood banks. Each site records instances of a range of predetermined errors and the associated corrective actions. Data is entered into a Microsoft Access™ database for subsequent analysis.

In 2007 a total of 148,441 requests were received of which 5,611 (equivalent to 1:26) had errors associated with them, a number of requests had more than one error associated with them.

The overall error rate for the six NZBS blood banks for the calendar year 2007 was 3.8% compared to 4.5% in 2006.

Figure 17.1 shows the error rate per 1,000 requests received by the six NZBS blood banks. Apart from BB 3, which introduced hand-labelling during the observation period and BB 4, the remaining four NZBS blood banks appear to have a steady error rate. The error rate for BB 4 could to be due to cord blood samples being inadequately labelled. In 2007 BB 4 were registering all cord blood samples, irrespective of whether they required testing. The other blood banks may only have been registering cord blood samples that required testing. This inadvertent inflation of sample numbers combined with poor labelling practice may explain the error rate for BB 4.

Figure 17.1 > Number of Requests with Errors per 1,000 Requests - 2007



Tables 17.1 and 17.2 summarise the total clerical and technical request form/sample errors recorded in 2007 that are required to be reported by blood banks according to NZBS policy. Errors that allow for correction are documented and a declaration is signed by the person responsible for the correction.

Of the specific clerical errors reported as required by NZBS policy, the following were the five most prevalent errors:

- Missing or incomplete patient details (24%)
- Patient details - discrepancy between sample and form (15%)
- Declaration not signed by phlebotomist (13%)
- Sample not signed (18%)
- Sticky (addressograph) label on sample (16%)

Table 17.1 > Total Clerical Errors and Required Action

Clerical Error	Action Required	Total
C01: Wrong Blood In Tube (WBIT)	New Sample	9
C02: Unlabelled Sample	New Sample	107
C03: Missing / Incomplete Patient Details – Patient details on specimen but not form	Correction	1,414
– No patient identification on form	New Sample	
– Given or family name not on sample	New Sample	
– Abbreviated, minor spelling errors, given names transposed	Correction	
– Single letter or number transposed	Correction	
C04: Patient Details: Discrepancy Between Sample And Form	New Sample	886
C05: Patient Details Do Not Agree With Historical Record	Phone follow-up	196
C06: Original Details Overwritten (Or Labels Overstuck) On Sample Or Form	New Sample	95
C07: Declaration Not Signed – Declaration and specimen not signed	New Sample	737
– Declaration signed, specimen not signed	Correction	
C08: Sample Not Signed	New Sample	1,025
– Both sample and form not signed		
– Sample not signed, form signed	Correction	
C09: Signature On Sample And Declaration Differ	New Sample	89
C10: No Date / Time Sample Collected (Sample And/or Form)	Phone follow-up	107
C11: Name / Signature Requesting Practitioner Not Given	Phone follow-up	266
C12: Sticky Label On Sample	New Sample	906
C13: Cord Blood - Labelled With Mother's Details Only	New Sample	18
All		**5,855**

17 Request Form and Sample Labelling Errors continued

Table 17.2 > Total Technical Errors and Required Action

Technical Error	Action Required	Total
T01: Haemolysed Sample	New Sample	8
T02: Wrong Tube Type	New Sample	114
T03: Insufficient Sample	New Sample	25
T04: Leaking / Broken Sample	New Sample	2
T05: Maternal Contamination of Cord Blood Sample	New Sample	1
T06: Other Technical Error	Consult	14
All		**164**

Table 17.3 summarises the different actions taken in response to the errors identified by the blood banks. More than one corrective action associated with each request form or sample may be recorded where errors were identified.

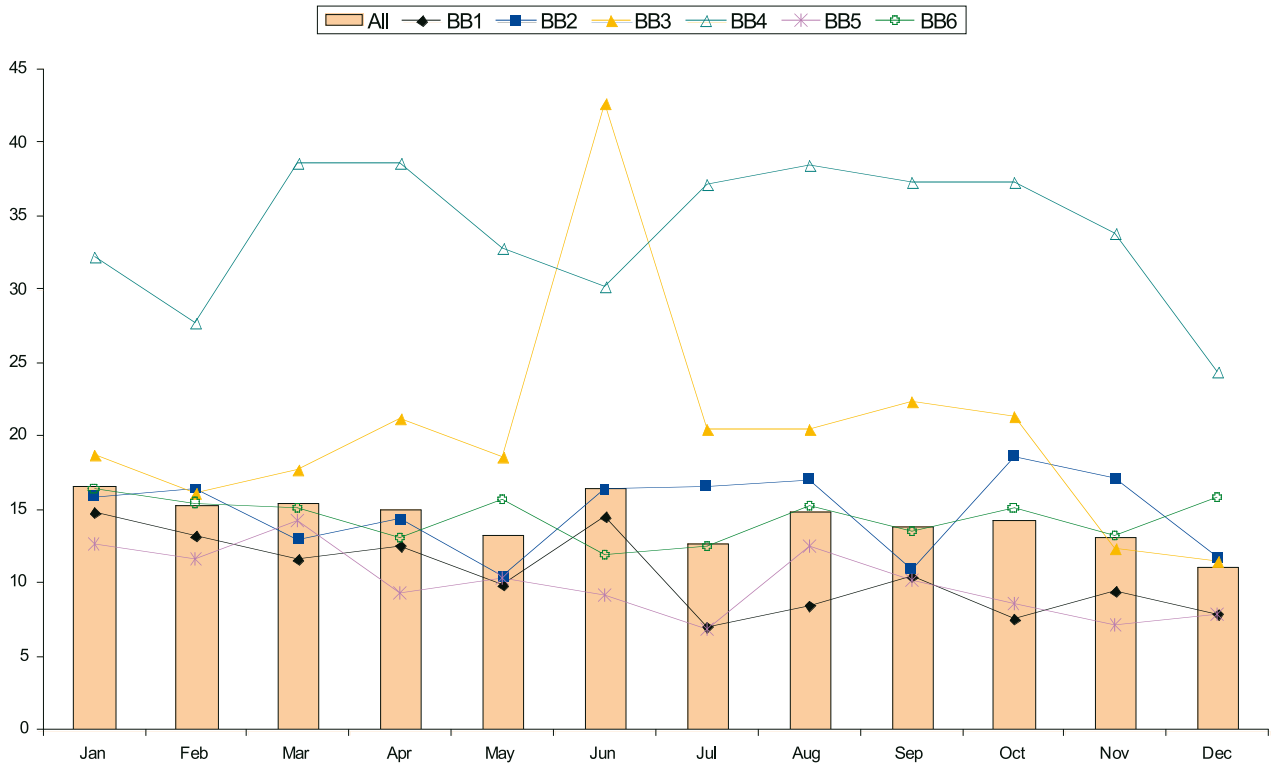
Table 17.3 > Summary of Actions taken in Response to Reported Errors

Action Taken	Totals
No Action Taken	461
Sample Discarded	1,790
Sample / Request Not Processed (Held)	27
New Sample Requested	2,129
Labelling Corrected By Collector	1,570
Correct Details Obtained By Telephone/Fax	1,011
Request Withdrawn	77
Compatibility Testing Done Using Earlier Sample	34
Other	458
All	**7,557**

Of the requests received, 2,129 failed to meet NZBS requirements and a new sample and request form were required for pre-transfusion testing. Of the errors detected, 38% required a request for collection of a new sample from the patient. The recollection rate for the six NZBS blood banks was 14 per 1,000 samples received. The request for the recollection of a blood sample meant that the patient was subjected to a second venepuncture and a potential delay in the provision of blood components.

Figure 17.2 shows the number of recollects per 1,000 requests for the six NZBS blood banks.

Figure 17.2 > Number of Request for Recollection of Sample per 1,000 Requests - 2007



Wrong Blood in Tube (WBIT)

A “wrong blood in tube” involves miscollection, where a pre-transfusion sample is tested and found to have an ABO blood group that differs from that in the historical record. It occurs as a result of collecting blood from the wrong patient or labelling the sample and request form with a different patient’s details.

Historical blood groups were available for 62% of the samples received by the six blood banks in 2007.

The raw WBIT rate can be corrected for silent WBIT errors; such errors occur when the wrong patient’s blood is collected, but the ABO and Rh D group of the blood in the tube happens by chance to match the blood group on the record. To correct for these, the raw rate is multiplied by a correction factor equal to 1/(1-Q), where Q represents the chance that two random individuals will have the same ABO Rh D groups.[7]

Table 17.4 shows the number of reported WBITs in 2007 and the corrected WBIT frequency for each of the six NZBS blood banks with 95% confidence intervals determined using the Wilson Score Method of binominal confidence levels.

17 Request Form and Sample Labelling Errors continued

Table 17.4 > Frequency of WBITs Reported in 2007

Site	Historic Groups	WBITs	Frequency*	WBIT prop	Lower CI	Upper CI
BB 1	29,240	5	1:3,655	0.00017	0.0001	0.0004
BB 2	18,012	1	1:11,258	0.00006	0.0000	0.0004
BB 3	6,366	0		0.00000	0.0000	0.0006
BB 4	8,250	1	1:5,156	0.00012	0.0000	0.0006
BB 5	17,614	0		0.00000	0.0000	0.0002
BB 6	12,911	2	1:4,035	0.00015	0.0001	0.0006
All	**92,393**	**9**	**1:6,416**	**0.00010**	**0.0001**	**0.0002**

**Corrected to account for silent errors. Corrected WBIT rate = No. historical groups / Number WBIT* correction Factor). The correction factor (1.6) is based on New Zealand blood group frequencies.*

The corrected frequency of WBIT for NZBS blood banks in 2006 was 1:5,089 compared to 1:6,416 in 2007.

Five of the six NZBS blood banks have identified incidences of WBIT, Table 17.5 summarises the NZBS individual corrected frequencies for WBIT from May 2006 - December 2007.

Table 17.5 > Total WBITs May 2006 - December 2007

Site	Historical Groups	WBITs	Frequency*	WBIT prop	Lower CI	Upper CI
BB 1	42,971	10	1:2,686	0.00023	0.0001	0.0004
BB 2	28,155	1	1:17,597	0.00004	0.0000	0.0001
BB 3	9,935	4	1:1,552	0.00040	0.0002	0.0010
BB 4	11,296	1	1:7,060	0.00009	0.0000	0.0005
BB 5	26,799	0		0.00000	0.0000	0.0001
BB 6	19,034	2	1:5,948	0.00011	0.0000	0.0004
All	**138,190**	**18**	**1:4,798**	**0.00013**	**0.0001**	**0.0002**

**correction factor applied*

NZBS blood banks require all pre-transfusion samples to be signed by the phlebotomist, who has also signed the declaration on the request form verifying that they have checked the identity of the patient (verbal or by checking the wristband). However the data prove that pre-transfusion samples are not always labelled at the bedside and that the patient's identity is not always confirmed by the phlebotomist. Efforts must focus on improving compliance in this area, in order to prevent transfusion of incompatible blood.

New Zealand Blood Service Standards

In New Zealand, blood and blood products intended for therapeutic purposes are defined as medicines and, therefore subject to the *Medicines Act 1981, Medicines Regulations 1984* and subsequent amendments. Medsafe is responsible for administering this legislation which includes the issuing of licenses to manufacture medicines. Medsafe carries out annual audits of all NZBS Manufacturing sites to ensure that good manufacturing practice standards are being met.

The NZBS standards outline the technical requirements used in the collection, manufacture, distribution and storage of blood and blood components. These standards in conjunction with the 'Code of Good Manufacturing Practice' (GMP) provide the basis for the NZBS Quality System.

The standards are in two volumes; firstly, the *Collection Standards* detail the requirements relating to donors and include detailed information on the selection and care of donors including an A-Z Guide; secondly, the *Manufacturing Standards* detail the requirements for premises, equipment and personnel. Also included are the requirements for processes used in the manufacture of blood and blood components. A separate document, the NZBS Quality Manual, outlines NZBS quality system policies and procedures.

The standards are owned by NZBS with the Clinical Advisory Group (CAG) being responsible for their development and maintenance. The Council of Europe *'Guide to the preparation, use and quality assurance of blood products'*, which is updated annually, is used as an external reference standard and NZBS has observer status on the Council of Europe committee responsible for its maintenance. In developing standards CAG takes account of other international standards relating to blood with the intention of ensuring that the standards are consistent with international best practice.

Changes to the standards are undertaken through a controlled process involving consultation with Medsafe (New Zealand Medicines and Medical Devices Safety Authority).

Medsafe approved a number of changes to the manufacturing Standards during 2007. These are outlined below.

Monitoring for Sterility of Blood Components

The NZBS Manufacturing Standards included a requirement for sterility testing of a range of blood components. This approach was based on early editions of the Council of Europe Guide.

Sterility testing requirements generally involve the testing of 1% of manufactured product at expiry with a minimum of 4 components per month.

The 11th Edition of the Guide, published in 2005, outlined a new approach to monitoring of bacterial contamination. This is described below.

'Although blood collection and processing procedures are intended to produce non-infectious blood components, bacterial contamination still may occur. Bacterial quality control testing in all blood components may be appropriate. However, for whole blood collection, bacterial cultures of platelets provide the best indication of the overall rate of contamination, provided that the sample for culture is obtained at a suitable sample volume and at a suitable time post collection.'

New Zealand Blood Service Standards continued

NZBS implemented a pilot system of bacterial monitoring of platelet components in Auckland in June 2004. This has since been extended to include all manufacturing sites. The system involves systematic sampling of platelet components on day two of storage using the Bac-T-Alert culture system. The results of testing are monitored using statistical process control methodology (NWA Quality Analyst system).

In May 2007 NZBS submitted an application to Medsafe

- Proposing that a new section on the microbiological safety of blood components be introduced into the *"Specification for Blood Components"* section of the Manufacturing Standards. This commits NZBS to maintaining systems for bacterial monitoring of platelet components that complies with the Council of Europe guideline.

- Requesting that the routine sterility testing of expired components be discontinued for all blood components manufactured using closed systems.

- Proposing that the requirement for 100% bacterial sterility testing of components that include an open processing step be maintained (this includes washed red cells, washed platelets and red cells ex liquid nitrogen).

Medsafe approved the submission in November 2007. The new systems have now been fully implemented.

Introduction of Nucleic Acid Testing for Hepatitis B Virus

NZBS introduced nucleic acid testing (NAT) for HIV and Hepatitis C virus in 2000. Testing is undertaken in small pools of up to 16 donations (mini pool testing). This significantly reduced the risk of transmission of these viruses by tested blood. The risk is currently estimated to be less than 1 in 2 million donations. The models used to assess risk internationally include a number of conservative assumptions. Risk estimates may therefore over-estimate risk. In practice, no cases of transmission by blood components for either of these viruses has been documented since the introduction of antibody testing (1985 for HIV and 1992 for Hepatitis C).

In contrast, between 0-2 probable cases of Hepatitis B transmission have been reported per year to NZBS during the last 6 years. This is consistent with reported data from other countries and in part reflects the endemic nature of this infection in New Zealand. In each case look back investigations have identified one donor with a classic 'core only' pattern of Hepatitis B markers.

The Informed Consent leaflet produced by NZBS for potential recipients of fresh blood components identifies for Hepatitis B that *'the estimated risk is less than 1 in 100,000 transfusions (less than 1 case per year in NZ)'*.

A study undertaken in 2004 identified that overall 7% of New Zealand donors had Hepatitis B core antibody, this indicating past exposure to infection with the virus. This identifies that routine core antibody testing is neither feasible, nor appropriate, in New Zealand.

During 2006 Chiron, the manufacturer of the NAT system used by NZBS, introduced a new assay. This detects Hepatitis B virus DNA in addition to HIV and Hepatitis C RNA. Levels of Hepatitis B DNA are however significantly lower than those for the other viruses. This means that single donation testing is required in order

to confidently identify potentially infectious donations. New fully automated testing platforms are now available to support single donation testing. A pilot study of 10,000 donations identified 2 confirmed Hepatitis B DNA positive donations. A further 2 donations contained possible Hepatitis B DNA at low levels. All 4 donations were collected from donors who were core antibody positive (and surface antigen negative).

The semi-automated NAT testing platforms currently purchased by NZBS in 2000 were in need of replacement. NZBS took a decision to replace these with the fully automated Tigris system thus enabling the introduction of single donation NAT for Hepatitis B DNA. The incremental cost to NZBS was low and the benefits potentially very valuable. Single donation NAT testing for HIV, HBV and HCV commenced in September 2007.

In December 2007 NZBS submitted an application to Medsafe to enable the Manufacturing Standards to be updated to reflect the implementation of Hepatitis B DNA testing. This was approved in March 2008.

Manufacture of Clinical Fresh Frozen Plasma by Apheresis

NZBS routinely manufactured clinical Fresh Frozen Plasma (FFP) from whole blood donations. Data obtained from haemovigilance schemes both in New Zealand and overseas has demonstrated that transfusion of FFP is associated with a significant risk of adverse reactions. These are predominantly allergic in nature and clinically not serious. Transfusion Associated Acute Lung Injury (TRALI) is increasingly recognised as a serious complication of transfusion of blood components and occurs most frequently following transfusion of components containing plasma. Nine to ten cases of TRALI were reported to the NZBS Haemovigilance Programme each year between 2005 and 2007.

The UK Serious Hazards of Transfusion (SHOT) report for 2005 indicates a reduction in the number of immune-mediated TRALI cases following introduction of a policy of using male only donors for clinical FFP and the plasma contribution of platelet pools. A reduction in both the number of TRALI cases and their clinical severity has been noted.

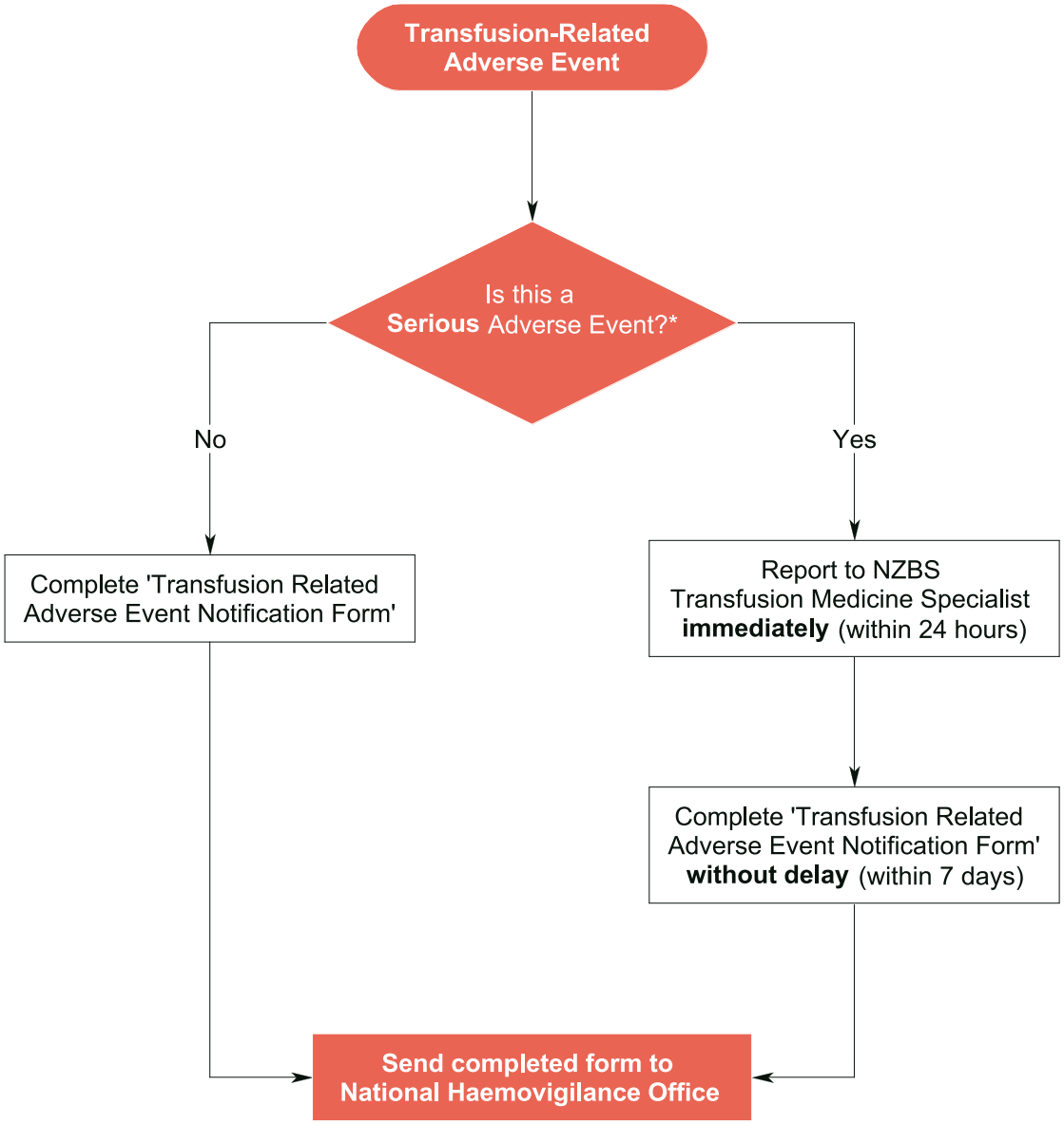
In January 2007 the AABB (American Association of Blood Banks) issued a bulletin containing recommendations to reduce the risk of TRALI. This included a move to the use of clinical FFP sourced only from male donors.

In order to maintain consistency with developing international practice, NZBS was keen to implement a system whereby clinical FFP is manufactured only from donations given by male donors. An initial assessment undertaken in 2006 indicated that this could not easily be achieved by continued reliance on FFP derived only from whole blood.

In May 2007 NZBS requested authorisation from Medsafe to amend the Manufacturing Standards to support manufacture of clinical FFP from apheresis plasma. The specification for the component was otherwise unchanged. Medsafe endorsed the proposal. Clinical FFP manufactured by apheresis, restricted to male donors with no history of transfusion, was progressively introduced from February 2008.

Appendix 1

Flowchart for Reporting Transfusion Related Adverse Events



Serious Events

A serious event is defined as any adverse event that:

- requires hospitalisation or a prolonged hospital stay
- results in persistent or significant disability or incapability
- necessitates medical or surgical intervention to prevent permanent damage or impairment of a body function
- is associated with severe temporary or permanent morbidity and/or mortality

All such should be reported to a NZBS Transfusion Medicine Specialist **immediately** (i.e. within 24 hours).

Appendix 2

Notification and Investigation of Adverse Transfusion Reaction Form page 1

Hospital:	Ward:	Consultant:

Patient NHI: **DOB:** **Sex:**

Surname:

Given Names:

Clinical advice is always available when severe transfusion reactions occur. Contact numbers can be obtained via the blood bank.

List Product(s) transfused & Donation/Batch No		Other details				
Whole blood/Red Cell products		Date of transfusion	/ /			
Platelet concentrate		Transfusion started	am / pm			
Fresh Frozen Plasma		Reaction noticed	am / pm			
Albumin		Amount transfused	ml			
Immunoglobulin			<¼	<½	<¾	>¾
Other products – specify		**Other blood products administered prior to reaction:**				

Baseline observations prior to reaction	**Temp:** °C	**Pulse:** /min	**BP:** / mm Hg

Nature of Reaction Tick or record details in relevant boxes.

Temperature peak °C	**Red urine:** ☐ Yes	☐ No	☐ Unknown
Pulse peak or trough /min	**Pain:** ☐ Chest pain	☐ Loin pain	☐ Abdo pain
BP peak or trough / mm Hg	**Unexpected bleeding:** ☐ Skin	☐ Wound	
Urticaria: ☐ Isolated ☐ Extensive	**Rash:** ☐ Macular, other _____		
Resp signs: ☐ Dyspnoea ☐ Stridor	☐ Wheeze	☐ Haemoptysis	☐ Pulmonary oedema
Systemic: ☐ Anaphylaxis/anaphylactoid reaction	**CNS disturbances:**		

Comments and further descriptions of symptoms & signs:

Medications & medical/surgical procedures:

Is further transfusion required in the next 24 hours? ☐ **Yes** ☐ **Possibly** ☐ **No**

Type of products required:

Record of any actions and investigations taken at bedside:

- ☐ Bags & giving set returned to Blood Bank
- ☐ EDTA & Serum samples to Blood Bank
- ☐ FBC ☐ Serum biochem ☐ Urine for Hb
- ☐ Coag screen ☐ Blood gases
- ☐ Blood culture from patient

Signature & print name Pager/locator

Follow up investigations should be performed if a moderate or severe reaction has occurred. Please send samples, this form, blood bag and attached IV set promptly to the Blood Bank. Please phone the Blood Bank staff to notify dispatch of samples. Turn over for recommendations on clinical assessment, blood samples required, and other relevant information.

Appendix 2

Notification and Investigation of Adverse Transfusion Reaction Form page 2

Guidelines for Management of Adverse Transfusion Reactions

First mild reaction

➢ **Mild febrile reaction**
- Temp up: < 1.5°C
- Stable haemodynamics
- No respiratory distress
- ***and*** no other symptoms

OR

➢ **Mild allergic reaction**
- Occasional urticarial spots
- ***and*** no other symptoms

Action:
1. Check labels & recipient ID
2. Slow transfusion
3. Consider giving medication:
   - ✶ Antipyretic for pyrexia, e.g. paracetamol
   - ✶ Antihistamine for urticaria
4. Continue transfusion at a slower rate with increased monitoring, e.g. BP/P/T 15-30 m
5. *If symptoms increase treat as a moderate or severe reaction*

Further transfusion and -

➢ **Recurrence of mild allergic reactions,**

OR

➢ **Recurrence of mild febrile reactions**

Action:
1. Consider giving premedication:
   - ✶ Febrile reaction – antipyretic (e.g. paracetamol)
   - ✶ Urticarial reaction – antihistamine
2. Hydrocortisone - not usually needed

Moderate and severe reactions: may include any of -

1. Fever: ≥1.5°C from baseline; or fever with rigors / chills
2. Unexpected tachycardia
3. Unexpected change of BP
4. Acute breathlessness, stridor or cyanosis; pharyngeal/ laryngeal oedema
5. Extensive erythematous or urticarial rash; pain up transfusion arm
6. JVP acutely elevated
7. Loin pain; haemoglobinuria
8. Severe apprehension

Action if a moderate or severe reaction is suspected:
1. **Stop** transfusion and review
2. **Check** label and recipient ID information is correct
3. **Replace** IV set; give saline to keep vein open and, or maintain BP
4. **Call** for medical assessment
5. **Obtain specimens:**
   - Blood group serology: 1 x 7 or 10 ml clotted (red) & 1 x 7 ml EDTA (lavender) tube *(collect away from site of transfusion)*
   - FBC and Serum biochemistry

   And consider need for:
   - Blood cultures if sepsis suspected
   - Blood gases if respiratory distress present
   - Urine to check for haemoglobinuria
   - Coagulation screen if bleeding
6. **Send** adverse reaction notification form, blood product with IV set attached (in plastic bag) to Blood Bank and specimens to relevant labs.
7. **Notify** Blood Bank by phone: discuss urgency of follow up tests and further transfusion needs.
8. **Discuss** with TMS* if severe reaction present
9. **Further treatment – depends on cause:**
   - Septic reaction likely: antibiotics (eg gentamicin & piperacillin)
   - Anaphylaxis/anaphylactoid reaction: adrenaline sc/im Adverse reaction recurs: discuss use of washed cellular products with TMS* / Haematologist
   - Other: based on clinical state, test results & TMS* consultation
   - HLA antibodies: Red cell and platelet products are now leucocyte-depleted. HLA antibodies are unlikely to cause clinical reactions.

✶ TMS = *NZ Blood Service Transfusion Medicine Specialist.*

Blood Bank Action: Blood Bank will: re-check the blood group of the patient and the units, re-screen for unexpected blood group antibodies, and when appropriate arrange for specialised microbiological cultures.

- Special methods are required to obtain microbiological samples from a unit, if sepsis is suspected.
- If a patient reacts to more than one unit, or has a severe reaction, it is essential that investigations are performed promptly. Blood Bank may provide modified blood products after appropriate investigations.

FOR ANY SEVERE TRANSFUSION REACTION AND ANY SPECIAL TRANSFUSION REQUIREMENT

➢ ***CONTACT TRANSFUSION MEDICINE SPECIALIST / HAEMATOLOGIST OR BLOOD BANK REGISTRAR IMMEDIATELY, CONTACT DETAILS CAN BE OBTAINED FROM THE BLOOD BANK.***

Prepared by the New Zealand Blood Service, 71 Great South Road, Epsom, Auckland. Telephone 09 523 5744 Fax 09 523 5754.

Appendix 3

Transfusion-Related Adverse Event Notification Form page 1

Event Identification Number (NZBS Office Use Only)

Haemovigilance | HV | | | | | | |

A. Patient Details

Hospital	Ward / Location	NHI Number	Date-of-birth / /	Gender

B. Nature Of Adverse Event

* *Notify a NZBS Transfusion Medicine Specialist Immediately.*

Type Of Adverse Event *(For definition of categories see 'Guidelines For Completing The Transfusion Related Adverse Events Notification Form' 111I042)*		***Please*** *(✓)*
(i) Incorrect Blood Component / Product Transfused *(Specify)*		
• ABO and/or Rh(D) incompatible	*	
• ABO and/or Rh(D) compatible	*	
• Other red cell incompatibility	*	
• Special requirements not met *(e.g. CMV-, irradiated; Specify)* _____	*	
• Inappropriate transfusion	*	
• Anti-D	*	
• Other *(Specify)*_____	*	
(ii) Acute Haemolytic And Other Severe Acute Transfusion Reaction *(Occurring <u>less</u> than 24 hours post transfusion)*	*	
(iii) Delayed Transfusion Reaction *(Occurring <u>more</u> than 24 hours post transfusion)*	*	
(iv) Non-Haemolytic Febrile Transfusion Reaction:		
• Mild		
• Moderate / Severe	*	
(v) Transfusion-Related Acute Lung Injury (TRALI)	*	
(vi) Transfusion-Associated Graft-versus-Host Disease (TA-GvHD)	*	
(vii) Post-Transfusion Purpura (PTP)	*	
(viii) Allergic Reaction:		
• Minor Allergic Reaction *(Urticarial or skin rash <u>without</u> fever or other symptoms)*		
• Anaphylactoid / Anaphylactic Transfusion Reaction	*	
(ix) Transfusion Associated Circulatory Overload (TACO)	*	
(x) Transfusion Transmitted Infection (TTI) *(Bacterial / viral / parasitic)*	*	
(xi) Equipment-related *(Specify)* _____		
(xii) Component-related *(Specify)*_____		
(xiii) Other type of reaction / event *(Specify)* _____		

Appendix 3

Transfusion-Related Adverse Event Notification Form page 2

Event Identification Number (NZBS Office Use Only)

Haemovigilance | HV | | | | | | |

C. Component / Product Transfused *(Record details of each component / product transfused)*

Component / Product	Donation / Batch Numbers *(Indicate whether or not modified e.g. irradiated, washed plasma etc)*
Red Cells	
Platelets (Apheresis)	
Platelets (Pooled)	
Fresh Frozen Plasma	
Cryoprecipitate	
Blood products	
Other	

C1. Date of transfusion / /	**C2. Time transfusion started**_____am / pm
C3. Volume transfused _____ ml	**C4. Was this transfusion an emergency** ☐ Yes ☐ No

D. Symptoms Present During Reaction *(Tick relevant boxes)*

☐ Fever / Temperature rise ____ °C	☐ Stridor / Wheeze	☐ Falling urinary output / Oliguria
☐ Chills / Rigors	☐ Falling O_2 saturation	☐ Haemoglobinuria
☐ Urticaria	☐ Rising pCO_2	☐ Jaundice
☐ Non-urticarial rash	☐ Loin pain	☐ Pain along infusion site
☐ Hypertension	☐ Chest pain	☐ Restlessness / Anxiety
☐ Hypotension	☐ GI symptoms (inc. abdo pain)	☐ Shock
☐ Tachycardia	☐ Unexpected bleeding	☐ No symptoms
☐ Dyspnoea	☐ Falling haemoglobin	☐ Patient under anaesthesia

☐ Chest X ray changes *(specify)*

☐ Other *(specify)*

D1. Patient's baseline observations prior to reaction

Temp _____Pulse _____BP_____

D2. Patient's observations at time of reaction

Temp _____Pulse _____BP_____

Appendix 3

Transfusion-Related Adverse Event Notification Form page 3

Haemovigilance

Event Identification Number (NZBS Office Use Only)

HV						

D2. Interval between start of transfusion and onset of symptoms

E. Patient History And Diagnosis

E1. What is the patient's primary diagnosis

E2. What was the reason for transfusion

E3. Other relevant medical and/or surgical history

E4. Pregnancy / miscarriage

☐ Yes <3 months ☐ Yes >3 months ☐ No ☐ Unknown

E5. Transfusion history

☐ Yes <3 months ☐ Yes >3 months ☐ No ☐ Unknown

E6. Pretransfusion haematology

a. If red cells transfused state pretransfusion Hb _____ Date / / Time_____ am / pm

b. If platelets transfused state pretransfusion platelet count _____ Date / / Time _____ am / pm

c. If plasma transfused state pretransfusion INR _____ Date / / Time _____ am / pm

d. If cryoprecipitate transfused state pretransfusion fibrinogen _____ Date / / Time_____ am / pm

F. Comments

Appendix 3

Transfusion-Related Adverse Event Notification Form page 4

Haemovigilance

Event Identification Number (NZBS Office Use Only)

HV						

G. *Imputability assessment*

Imputability Scale		Explanation	Event (✓)
NA	Not assessable	When there is insufficient data for imputability assessment	☐
0	Excluded	When there is conclusive evidence beyond reasonable doubt for attributing the event to alternative causes	☐
0	Unlikely	When the evidence is clearly in favour of attributing the event to causes other than the transfusion	☐
1	Possible	When the evidence is indeterminate for attributing the event either to the transfusion or alternative causes	☐
2	Likely, probable	When the evidence is clearly in favour of attributing the event to the transfusion	☐
3	Certain	When there is conclusive evidence beyond reasonable doubt for attributing the event to the transfusion	☐

Assessment Made In Consultation With:

☐ Patient's Doctor ☐ Patient's Nurse ☐ Transfusion Nurse Specialist

☐ NZBS Transfusion Medicine Specialist ☐ NZBS MO

☐ Other *(specify)*: _____

Completed By: _____

H. *Notification And Reporting*

H1. NZBS TMS informed ☐ Yes ☐ No

TMS name _____ Time_____ am / pm Date / /

H2. Notification form completed by Name_____ Date / /

Tel _____ Fax_____ Email _____

Please send completed form to:

National Haemovigilance Office
New Zealand Blood Service
Private Bag 7904
WELLINGTON

04 380 2243
04 389 5608
haemovigilance@nzblood.co.nz

NZBS Office Use Only

Notification Form Received Date / / Acknowledgement Email Sent ☐ Yes ☐ No Date / /

Follow Up Form(s) Sent *(indicate below ✓)* Date / /

☐ Incorrect Blood Component Transfused ☐ Transfusion-Associated Graft versus Host Disease

☐ Transfusion Reaction ☐ Transfusion Transmitted Bacterial Infection

☐ Post Transfusion Purpura ☐ Transfusion Transmitted Viral Infection

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Disclaimer

Protected Quality Assurance Activity

Haemovigilance has been declared a 'protected quality assurance activity' under section 54 of the Health Practitioners Competence Assurance Act 2003 as notified by the Health Practitioners (Quality Assurance Activity: New Zealand Blood Service) Notice 2006, published in the New Zealand Gazette on 6 April 2006.

The effect of this declaration is that subject to certain exceptions:

- any information that becomes known solely as a result of Haemovigilance is confidential; and
- any documents brought into existence solely for the purposes of Haemovigilance are confidential; and
- the persons who engage in Haemovigilance in good faith are immune from civil liability.

Patient Privacy

Patient identification in the form of NHI (National Health Index) number is collected as part of the initial notification of events. This identifier is used solely to enable follow up of patients in serious events or where further information is required to complete (or verify) the initial notification.

Patient information may subsequently be shared with only those DHB and NZBS health professionals directly involved in the reporting, investigation and management of individual Haemovigilance events.

The electronic data relating to the cases on which this annual report are based have been placed into an archival database from which the NHI information and unique Haemovigilance number have been removed. Patient identifier information has also been removed from the original notification forms. These have then been placed into secure document storage according to NZBS policy.

From the information held in the electronic and paper archives it is not possible to identify individual patients.

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