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Vox Sanguinis

INTERNATIONAL FORUM

Haemovigilance

Six years ago we devoted an International Forum to haemovigilance [1]. At that time a haemovigilance system had been established in seven of the 17 countries from which a contribution to the Forum was received. It therefore seemed of interest to investigate how haemovigilance has developed since then, and to enquire what the impact will be of the new European Union (EU) Blood Directive [2] that will be implemented in November 2005. Furthermore, data from haemovigilance may now be available. The questions listed below were sent to many countries. We obtained a record number of 24 contributions to this Forum.

Question 1. If a haemovigilance system had not been established in your country in 1999, has one been adopted since then, and, if not, will it be established in the near future?

Question 2. Is participating in the haemovigilance system in your country legally obligatory, or is it voluntary?

Question 3. Is reporting on transfusion-related adverse events and reactions the main purpose of haemovigilance, or are other aspects, such as the misuse of blood products, also included?

Question 4. Which adverse events must be reported?

Question 5. Could you provide us with the results of haemovigilance in the last 2 years?

Question 6. For European countries: will you adapt your haemovigilance program after the implementation of the new EU Blood Directive in November 2005?

In all but a few of the participating countries, a full haemovigilance system is now in force. In Germany only adverse transfusion reactions have to be reported, in the Czech Republic the reporting is restricted to serious transfusion reactions, and in Spain and South Africa the system is still being developed. The situation in the USA is complex. It is obligatory to report all fatal transfusion reactions to the Food and Drug Administration (FDA), but no official full haemovigilance system is used (see the contributions of the three American participants). In Québec (Canada) deaths and severe adverse reactions must be reported to the Health Canada regulatory body by the blood manufacturers, but the hospitals or physicians are not obliged to report.

In most of the countries, reporting is obligatory and in all European countries the reporting of serious transfusion reactions will become mandatory after the new EU Blood Directive is implemented in November 2005.

In only a minority of countries is reporting restricted to adverse reactions occurring after the transfusion of blood products, including transmitted infectious diseases. In most countries, additional reporting is required, or desired, ranging from reporting the misuse of blood products (i.e. not based on the proper indications), to reporting data on virtually the whole blood transfusion chain. For details, the reader is referred to the answers to question 3.

A host of interesting results of reporting under the auspices of haemovigilance have been included in the contributions to this Forum. Most are from individual studies, but there are some important general points.

(1) Acute and delayed haemolytic transfusion reactions still occur regularly, the former often as a result of ABO incompability.

(2) A surprisingly large number of cases of transfusion-related acute lung injury (TRALI) are reported, and although they were not all definitely proven, it seems that the frequency of TRALI has, to date, been underestimated. It appears that in the USA (see Menitove & Lipton) TRALI is the leading cause of transfusion-related fatalities. This raises the question of whether active measures should be taken to prevent TRALI [e.g. testing the serum of multiparous donors and donors with a history of blood transfusion for human leucocyte antigen (HLA) and granulocyte antibodies, to use male donors exclusively for fresh-frozen plasma (FFP) and platelet pools, as implemented in the UK, and to use SD (solvent detergent) plasma].

(3) There have been many cases of severe anaphylactic reactions after transfusion. In Denmark, three of 12 cases of severe anaphylactic reactions appeared to be caused by antibodies to immunoglobulin A, but in the other nine cases the cause was unknown. This indicates that anaphylactic transfusion reactions are still a serious problem.

(4) Bacterial contamination of blood products is still a frequent occurrence.

(5) Only two cases of post-transfusion purpura have been diagnosed.

(6) Although one case of transfusion-related graft vs. host disease (GvHD) has been seen in Denmark, this complication is virtually restricted to Japan.

(7) The number of cases of transmitted viral disease is low and, as shown by Rebibo *et al.* (France), the transmission of human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) is further reduced by nucleic acid amplification technology (NAT) testing.

In all European countries (except Russia?) the haemovigilance system will be adapted, if necessary, to the new EU Blood

Directive after its implementation in November 2005. This will mean that reporting serious transfusion reactions will become mandatory in all European countries. In general, however, the haemovigilance system will go much further than required by the Directive. Even in Switzerland (which is not a member of the EU) and in South Africa the Directive will be followed.

In conclusion, haemovigilance has clearly become an integral and important aspect of transfusion medicine. The results of reporting clearly show which untoward reactions are still a problem and may facilitate finding means to prevent them. It is also clear that the EU Blood Directive has, and will continue to have, a great impact on the practice of haemovigilance.

We wish to thank the participants for their detailed contributions to this Forum.

References

1 Engelfriet CP, Reesink HW, Brand B, Lévy G, Williamson LM, Manitove JE, Heier HE, Jørgensen, Politis C, Seyfried H, Smit Sibinga CTh, Faber J-C, Angel Vesga M, Selinov E, Danilova T, Tadokoro K, Krusius T, Hafner V, Reali G, d'Almeida Gonçalves J: International Forum. Haemovigilance systems. *Vox Sang* 1999; **77**:110–120

2 *Commission Directive 2005/61/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events*. Official Journal of the European Union

C. P. Engelfriet
Sanquin Research and Sanquin Diagnostic Services
PO Box 9190
NL-1006 AD Amsterdam
the Netherlands
E-mail: p.engelfriet@sanquin.nl

H. W. Reesink
Sanquin Blood Bank North-West and Sanquin Diagnostic Services
PO Box 9137
NL-1006 AC Amsterdam
the Netherlands
E-mail: h.reesink@sanquin.nl

G. Henn & W. R. Mayr

Question 1

In 1999, a compulsory haemovigilance system was put in place in Austria. It took 2–3 years to become fully established.

Question 2

The haemovigilance system is legally obligatory.

Questions 3

Adverse reactions, near-miss events and topics such as misuse of blood or deficiency of blood bags, etc., are all included in the system.

Table 1 Haemovigilance in Austria, 2004

	n	%
Allergic reaction	191	35
Febrile non-haemolytic TR	190	35
Non-febrile, non-haemolytic TR	127	23
Suspected bacterial contamination	17	3
Haemolytic TR	6	1
Delayed TR	1	0·2
Suspected viral infection	6	1
Products defect	18	3
PPT	1	0.2
	557	
Other events not mentioned above	2	
Near-miss events	60	

(From OEBIG, Austrian Hemovigilance Report, 2004)
TR, transfusion reaction.
All results can be followed up at www.oebig.at

Question 4

Adverse events that must be reported are suspected bacterial, viral or other infection that could be transmitted by blood products, acute non-haemolytic transfusion reaction, ABO incompatibility, transfusion against clinically relevant antibodies, transfusion of 'wrong' blood, transfusion-associated graft-vs.-host disease (GvHD), transfusion-related acute lung injury (TRALI), post-transfusion purpura and delayed transfusion reaction.

Question 5

The results of haemovigilance in the last 2 years are shown in Table 1.

Question 6

The haemovigilance programme will be adapted slightly to comply fully with the European Union Blood Directive.

Gabriela Henn
Wolfgang R. Mayr
Blood Donation Center for Wien, Niederösterreich and Burgenland
Austrian Red Cross
Wiedner Hauptstraße 32
A-1040 Wien/Austria
E-mail: gabriela.henn@roteskreuz.at

S. Olyntho & S. Wendel

Question 1

The Brazilian regulatory authorities have discussed extensively, since 2001, the need to establish a haemovigilance system [1]. This started as part of a larger, voluntary pilot project named the 'Sentinel Project' [2]. This project aims to

collect data on adverse effects related to blood components, laboratory reagents, hospital equipment and medicinal drugs. As a pilot project, 96 hospitals are official participants. Unfortunately, as far as blood transfusion services (BTS) are concerned, this project is not representative of the whole country. Nevertheless, all BTS are legally obliged to send all data concerning blood transfusions (based on a standard questionnaire) to the Brazilian Ministry of Health [3]. We do not consider this as an integrated haemovigilance system, given that the data are not fully analysed or reported throughout the country. Thus, we shall refer to the 'Sentinel Project' to answer the next questions, instead of the obligatory transfusion data required by the Ministry of Health.

Question 2

As stated above, there is a larger project that includes the haemovigilance system on a voluntary basis, where confidentiality is guaranteed.

Question 3

The main purpose of the report is focused on the adverse events related to transfusions; the clinical indication for the transfusion is also required, which can lead to the analysis of the misuse of blood components.

Question 4

We report on immediate (symptoms starting within the first 24 h after transfusion), and late, adverse events.

Immediate adverse events include the febrile non-haemolytic, haemolytic, allergic and anaphylactic reactions, bacterial contamination, transfusion-related acute lung injury (TRALI), circulatory overload, hypotensive reactions and non-immune haemolysis.

Late adverse events include delayed haemolytic reactions, transfusion-associated graft-vs.-host disease, erythrocyte alloimmunization and seroconversion to blood-borne diseases.

Question 5

The data sent to the 'Sentinel Project' have been collected for ≈ 3 years now, and are still under analysis for the moment; unfortunately, no national reports have been produced so far.

Question 6

The question does not apply.

References

1 Brazilian Act 10.205, March 21, 2001: D.O.U. – Diário Oficial da União; Poder Executivo, de 22 de Março de 2001, also available at http://e-legis.anvisa.gov.br/leisref/public/showAct.php?id=7479&tword= (last checked on 19/12/2005)
2 Brazilian Ministry of Health – Hemovigilance Technical Manual: http://www.anvisa.gov.br/divulga/public/sangue/hemovigilancia/manual_atualizado_jul2004.pdf (last checked on 19/12/2005)
3 Brazilian Ministry of Health Act: Agência Nacional de Vigilância Sanitária, Resolução da Diretoria Colegiada (RDC) 153, June 14, 2004: D.O.U. – Diário Oficial da União; Poder Executivo, de 24 de Junho de 2004, also available at http://e-legis.anvisa.gov.br/leisref/public/showAct.php?id=11662&tword= (last checked on 19/12/2005)

Sylvia Olyntho
Médica Assistente – Banco de Sangue
Attending Physician – Blood Bank
Hospital Sirio Libanês
Rua Adma Jafet 91
São Paulo, Brasil 01308-050
E-mail: olynthos@ihsl.com.br

Silvano Wendel
Diretor Médico – Banco de Sangue
Medical Director – Blood Bank
Hospital Sirio Libanês
Rua Adma Jafet 91
São Paulo, Brasil 01308-050
E-mail: snwendel@uninet.com.br

P. Robillard

Question 1

A new haemovigilance system was implemented in Québec, Canada, in 2000. This haemovigilance system was created as part of a complete reorganization of the blood system in Québec that occurred in 1998 with the designation of 20 regional hospitals that would oversee the transfusion activities of all Québec hospitals.

Transfusion safety officers were hired in those designated hospitals with, as a major role, the investigation and reporting of adverse transfusion events. This responsibility is exercised not only within their own hospital but also in all hospitals for which they are responsible in terms of transfusion medicine activities.

A complete description of the Québec Haemovigilance System has been published previously [1].

Question 2

In Canada, deaths that might be related to transfusion and serious adverse transfusion reactions should be reported to Health Canada regulatory body by the blood manufacturers. There is, however, no obligation for hospitals or physicians to report those events to the manufacturers or to Health Canada.

Participation in the Québec Haemovigilance System is voluntary. However, the presence of personnel dedicated to the investigation and reporting of adverse transfusion events (namely the transfusion safety officers) ensures that reporting is of good quality in Québec.

Question 3

The Québec Haemovigilance System reports on incidents, defined as all errors recognized before the start of transfusion,

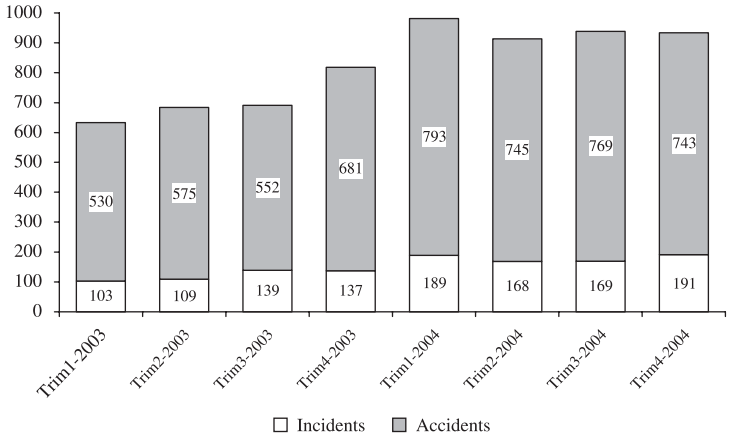

Fig. 1 Trends in reporting of incidents and accidents to the Québec Haemovigilance System by trimester (2003–2004).

and accidents, defined as all adverse transfusion reactions and all errors recognized after the start of transfusion, even if no reaction occurred. The scope of reporting includes not only fresh blood components (or labile products) but also plasma derivatives such as intravenous immune globulin, albumin, coagulation products, etc. (under pharmacovigilance in many countries).

There is also a component of surveillance of blood utilization that has started. It will be possible to study the appropriateness of blood utilization once a central transfusion registry has been established. This will occur in the near future.

Question 4

In the Québec Haemovigilance System, all adverse transfusion events are reportable to the Québec Health Ministry. All transfusion errors identified prior to the start of transfusion (incidents) are to be reported. All transfusion reactions, whether minor or serious, are to be reported along with transfusion errors not leading to a reaction. The latter two are grouped under the name 'accidents'. The accidents are classified with respect to severity and strength of association with transfusion. Severity is classified into four categories: death; vital threat; long-term morbidity; and minor or no morbidity. Association with transfusion (or imputability) is classified into five categories: definite; probable; possible; unlikely; or excluded.

For labile blood components, data on units transfused are obtained through hospital monthly reports on utilization. These data are used as denominators for incidence rate calculations. As for plasma derivatives, data on utilization are incomplete, preventing their use for incidence rate calculation.

Question 5

From 2000 to 2004, a total of 2335 incidents and 7606 (6899 for labile components and 707 for plasma derivatives) accidents possibly, probably or definitely associated with transfusion, were reported. The results for 2003 and 2004 are shown in Fig. 1. Table 2 shows that the majority of reported incidents occurred on different hospital wards (including emergency room, intensive care units and operating theatre). Many of the errors reported related to incorrect patient identification. In Table 3 the number and proportion of accidents that were reported for 2003 and 2004 are presented. Minor reactions account for the vast majority of cases. The category 'other' mainly includes events that did not cause reactions in recipients but that were deviations from standard procedures related to transfusion, such as an excessive transfusion time or wrong type of fluid used for administration. Three deaths were reported in 2003 and four in 2004. Table 4 presents data on the overall incidence of transfusion accidents by type of component. It is worth noting that the incidence is higher for platelet transfusions than for other products and that there is no difference between apheresis platelets and whole blood-derived platelets (pools of five units). Tables 5 and 6 present the incidence of selected accidents for red blood cells, platelets and fresh frozen plasma in 2003 and 2004. These haemovigilance data have already been used by advisory committees to make recommendations in order to improve blood safety in Québec [3].

Question 6

Not applicable.

References

1 Robillard P, Nawej KI, Jochem K: The Quebec hemovigilance system: description and results from the first two years. *Transfus Apheresis Sci* 2004; **31**:111–122

2 Williamson L, Cohen H, Love E, Jones H, Todd A, Soldan K: The Serious Hazards of Transfusion (SHOT) initiative: the UK approach to haemovigilance. *Vox Sang* 2000; **78** (Suppl. 2):291–295

3 Page D, Robillard P, Delage G, Poulin C: The Quebec Hemovigilance Committee: an important partner in blood safety. *Canadian Society for Transfusion Medicine Conference*. Book of abstracts 2005:58

Table 2 Incidents reported to the Québec Haemovigilance System in 2003 and 2004

Source of errors	2003 (*n* = 488)				2004 (*n* = 717)			
	n	%	*n*	%	*n*	%	*n*	%
Ward			387	79·3			587	81·9
Wrong name on tube	105	27·1		21·5	158	26·9		22·0
Incorrect conservation procedure	60	15·5		12·3	70	11·9		9·8
Component discarded (wasted)	58	15·0		11·9	116	19·8		16·2
Discrepancy between request form & specimen	53	13·7		10·9	61	10·4		8·5
Wrong blood in tube	43	11·1		8·8	61	10·4		8·5
Incorrect labelling	32	8·3		6·6	43	7·3		6·0
Wrong identification on request form	17	4·4		3·5	20	3·4		2·8
Wrong identification on both specimen and request form	13	3·4		2·7	15	2·6		2·1
Order for wrong patient	9	2·3		1·8	15	2·6		2·1
Wrong component ordered	3	0·8		0·6	7	1·2		1·0
Administrative errors	0	–		–	38	6·5		5·3
Others	11	2·9		2·2	29	4·9		4·0
Subtotal[a]	387[a]	100			587[a]	100		
Blood bank			94	19·3			121	16·9
Testing procedure error	45	47·9		9·2	50	58·7		7·0
Transcription error	16	17·0		3·3	20	16·5		2·8
Product issued for wrong patient	12	12·8		2·5	10	8·3		1·4
Wrong type of product issued	10	10·6		2·0	7	5·8		1·0
Product discarded (wasted)	3	3·2		0·6	8	6·6		1·1
Inappropriate storage condition	2	2·1		0·4	4	3·3		0·6
Incorrect labelling	0	–		–	7	5·8		1·0
Administrative errors	0	–		–	8	6·6		1·1
Others	6	6·4		1·2	13	10·7		1·8
Subtotal[a]	94[a]	100			121[a]	100		
Other sources			7	1·4			9	1·3
Product discarded (wasted)	5	71·4		1·0	3	33·3		0·4
Incorrect labelling	1	14·3		0·2	5	55·5		0·7
Administrative error	0	–		–	1	11·1		0·1
Other	1	14·3		0·2				
Subtotal[a]	7[a]	100			9[a]	100		

[a]The total could exceed 100% as one reported event may involve several errors.

Table 3 Type of accidents related to labile blood components reported to the Québec Haemovigilance System in 2003 and 2004

Accident	2003 (*n* = 1794)		2004 (*n* = 2223)	
	n[a]	%	*n*[a]	%
Mild allergic reaction	446	24·9	496	22·3
Severe allergic reaction	35	2·0	32	1·4
Febrile non-haemolytic reaction	809	45·1	890	40·1
Acute haemolytic transfusion reaction	15	0·8	11	0·5
Delayed haemolytic transfusion reaction	17	0·9	17	0·8
Delayed serological reaction	158	8·8	139	6·3
Bacterial contamination	9	0·5	7	0·3
Transfusion-related acute lung injury	6	0·3	8	0·4
Circulatory overload	77	4·3	82	3·7
Hypotensive reaction	7	0·4	8	0·4
Incorrect blood component transfused[b]	38	2·3	28	1·3
ABO and Rhesus incompatibilities	9	0·5	12	0·5
Transfused component was not ordered	2	0·1	1	0·05
Wrong product transfused	24	1·3	13	0·6
Compatible component transfused to a wrong person	3	0·2	2	0·1
Unknown diagnosis	24	1·3	55	2·5
Other	188	10·5	452	20·3

[a]The total could exceed 100% as one reported adverse event may involve several diagnoses.
[b]Item created in accordance with the definition of the Incorrect Blood Component Transfused (IBCT) category of the Serious Hazards of Transfusion (SHOT) Scheme [2]. The results apply only to labile blood components because, as previously noted, we do not have accurate denominator data for plasma derivatives.

Table 4 Incidence of accidents by type of components reported to the Québec Haemovigilance System

Components	Transfused units	Reported ATRs	Ratio per units transfused
2003			
Red blood cells	178 499	1293	1 : 138
Whole blood	265	2	1 : 133
Platelets			
Apheresis	4603	61	1 : 75
WBDP	78 423	253	1 : 310
Pools of 5 WBDP units	15 685[a]	253	1 : 62
Plasma	42 215	136	1 : 310
Cryoprecipitate	18 200	42	1 : 433
Granulocytes	33	–	–
Total	322 238	1787	1 : 180
2004			
Red blood cells	199 363	1639	1 : 122
Whole blood	208	1	1 : 208
Platelets			
Apheresis	9188	126	1 : 73
WBDP	60 259	213	1 : 283
Pools of 5 WBDP units	12 052[a]	213	1 : 57
Plasma	46 471	230	1 : 202
Cryoprecipitate	18 634	14	1 : 1331
Granulocytes	25	0	–
Total	334 148	2223	1 : 150

[a]Not included in total.

ATR, adverse transfusion reaction; WBDP, whole blood-derived platelets.

Table 5 Incidence by type of accident related to labile blood components reported to the Québec Haemovigilance System in 2003

			Platelets							
	RBC (178 499 units)		Apheresis (4603 units)		WBDP (15 685 pools)		Plasma (42 215 units)		All products (322 238 units)	
Accident	*n*	Ratio	*n*	Ratio	*n*	Ratio[a]	*n*	Ratio	*n*[b]	Ratio
Mild allergic reaction	216	1 : 826	30	1 : 153	115	1 : 136	67	1 : 630	446	1 : 723
Severe allergic reaction	13	1 : 13 731	3	1 : 1534	7	1 : 2241	12	1 : 3518	35	1 : 9207
Febrile non-haemolytic reaction	652	1 : 274	25	1 : 184	103	1 : 152	28	1 : 1508	809	1 : 398
Acute haemolytic transfusion reaction	15	1 : 11 900	–	–	–	–	–	–	15	1 : 21 483
Delayed haemolytic transfusion reaction	17	1 : 10 500	–	–	–	–	–	–	17	1 : 18 955
Delayed serological reaction	144	1 : 1240	2	1 : 2302	11	1 : 1426	1	1 : 42 215	158	1 : 2039
Bacterial contamination	5	1 : 35 700	2	1 : 2302	–	–	2	1 : 21 108	9	1 : 35 804
TRALI	1	1 : 178 499	–	–	1	1 : 15 685	4	1 : 10 554	6	1 : 53 706
Circulatory overload	60	1 : 2975	–	–	3	1 : 5228	14	1 : 3015	77	1 : 4185
Hypotensive reaction	6	1 : 29 750	–	–	–	–	1	1 : 42 215	7	1 : 46 034
Death	1	1 : 178 499	–	–	1	1 : 15 685	1	1 : 42 215	3	1 : 107 413
Incorrect blood component transfused	32	1 : 5578	–	–	2	1 : 7843	4	1 : 10 554	38	1 : 8480
ABO and Rhesus incompatibilities	7	1 : 25 500			1	1 : 15 685	1	1 : 42 215	9	1 : 35 804
Transfused component was not ordered	2	1 : 89 250							2	1 : 161 119
Wrong product transfused	20	1 : 8925			1	1 : 15 685	3	1 : 14 072	24	1 : 13 427
Compatible component transfused to the wrong person	2	1 : 89 250					1	1 : 42 215	3	1 : 107 413
Total[c]	1318	1 : 135	62	1 : 74	252	1 : 62	139	1 : 304	1794	1 : 180

[a]Ratios were calculated per pools of 5 units of whole blood-derived platelets (WBDP).

[b]The sum of columns could be less than the reported total because accidents related to whole blood, cyoprecipitate and granulocytes are not shown.

[c]The sum of rows could exceed the total as one reported adverse event may involve several diagnoses.

RBC, red blood cells; TRALI, transfusion-related acute lung injury.

Table 6 Incidence by type of accident related to labile blood components reported to the Québec Haemovigilance System in 2004

	RBC (199 363 units)		Platelets: Apheresis (9188 units)		Platelets: WBDP (12 052 pools)		Plasma (46 471 units)		All products (334 148 units)	
Accident	***n***	**Ratio**	***n***	**Ratio**	***n***	**Ratio**[a]	***n***	**Ratio**	***n***[b]	**Ratio**
Mild allergic reaction	246	1 : 810	72	1 : 128	96	1 : 126	72	1 : 645	497	1 : 672
Severe allergic reaction	8	1 : 24 920	3	1 : 3063	11	1 : 1096	10	1 : 4647	32	1 : 10 442
Febrile non-haemolytic reaction	725	1 : 275	37	1 : 248	81	1 : 149	49	1 : 948	893	1 : 374
Acute haemolytic transfusion reaction	11	1 : 18 124	–	–	–	–	–	–	11	1 : 30 377
Delayed haemolytic transfusion reaction	16	1 : 12 460	–	–	1	1 : 12 052	–	–	17	1 : 19 656
Delayed serological reaction	130	1 : 1534	3	1 : 3063	6	1 : 2009	–	–	139	1 : 2404
Bacterial contamination	5	1 : 39 873	1	1 : 9188	1	1 : 12 052	–	–	7	1 : 47 735
TRALI	5	1 : 39 873	1	1 : 9188	1	1 : 12 052	1	1 : 46 471	8	1 : 41 769
Circulatory overload	68	1 : 2932	1	1 : 9188	2	1 : 6026	11	1 : 4225	82	1 : 4075
Hypotensive reaction	7	1 : 28 480	1	1 : 9188	–	–	–	–	8	1 : 41 769
Death	3	1 : 66 454	–	–	–	–	1	1 : 46 471	4	1 : 83 537
Incorrect blood component transfused	23	1 : 8668	–	–	1	1 : 12 052	4	1 : 11 618	28	1 : 11 934
ABO and Rhesus incompatibilities	10	1 : 19 936					2	1 : 23 236	12	1 : 27 846
Transfused component was not ordered	1	1 : 199 363							1	1 : 334 148
Wrong product transfused	10	1 : 19 936			1	1 : 12 052	2	1 : 23 236	13	1 : 25 704
Compatible component transfused to the wrong person	2	1 : 99 682							2	1 : 167 074
Total[c]	1639	1 : 122	126	1 : 73	213	1 : 57	230	1 : 202	2223	1 : 150

[a]Ratios were calculated per pools of 5 units of whole blood-derived platelets (WBDP).

[b]The sum of columns could be less than the reported total as accidents related to whole blood, cyoprecipitate and granulocytes are not shown in the table.

[c]The sum of rows could exceed the total as one reported adverse event may involve several diagnoses.

RBC, red blood cells; TRALI, transfusion-related acute lung injury.

Pierre Robillard
Institut National de Santé Publique du Québec
4835 Christophe-Colomb
Montréal, QC, Canada H2J 3G8
E-mail: pierre.robillard@inspq.qc.ca

P. Turek

Question 1

Collection of information on untoward reactions to blood components in recipients has a long tradition in the Czech Republic. Duty to report post-transfusion reactions was introduced by a Ministerial Decree in 1976. Since then, reports of untoward effects of transfusion (both mild and severe) have been collected and analysed at a local hospital level. Severe reactions and transfusion-related deaths had to be reported to the Ministry of Health. In 1997, blood components were implemented into the Drug Law and obligatory reporting was artificially narrowed to only 'adverse effects related to the quality of the product (drug)'. Reporting of other adverse effects became voluntary (data being collected by the Blood Transfusion Society) with very low effectivity. A new law has now been prepared for Parliamentary discussion, which should extend obligatory reporting, at least to the scope of the European Union Blood Directive, probably the reporting of adverse effects and events not related to the quality of the product will also be included.

Question 2

Reporting of severe adverse effects related to the quality of the product is obligatory; other parts of haemovigilance are voluntary at present. A complex obligatory system of haemovigilance with monitoring of all adverse effects and events in donors and/or recipients and reporting severe effects and events is in preparation.

Question 3

The new system in preparation should also cover confusions (i.e. the wrong unit to the wrong patient) and near-misses, but not misuse in the sense 'non-adherence to indication criteria'.

Question 4

All adverse events in the blood chain should be monitored and documented. Severe adverse events, which may affect

Table 7 Use of blood components and transfusion-related adverse reactions in Czech Republic 2003

	Units issued		
	Red cells 414 thds.	Platelet (therap. doses) 22·6 thds.	Plasma (240 ml) 170 thds.
Acute immune haemolysis	2	0	0
Delayed immune haemolysis	4	0	0
FNHTR	300	11	21
Allergy/anaphylaxis	92	42	101
TRALI	1	0	0
Post-transfusion purpura	1	0	0
Bacterial/sepsis	0	0	0
Transmission of infection	0	0	0

(There is a general feeling that adverse effects are underreported)
FNHTR, febrile non-haemolytic transfusion reaction; thds., thousands; therap., therapeutic; TRALI, transfusion-related acute lung injury.

persons different from those in whom the problem was diagnosed, should be reported.

Question 5

No severe adverse effects related to the quality of the product were reported in 2003 and 2004. Results from the voluntary system in 2003 are shown in Table 7.

Question 6

It is expected that a new law which covers at least the European Union Blood Directive matters will be agreed on by the end of this year.

Petr Turek
General Faculty Hospital, Prague,
U Nemocnice 2, 128 00 Prague, Czech Republic
E-mail: turek.petr@vfn.cz or turek.petr@centrum.cz

T. Krusius & S. Koskinen

Question 1

During the last few years, a voluntary haemovigilance system has been introduced in Finland. The system is not regulated by legislation. Hospitals report serious adverse reactions, transfusion of incorrect blood components and near-miss events, on a patient basis, to the Finnish Red Cross Blood Service. The Blood Service assists hospitals in clearing up adverse reactions by performing necessary laboratory tests, maintaining a national registry, drawing up annual reports and assisting in training hospital staff. Reporting has become more active from year to year.

Question 2

At present, the reporting of adverse reactions is voluntary, but the situation will change following implementation of the European Union (EU) Directive into Finnish legislation. The new blood service law, which will come into force 1 November 2005, makes reporting legally mandatory.

Question 3

Hospitals are also encouraged to report, voluntarily, transfusions of incorrect blood components, near misses and the annual number of mild adverse reactions (e.g. mild allergic and non-haemolytic febrile transfusion reactions). The goal is to use haemovigilance data in developing hospital transfusion processes and training of staff.

A separate national database for benchmarking the clinical use of blood components has been established. Information from this database is used to improve the clinical use of blood components.

Question 4

Hospitals report acute and delayed immunological haemolysis, non-immunological haemolysis, anaphylaxis and anaphylactoid reactions, post-transfusion bacterial and viral infections, transfusion-related acute lung injury (TRALI), post-transfusion purpura (PTP), graft-vs.-host disease (GvHD) and other clinically serious reactions. The same adverse reactions are mandated by the EU Directive to be reported.

Question 5

See Table 8.

Table 8 Transfusion-associated serious adverse reactions, incorrect blood components transfused and near-miss events in Finland 2003–2004

	2004	2003
Acute immunological haemolysis	4	3
Delayed immunological haemolysis	5	3
Non-immunological haemolysis	0	0
Anaphylaxis/anaphylactoid reaction	25	7
Post-transfusion bacterial or viral infection	2	2
TRALI	3	4
PTP	0	1
GvHD	0	0
Other serious adverse reaction	0	0
Incorrect blood component transfused, no symptoms	22	9
Near miss event	6	2
Red cell components distributed (units)	255 377	270 620
Platelet components distributed (clinical doses)	34 858	34 950
Fresh-frozen plasma distributed (units)	40 684	45 196

GvHD, graft-vs.-host disease; PTP, post-transfusion purpura; TRALI, transfusion-related acute lung injury.

Question 6

The Parliament has passed a new law on blood service activities based on the EU directive. The Ministry of Social Welfare and Health is preparing a decree on haemovigilance and traceability. The decree is based on the Commission Directive on haemovigilance and mandates hospitals to report serious adverse reactions and events to the blood establishment which is responsible for assisting hospitals in clearing up serious adverse reactions by performing necessary laboratory tests and lookback procedures, to maintain a haemovigilance registry and to forward patient-based and annual reports to the health authorities.

Tom Krusius
Medical Director
Finnish Red Cross Blood Service
E-mail: tom.krusius@bts.redcross.fi

Sinikka Koskinen
Clinical specialist
Finnish Red Cross Blood Service
E-mail: sinikka.koskinen@bts.redcross.fi

E. Taaning & J. Jørgensen

Question 1

The Danish Registration of Transfusion Risk (DART) was established in 1999 [1].

Question 2

The reporting of data to DART and The Danish Transfusion Database (DTDB) is voluntary and confidential, whereas official bodies, as a legal obligation, provide other data.

Question 3

In Denmark, data concerning nearly all parts of the transfusion chain, from collection of blood through to the production of blood components and to the registration of transfusion and complications, has been collected for years. Haemovigilance data collected in Denmark are as follows.

(1) Data concerning blood collections, production of blood components, transfused components, and components not used for transfusion, have been produced by the central health authorities [The Danish Medicines Agency (DMA)] since 1994. Data are published in annual reports.

(2) Statistics of complications in connection with blood collection have been made by The Blood Donors in Denmark (BiD) since 1998.

(3) Data concerning the number of donors found to be positive in screening for viral markers [hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and human T-cell lymphocytotrophic virus (HTLV)] and data concerning the number of patients infected with these viruses as a result of blood transfusion and the result of lookback programmes for HCV and HIV, have been collected by The Department of Epidemiology, The State Serum Institute, since 1985.

(4) DART provides an analysis of risks in connection with transfusion of blood and blood components and 'near-miss' events in Denmark. DART was launched by the Danish Society of Clinical Immunology (DSKI), and the collection of reports from all of Denmark began in January 1999. The organization is very similar to the Serious Hazards of Transfusion (SHOT) initiative in the UK. The first DART report was published in 2000 [2].

(5) The DTDB collects data concerning the use of blood components. The following data are registered for each hospitalized patient: number of blood components transfused; age, gender, diagnoses and treatments; and haemoglobin concentration, platelet count and coagulation parameters.

The DTDB makes it possible to validate the transfusion praxis of a department by comparison, for example, of the praxis before and after a change in policy, of the actual praxis with the official or intended transfusion policy, or to compare the praxis for patients with the same diagnosis undergoing similar treatment in another setting. The first report was published in 2001 [2].

Question 4

The following adverse events are reported to DART.

(1) Incorrect blood components transfused (IBCT).

(2) Acute transfusion reactions (ATR).

(3) Delayed transfusion reactions (DTR).

(4) Transfusion associated graft versus host disease (TA-GvHD).

(5) Transfusion related acute lung injury (TRALI).

(6) Post transfusion purpura (PTP).

(7) Transfusion transmitted infection (TTI).

Question 5

During the first 6 years, DART received 124 reports. In Denmark, ≈ 450 000 blood components are transfused per year. Thus, the report rate was 4·2 per 100 000 components transfused. The number of reports varied only a little from year to year.

The distribution of the events, according to reporting categories, is shown in Fig. 2. About half of the severe events concerned the transfusion of incorrect blood components (IBCT) (54%), and 40% concerned immunological complications. Only 6% of the reported events concerned TTI.

The IBCT events (67 cases) included 10 cases with transfusion of ABO major-incompatible units of red cells (one blood group B patient died after receiving 100 ml of type A blood). In 24 cases, the unit was labelled with the name and social security number of another person, but nevertheless given to the wrong patient. In 43 cases, the unit was dedicated to the patient, but the type of component was wrong.

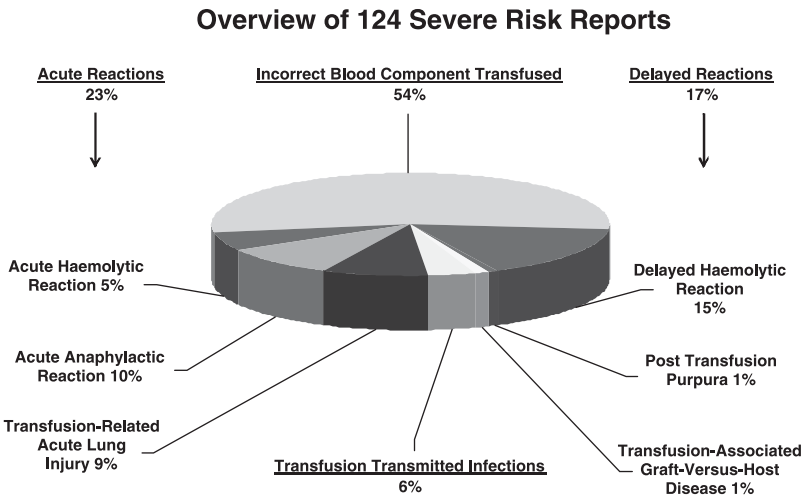

Fig. 2 Overview of 124 severe risk reports received by DART during the first 6 years.

Table 9 Transfusion-related mortality/morbidity or clinical outcome [definitions used by the Serious Hazards of Transfusion (SHOT) initiative] and imputability for the relationship between the reaction and the transfusion

Clinical outcome	IBCT	ATR[a]	TRALI	DHR	PTP	TA-GvHD	TTI	Total
Death	2			1		1		4
Major morbidity	10	11	7		1		2	31
Minor or no morbidity	55	7	4	18			5	89
Total	67	18	11	19	1	1	7	124

AAR, acute anaphylactic reaction; AHTR, acute haemolytic reaction; ATR[a], acute transfusion reaction (AHTR and AAR); DHR, delayed haemolytic reaction; IBCT, incorrect blood component transfused; PTP, post transfusion purpura; TA-GvHD, transfusion-associated graft-versus-host disease; TRALI, transfusion-associated acute lung injury; and TTI, transfusion transmitted infection.

The immunological complications included six acute haemolytic reactions (two anti-Wr[a], two anti-Fy[a] and two undetermined), 12 acute anaphylactic reactions (three anti-immunoglobulin A and nine unknown), 11 TRALI, 19 delayed haemolytic reactions (one patient with anti-c in plasma died), one PTP (anti-HPA-1a in serum), and 1 TA-GvHD (the patient died). The transfusion-transmitted infections included three cases of hepatitis A virus and four cases of bacterial contamination of platelets.

The frequency of immunological complications caused by fresh-frozen plasma was four times higher than that of complications caused by red cells.

The clinical outcome is listed in Table 9. Four patients died, corresponding to 0·1 per 100 000 transfused components. Thirty-one patients had a severe reaction, corresponding to 1·1 per 100 000 transfused components.

The collection of near-miss reports began as a pilot study, involving the five largest transfusion centres in 2001. A near-miss failure is defined as any error that, if undetected, could result in the determination of a wrong blood group, or issue of an incorrect or inappropriate component, but which was recognized before transfusion occurred. Half of the events reported were failures related to the collection of blood samples from the patients. A more detailed analysis of the 'sample failures' showed that a technician did not collect 75% of the blood samples, 55% were not collected during normal working hours and 60% were collected in an acute situation. Only 20% of the wrong samples were taken in a routine situation.

Question 6

Yes, we will continue the collection of data for the haemovigilance programme in parallel with registration to the EU.

References

1 Jorgensen J, Taaning E: DART – A Voluntary System of Haemovigilance in Denmark. *Transfus Alternatives Transfus Med* 2003; 5:260–264

2 http://www.dtdb.dk Papers and reports on haemovigilance in Denmark

Ellen Taaning
Herlev Hospital, University of Copenhagen
Department of Clinical Immunology and Blood Bank
75 Herlev Ringvej
DK-2730 Herlev
Denmark
E-mail: elta@herlevhosp.dk

Jan Jørgensen
Aarhus University Hospital, Skejby Sygehus
Department of Clinical Immunology
Regional Blood Transfusion Centre
Brendstrupgaardsvej
DK-8200 Aarhus N
Denmark
E-mail: janjorgensen@dadlnet.dk

D. Rebibo, L. Hauser, P. Zorzi, J. F. Legras, A. Slimani, M. Vo-Mai, J. H. Trouvin & G. Andreu

Question 1

A haemovigilance system was established in France in 1994 [1]. The French Health Products Safety Agency [Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS)] is in charge of the whole haemovigilance network.

Question 2

Participation in the haemovigilance system is legally obligatory.

Question 3

Traceability of blood components is a critical step to ensure satisfactory functioning of the haemovigilance network. Therefore, all data related to traceability of blood components are recorded and analysed each year.

As related to recipients' adverse reactions, the founding decree of haemovigilance states that, 'Any person, physician, pharmacist, dental surgeon, midwife or nurse who observes an effect unexpected or undesirable due or likely due to Labile Blood Components (LBC), must notify it without delay' [1]. The notification of adverse reactions in recipients of blood components is compulsory, regardless of the severity of the reaction. In addition, 'severity 0' reactions, which consist of the transfusion of an inappropriate blood component as a result of a dysfunction at any step of the transfusion chain, without any clinical or biological adverse reaction, has to be declared.

The haemovigilance network gathers all the data relating to the epidemiological follow-up of donors. These data are transferred to the National Institute of Sanitary Surveillance (INVS), and form the basis for an annual evaluation of the residual risk of virus transmission [hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and human T-cell lymphocytotrophic virus (HTLV)] by transfusion, which is regularly published in the literature [2]. Moreover, since 2002, any postdonation information that may affect transfusion safety is notified daily to the AFSSAPS, and reported in an annual survey. Currently, information on adverse reactions in donors are kept at the regional blood centres and are not presented in a national annual report.

Question 4

At present, the following adverse events must be reported at a national level:

- adverse reactions (immediate or delayed) in recipients of blood components, regardless of the degree of severity;
- 'severity 0' reactions (see the response to question 3 for definition); and
- postdonation information that may affect the transfusion safety and quality of the products.

Question 5

In 2003–2004, 5 003 759 blood components (BC) were collected for transfusion: 4 059 240 red cell concentrates (RCC); 363 546 apheresis platelet concentrates (APC); 50 368 pooled platelet concentrates (PPC) prepared from buffy-coat; and 530 605 units of therapeutic fresh-frozen plasma (FFP).

The global traceability of BC is stable, ranging from 97·88% to 98·98%.

Recipient's adverse reactions

All recipient's adverse reactions are declared, regardless of their severity or transfusion imputability. The adverse reactions are categorized according to:

- their type: immediate (less than 8 days after transfusion), or delayed;
- their severity, graded as: 0, absence of clinical and/or biological signs; 1, immediate reaction with absence of vital threat or long-term threat; 2, long-term morbidity; 3, vital and immediate threat; and 4, death of the recipient; and
- the imputability of transfusion, graded as: 0, excluded; 1, doubtful; 2, possible; 3, probable; and 4, definite.

Main results

The overall incidence of the recipient's adverse reactions was stable during 2003 and 2004, at 3 per 1000 BC.

A total of 15 185 reactions were notified, among which 42% (n = 6378) have an imputbility of 3 or 4; 64·3% (n = 4101) of the latter are immediate reactions; and 35·7% (n = 2276) are delayed reactions.

In the following text, data will be provided for all imputability levels (0 to 4), and some analysis of data considering only imputability 3 and 4 will be specifically mentioned.

Immediate adverse reactions

Adverse reactions are described below.

(1) ABO incompatibility. Forty-two ABO incompatibilities were reported, of which 30 had an imputability of 3 or 4; among the latter, 20 were related to RCC, nine to APC and one to FFP transfusion. Considering the severity of RCC-related cases, we observed 14 grade 1, three grade 3 and three grade 4.

(2) Transfusion-transmitted bacterial contamination (TTBC). A total of 493 suspicions of TTBC were reported, and 12

Table 10 Transfusion-transmitted bacterial contamination (TTBC) incidence during the period 2003–2004

	1 TTBC/N BC		
Blood components	**All severity**	**Severity 3**	**Death**
Apheresis platelet concentrates	1/60 591	1/121 182	1/181 773
Pooled platelet concentrates	1/50 368	–	–
Red cell concentrates	1/811 848	1/2 029 620	1/4 059 240
Total blood components	1/416 980	1/1 000 752	1/1 667 920

BC, blood components; TTBC, transfusion-transmitted bacterial contamination.

Table 11 Evolution of the residual risk for hepatitis C virus (HCV), human immunodeficiency virus (HIV) and hepatitis B virus (HBV)

	Residual risk per 10^6 donations		
	Before NAT	**After NAT for HIV and HCV**	
Viruses	**1998–2000**	**2001–2003**	**2002–2004**
HIV	0·73	0·32	0·26
HCV	1·16	0·1	0·17
HBV	1·81	1·57	0·42

NAT, nucleic acid amplification testing.

cases with positive culture in BC were confirmed with imputability 3 or 4. The incidence of this type of reaction (imputability 3 or 4), according to BC types is reported in Table 10. As we have haemovigilance data records since 1994, it was of interest to analyse the evolution of the incidence of TTBC between 1994 and 2004. It shows a significant decrease for all kinds of BC and severity, but relatively unchanged for deaths. This is more evident for platelet concentrates, as shown in Fig. 3.

(3) Transfusion-related acute lung injury (TRALI). Forty-seven cases of TRALI were notified: 30 with a strong association with transfusion (imputability 3 and 4) and complying with rigorously defined criteria for diagnosis; 13 were related to RCC (incidence = 1/312 249); 12 were related to APC (incidence = 1/30 296); and five were related to plasma (incidence = 1/106 221). We observed four fatalities – one related to RCC, and the remaining three to APC transfusion.

(4) Volume overload. A total of 442 volume overload events were notified, with five deaths with imputability 3 and 4.

Delayed adverse reactions

A huge majority (94·6%) of these type of reactions involves the occurrence of red cell antibodies after transfusion.

Regarding viral transmission, 214 viral contaminations in relation to blood transfusion were initially notified. However, only two were considered of high imputability (imputabilities 3 and 4) after analysis. These two cases (one for HBV and the other for cytomegalovirus), corresponded to donations obtained during the window period and both occurred in 2003.

The residual risk for HCV, HIV and HBV has been calculated over a longer period of time, from 1998 to 2004 [2]. The results, expressed as the residual risk per million donations, are shown in Table 11. A significant decrease is observed for the three viruses, in part related to the implementation of nucleic acid amplification technology (NAT) testing for HIV and HCV in 2001.

Donor haemovigilance

Since April 2002, postdonation information that may affect transfusion safety has been notified to the national authority

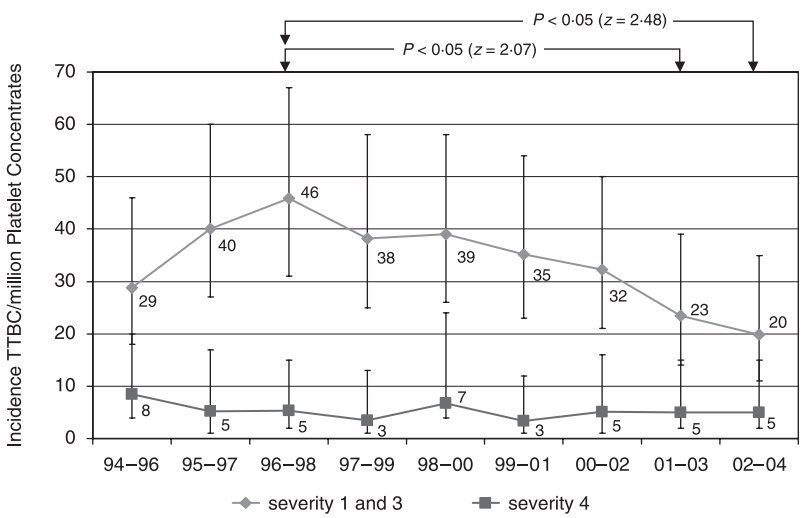

Fig. 3 Evolution of the incidence of platelet concentrates [apheresis platelet concentrates (APC) and pooled platelet concentrates (PPC)] and transfusion-transmitted bacterial contamination (TTBC) between 1994 and 2004.

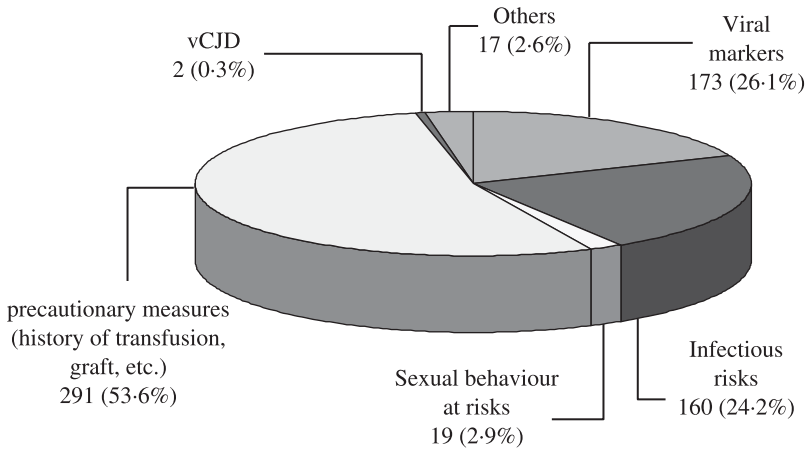

Fig. 4 Postdonation information between 2002 and 2004.

(AFSSAPS): 570 notifications were received in 2003 and 2004.

The most important part of the postdonation information concerns precautionary measures such as a previous history of transfusion, neurosurgery and infectious risks after donation (like flu-syndrome, urinary or digestive infection). The main results (analysis of the total number of notifications received from April 2002 to December 2004) are shown in Fig. 4.

Question 6

The haemovigilance network organization shall be reinforced in the process of Directive transposition in the National Legislation. The decree of transposition is in its final steps before publication.

In regard to reporting, the main new dispositions will be the reporting of every severe event (as defined in the European Directives), and of every severe reaction occurring in blood donors.

The new regulation will also emphasize the importance of regular evaluation of all the reported events, as well as the organization of all kind of studies (clinical, epidemiological, etc.) dedicated to adverse events and reactions.

In regard to the network organization, the role of all the participants (hospital- and clinic-based haemovigilance correspondents, blood transfusion establishment haemovigilance correspondents, Regional co-ordinators for Haemovigilance) and the respective responsibilities of all the institutions involved at a national level (AFSSAPS, EFS, military blood transfusion centre – CTSA – and InVS) and at a regional level (Regional Direction for Social and Sanitary Action – DRASS) have been fully redefined, in order to build a coherent and functional network.

Moreover, an AFSSAPS National Commission of Haemovigilance will be created, in charge of giving advice on the haemovigilance data, proposing complementary surveys and studies to be performed in the field of haemovigilance, and giving advice to the General Director of AFSSAPS on new safety measures to be taken to prevent the recurrence of adverse events and/or reactions.

We expect that this new regulation will be published and the whole new organization will be in place before the end of 2005. Finally, as far as we know, this project of new regulation in France is expected to comply with all the dispositions set in the ongoing project of the EU Technical Directive regarding traceability requirements and notification of serious adverse reactions and events.

References

1 Décret n° 94-68 du 24 janvier 1994 relatif aux règles d'hémovigilance pris pour application de l'article L.666-12 du code de la santé publique et modifiant ce code (deuxième partie: décrets en Conseil d'Etat)

2 Pillonel J, Laperche S: et l'Etablissement Français du Sang: Trends in risk of transfusion-transmitted viral infections (HIV, HCV, HBV) in France between 1992 and 2003 and impact of nucleic acid testing (Nat). *Eurosurveillance* 2005; 10:1–3

Danielle Rebibo
100, Avenue de Suffren
75015 Paris
France
E-mail: danielle.rebibo@efs.sante.fr

Lisette Hauser (E-mail: lisette.hauser@efs.sante.fr)
Ahmed Slimani (E-mail: ahmed.slimani@efs.sante.fr)
Georges Andreu (E-mail: georges.andreu@efs.sante.fr)
100, Avenue de Suffren
75015 Paris
France

Pierrette Zorzi (E-mail: Pierrette.ZORZI@afssaps.sante.fr)
Jean-François Legras
(E-mail: Jean-Francois.LEGRAS@afssaps.sante.fr)
Maiphuong Vo-Mai
(E-mail: Maiphuong.VOMAI@afssaps.sante.fr)
Jean-Hugues Trouvin
(E-mail: Jean-Hugues.TROUVIN@afssaps.sante.fr)
143, 147 Boulevard Anatole France 93285
Saint-Denis Cedex
France

V. Kretschmer, B. Keller-Stanislawski & D. Mentzer

Question 1

Germany has implemented a haemovigilance system, which is part of the pharmacovigilance system. The mandate, competence and responsibilities of the pharmacovigilance system are described in the German Drug law (AMG) and are fully compliant with European Drug Regulation.

In Germany, the producer (e.g. blood donation service/blood transfusion institute) of blood components has to apply for a marketing authorisation and therefore this process is regulated as for all other pharmaceuticals. Once a new blood component has been authorised through the Paul-Ehrlich-Institute (PEI), as the competent authority, all suspected serious adverse reactions following a transfusion have to be reported immediately (or at least not later than 15 days) by the marketing authorisation holder of the blood component to the PEI.

Unless other requirements have been laid down as a condition for granting marketing authorisation, reports of all adverse reactions must be submitted to the PEI in the form of a periodic safety update report (PSUR), immediately upon request or at least every 6 months after marketing authorisation and until the the product is placed on the market. PSURs shall also be submitted immediately upon request, or at least every 6 months during the first 2 years after the product has been initially placed on the market, and once a year for the following 2 years. Thereafter, the reports shall be submitted at three-yearly intervals, or immediately upon request. For blood products, annual PSURs are required in the event of a recall, a serious adverse reaction or a suspected serious adverse reaction.

Transfusion errors need not be reported to the PEI because, in general, the reaction is caused by inappropriate use rather than by the blood component itself. Therefore, at a national level, an overview concerning the current incidence of ABO-incompatible transfusions in Germany is not available. Moreover, it should be mentioned that these reporting requirements describe the obligations of the blood donation service/blood transfusion institute, whereas the reporting obligations of physicians are described in the transfusion law (TFG), which came into force in July 1998.

According to the transfusion law it is mandatory for physicians to immediately report all adverse events (including transfusion errors) following a transfusion to the transfusion officer of the unit and the transfusion chief co-ordinator of the hospital. In addition, all adverse reactions following transfusion must be reported to the blood donation centre and, in the event of serious adverse drug reactions, it is also mandatory for physicians to notify the PEI.

The PEI has a responsibility to inform the federal health authorities of the states as the national competent authority for blood components.

In summary, reporting requirements of transfusion reactions in Germany are described in two different laws: the drug law (AMG) and the transfusion law (TFG).

Additionally, all physicians in Germany have to report suspected adverse drug reactions, according to their codex of health care professionals, to the Drug Commission of the German Medical Association (AKdÄ). The PEI and the AKdÄ exchange information regarding suspected adverse drug reactions.

Question 2

See the answer to Question 1.

Question 3

See the answer to Question 1. The reporting is not related to aspects of blood transfusion other than adverse reactions and transfusion-transmitted infections.

Question 4

See the answer to Question 1.

Question 5

Data of the PEI. In 2002 and 2003, a total of 376 serious suspected transfusion reactions, including bacterial contaminations, were reported to the PEI (Table 12) together with 1778 non-serious transfusion reactions (Table 13). In 2002 and 2003 no transmission of hepatitis C virus (HCV) or human immunodeficiency virus (HIV), but a total of seven cases of transfusion related (certain or probable) hepatitis B virus (HBV) infections were reported to the PEI within this period.

Question 6

Germany will certainly adapt its haemovigilance programme in accordance with the implementation of the new EU Blood Directive. At present the details of the issue regarding the reporting of transfusions errors are under discussion.

Table 12 Overview of the serious transfusion reactions reported to the Paul-Ehrlich-Institute (PEI) in 2002 and 2003

	2002	2003	Total
Haemolytic reaction (transfusion errors)	10 (1)	9 (3)	19 (4)
Allergic reaction (including purpura)	110	95	205
Bacterial Infection	16	11	27
Transfusion-related acute lung insufficiency (TRALI causality certain)	25 (3)	35 (11)	60 (14)
Febrile reaction	24	29	53
Others	12	0	12
Total	197	179	376

Table 13 Overview of the non-serious suspected transfusion reactions reported to the Paul-Ehrlich-Institute (PEI) in 2002 and 2003

	Haemolytic TR[a]	Allergic TR	TRALI[b]	Bacterial TR	Febrile TR	Inadvertent use	Other TR
2002	12	585	33	6	362	0	137
2003	17	338	43	5	168	1	71

[a]TR, transfusion reaction.
[b]TRALI, transfusion-related acute lung insufficiency.

V. Kretschmer
Institute for Transfusion Medicine and Haemostaseology
University Hospital
Conradistrasse
Marburg D35033
Germany
E-mail: kretschv@mailer.uni-marburg.de

B. Keller-Stanislawski
D. Mentzer
Department Safety of Medicines and In Vitro-Diagnostics
Paul-Ehrlich-Institute
Paul-Ehrlich-Str. 51-59
63225 Langen
Germany
E-mail: kelbr@PEI.de

C. Politis

Question 1

The Hellenic National Co-ordinating Haemovigilance Centre (for short, SKAE, from its name in Greek) was founded in November 1995 and quickly developed a wide range of activities. SKAE is a founder member of the European Haemovigilance Network and organized the 4th European Haemovigilance Seminar in Athens in 2001.

Question 2

Participation in the system is voluntary. In 2003, 48 (50%) of the blood services participated, representing 46% of the country's blood supply.

Question 3

SKAE's declared objectives include the collection, recording and analysis of information on adverse events throughout all stages of the donation and transfusion of blood and blood products. In particular, the recording of adverse events is not limited to those occurring in the recipient; SKAE is already recording and studying adverse events at the other end of the blood chain, in all kinds of donors. Another interest, dating from the first days of SKAE, is in the epidemiological surveillance of viral infections in blood donors.

Question 4

SKAE requests that all adverse events be reported. Thus, all those associated with viral, bacterial or parasitic infectious agents are required, as well as those of a non-infectious nature. The latter include immediate reactions during blood transfusion (haemolytic, wrong blood, non-haemolytic febrile, allergic and anaphylactic, bacterial contamination, TRALI), delayed effects [delayed haemolytic reactions, alloimmunization against red cells, human leucocyte antigen (HLA) or platelet antigens, graft vs. host disease (GvHD)], post-transfusion purpura and alanine aminotransferase (ALT) elevation.

Question 5

Participating blood services issued 371 456 blood components in 2003 (265 326 red blood cells, 88 442 fresh-frozen plasma and 17 688 platelets). A total of 21 serious adverse events were recorded, for an overall rate of 0·6 per 10 000 units. The breakdown of type of event was as follows:

- allergic or anaphylactic, 10;
- haemolytic, 5 (one caused by ABO incompatibility);
- non-haemolytic febrile, 4;
- TRALI, 1; and
- bacterial contaimination, 1.

Furthermore, 435 adverse events of all levels of severity were recorded (11·7 per 10 000 units). The vast majority of these were non-haemolytic febrile reactions (207, 47·6%) or allergic and anaphylactic events (204, 46·9%).

Data were obtained in 2003 on 62 218 blood donors, among whom 32 severe adverse events were recorded (0·5 per 1000 donors). The majority of these (29, 91%) were loss of consciousness, with most (18) caused by hypovolemia. Serious injuries or accidents were reported in 56 cases (0·9 per 1000 donors), 37 of which (66%) were soft tissue damage, while the remaining 19 (34%) were falls.

Question 6

There will be developments in haemovigilance in Greece in response to the new European Union Blood Directive, but the full extent of these will become clear when the further 'daughter' Directives are issued. One necessary step is that reporting will become mandatory, as far as serious adverse events are concerned. However, SKAE is proposing to support

a programme that will go far beyond this, including the reporting of all adverse events, not only in recipients but also in donors, and also a range of other activities, such as the development of quality indicators, educational programmes, extensive collaboration with the relevant scientific societies (haematologists and others), meetings at national, regional and local levels, and the development of guidelines.

Acknowledgements

SKAE operates as a network, whose regional co-ordinators are A. Manitsa (for Northern Greece), G. Martinis (Thrace), O. Marandidou (Piraeus and Southern Greece), E. Zervou (Epirus and Western Greece) and M. Hatzitaki (Thessaly).

C. Politis
Director
3rd Regional Blood Transfusion Centre
Athens General Hospital 'George Gennimatas'
154 Messogeion Avenue
GR 115 27 Athens, Greece
E-mail: cpolitis@hol.gr

Emer Lawlor & Stefan Laspina

Question 1
The National Haemovigilance Office (NHO) in the Republic of Ireland was set up in October 1999 and the scheme has been fully operational since January 2000. Prior to this date, individual hospitals sent reports to the UK Serious Hazards of Transfusion (SHOT) initiative. Annual Reports have been published yearly since 2000.

Question 2
The scheme is not mandatory, but reporting has been considered to be part of the professional responsibility of all healthcare professionals and is anonymised.

Question 3
The scheme incorporates both a reporting system for serious adverse reactions and events to the NHO, and a strong educational component covering transfusion medicine in the hospitals. When the NHO was set up, the Department of Health and Children funded the appointment of Transfusion Surveillance Officers (TSOs) in each hospital or group of hospitals, depending on size. These TSOs (who come from a nursing or laboratory background) report serious adverse events and reactions, including the inappropriate use of blood components, and also have an audit and education role.

Reports of misuse of blood components or products are collected as inappropriate transfusions within the Incorrect Blood Component Transfused category (see the answer to question 4).

Question 4
The following categories of transfusion-related events and incidents are reportable:

- incorrect blood component/product transfused (This category is made up mostly of inappropriate transfusions and errors occurring along the transfusion chain, but also includes adverse events relating to the infusion of anti-D or factor concentrates. Adverse reactions associated with these products are reported to the Irish Medicines Board pharmacovigilance scheme.);
- severe acute anaphylactoid or anaphylactic transfusion reaction;
- transfusion-associated circulatory overload;
- acute haemolytic or other severe transfusion reaction;
- delayed haemolytic transfusion reaction;
- transfusion-related acute lung injury;
- suspected transfusion-transmitted infection;
- predeposit autologous donor incident;
- post-transfusion purpura; and/or
- transfusion-associated graft-vs.-host disease.

Question 5
During the period from 1 January 2002 to 21 December 2003, 335 reports were received by the NHO. The reports received have been categorized in Table 14. The commonest reports 202 (60%) were received in the incorrect blood component/product transfused (IBCT) category. IBCTs are classified by severity, with level 1 events those with a real potential for permanent injury or to be life threatening, level 2 events very unlikely to cause permanent harm or have the potential for minimal or transient harm, and level 3 events being those with no realistic potential for harm. A total of 103 (51%) of the 202 IBCT incidents in the 2 years were considered as being level 1.

There were 24 transfusion-associated circulatory overload (TACO) reports, a number of which were considered to represent inappropriate transfusions.

Viral transmission through transfusion was excluded in six of the seven suspected transfusion-transmitted infection reports submitted. Four reports related to suspected hepatitis B virus (HBV), two to hepatitis C virus (HVC) and one to human immunodeficiency virus (HIV). In one case of suspected hepatitis B transmission, transmission through transfusion could not be definitively excluded but was considered unlikely in view of other risk factors in the recipient. There were no reports received in the transfusion-associated graft-vs.-host disease (TA-GvHD) or post-transfusion purpura (PTP) categories in either year.

Two adverse reactions – a TRALI and a TACO – were associated with patient mortality throughout this period.

Question 6
After 8 November 2005, reporting of all serious reactions affecting the quality and safety of a blood component will be

Table 14 Incidents: 2002–2003

Year	IBCT	A/A	TACO	DHTR	AHOSTR	PAD	TTI	TRALI	Total incidents
2002	87	31	10	9	8	5	3	2	155
	56%	20%	7%	6%	5%	3%	2%	1%	100%
2003	115	23	14	9	8	6	4	1	180
	64%	13%	8%	5%	4%	3%	2%	1%	100%
Total	202	54	24	18	16	11	7	3	335
	60%	16%	7%	6%	5%	3%	2%	1%	100%

A/A, severe acute anaphylactoid or anaphylactic reaction; AHOSTR, acute haemolytic or other severe transfusion reaction; DHTR, delayed haemolytic transfusion reaction; IBCT, incorrect blood component/product transfused; PAD, predeposit autologous donor incident; TACO, transfusion-associated circulatory overload; TRALI, transfusion-related acute lung injury; TTI, suspected transfusion-transmitted infection.

mandatory. Reporting of serious adverse events occurring in hospitals and which are associated with an adverse reaction in the patient (such as an ABO-incompatible transfusion) will also be mandatory. However, reporting of adverse events unassociated with patient harm, although not mandatory, will continue to be reported as part of professional responsibility, including cases of transfusion-associated circulatory overload.

Emer Lawlor
Director, National Haemovigilance Office
Irish Blood Transfusion Service
National Blood Centre
James's Street
Dublin 8
E-mail: emer.lawlor@ibts.ie

Stefan Laspina
Irish Blood Transfusion Service
National Blood Centre
James's Street
Dublin 8
E-mail: stefan.laspina@ibts.ie

G. Grazzini, H. J. Hassan & G. Aprili

Question 1

A national transfusion-transmissible infections (TTIs) surveillance system has been in place in Italy for human immunodeficiency virus (HIV) since 1989, and for hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis since 1999, coordinated by the Transfusion Methodologies Division of the Istituto Superiore di Sanità (ISS; Italian National Institute of Health). The surveillance system is aimed at reporting all cases of blood donors confirmed to be positive for biological markers of HBV, HCV, human immunodeficiency virus (HIV)-1/2 and syphilis, thus obtaining epidemiological data necessary to estimate prevalence and incidence of the main TTIs and to evaluate their residual risk [1,2]. Blood transfusion centres (BTCs), which in Italy are systematically located at hospitals, are entrusted to collect data, filling in a single record for each identified case. Data are locally gathered by 22 Regional Blood Transfusion Co-ordinating Centres (RBTCCs) and sent to the ISS for storage and evaluation. National reporting is periodically performed.

Recently, in order to facilitate data collection, transmission and evaluation, the ISS has produced special software, named SMITT (Sorveglianza Malattie Infettive Trasmissibili con la Trasfusione/TTIs Surveillance), which has been delivered to BTCs nationwide.

By means of electronic import–export procedures, locally collected data are sent annually to the RBTCCs, entrusted to transmit regional data to the ISS, thus permitting national evaluations to be carried out.

Beyond the TTIs surveillance system, the ISS established a complete national haemovigilance system in October 2004, following appropriate scientific assessment performed together with transfusion medicine specialists, and consultation meetings with the RBTCCs medical directors.

Before starting the programme, the ISS produced another dedicated software, named PETRA (Programma Errori Trasfusionali e Reazioni Avverse/Transfusion errors and adverse events program), which was also delivered to BTCs nationwide. BTCs are entrusted to collect data on a hospital basis; hence, they are entitled to receive specific information about identified transfusion-related adverse events and reactions from blood users. As for the surveillance of TTIs, BTCs store and manage information, filling in a single record for each identified case and, by means of electronic procedures, locally collected data are periodically sent to the RBTCCs, entrusted to gather and transmit the whole of the regional data to the ISS. RBTCCs can elaborate their data, so that local epidemiological reports are readily available, before national reporting is performed. To assure traceability, each SMITT and PETRA record is automatically coded and univocally identified by the national code of the relevant BTC.

Question 2

Since 1990, the Italian legislation on blood transfusion has established that adverse reactions associated with blood transfusion must be reported to BTCs.

Collection of data by governmental authorities was not requested until 1997, when a decree established that a haemovigilance system had to be put in place by national authorities (Ministry of Health and ISS). The first focus was on the prevention of viral TTIs.

At present, participation in the haemovigilance system is highly recommended by institutional bodies (ISS and RBTCCs). In the meantime, the Italian Government is bringing into force a decree to comply with Directive 2002/98/EC of the European Parliament and of the Council, thus making it obligatory to notify to the competent authority 'any serious adverse events (accidents and errors) related to the collection, testing, processing, storage and distribution of blood and blood components which may have an influence on their quality and safety, as well as any serious adverse reactions observed during or after transfusion which may be attributed to the quality and the safety of blood and blood components' [3].

Question 3

Reporting on adverse events and reactions remains the main purpose of the system. Appropriateness of blood products use is not directly included. Nevertheless, evaluations on this issue can be extrapolated from reported data concerning patient's clinical history and diagnostic procedures. Furthermore, if 'misuse' of blood products is to be extensively intended as 'incorrect' blood component transfusion, PETRA includes the identification of transfusion process errors and near misses and the relevant data collection (see the answer to question 4).

All hospitals are required by law to have in place a hospital transfusion committee.

Question 4

The following serious adverse events and reactions are required to be reported:

- haemolytic transfusion reactions, caused by incompatible ABO, Rh, non-ABO-Rh blood component transfusion;
- non-immunological transfusion reactions;
- transfusion-related acute lung injury (TRALI);
- post-transfusion purpura (PTP);
- transfusion-associated graft-vs.-host disease (TA-GvHD);
- post-transfusion bacterial infections; and
- others, possibly including post-transfusion viral and parasitic infections.

Data collection is detailed, with the following sections included in each haemovigilance record:

- essential patient's history;
- type of adverse event/reaction and/or transfusion process error;
- blood component and pretransfusion compatibility tests;
- patient's reported signs and symptoms;
- pertinent diagnostic procedures performed on the patient before and after transfusion;
- bacterial contamination tests (patient and blood component);
- adverse event/reaction treatment;
- patient's outcome;
- transfusion process error details; and
- general data on the person responsible for managing the record.

Importantly, transfusion process errors and near misses must be reported. For this purpose a special section of the haemovigilance record is dedicated to the collection of detailed information concerning identified errors and near misses, according to the process phases in which they can occur, from blood component request, through sample collection, to transfusion.

Question 5

The first official data from PETRA will be available in 2006, reporting 2005 national haemovigilance activity. Preliminary data might be available by the end of 2005.

Available data concerning positivity of viral markers in blood donors, collected by SMIT1 for 2003, indicate the participation of 81% of BTCs, covering about 90% of blood donated in Italy (2 400 000 donations); the incidence per 100 000 donations, evaluated in repeat donors, was 1·8 for HIV, 2·9 for HCV, 2.3 for HBV and 13·2 for syphilis; and the prevalence per 100 000 donations, evaluated in first-time donors, was 12·4 for HIV, 228·5 for HCV, 362·6 for HBV and 113·4 for syphilis [1].

Question 6

The Italian haemovigilance system complies substantially with Directive 2002/98/EC, even if data collection about blood donors' serious adverse reactions has not yet been included.

Directive 2002/98/EC (Article 29) establishes the definition of a Community procedure for notifying serious adverse reactions and events and notification format, and for this purpose a Regulatory Committee was put in place to support the issue of a specific Directive by the European Commission, for which works are in progress [4]. Modifications to the present national programme could be adopted in the future, in order to comply with forthcoming requirements.

References

1 Gonzalez M, Règine V, Piccinini V, Vulcano F, Giampaolo A, Hassan HJ: Residual risk of transfusion-trasmitted human immunodeficiency virus, hepatitis C virus, and hepatitis B virus infections in Italy. *Transfusion* 2005; 45:1670–1676

2 Velati C, Romanò L, Baruffi L, Pappalettera M, Carreri V, Zanetti AR: Residual risk of transfusion-transmitted HCV and HIV infections by antibody-screened blood in Italy. *Transfusion* 2002; 42:989–993

3 Directive 2002/98/EC of the European Parliament and of the Council, of 27 January 2003. Setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC. *Official Journal of the European Union*, 08 February 2003; L33:30–40

4 European Commission: *Health & Consumer Protection Directorate-General. Directorate C, Public Health and Risk Assessment. Blood Regulatory Committee Summary Report, 19 January 2005*. Luxembourg, EC, 31 May 2005 (http://europa.eu.int/comm/health/ph_threats/human_substance/documents/blood_rc_en.pdf)

Giuliano Grazzini
Dipartimento Diritto alla Salute Regione Toscana
CRCC (Centro Regionale di Coordinamento e Compensazione)
Via Alderotti, 26/n
50139 Firenze,
Italy
E-mail: giuliano.grazzini@simti.it

Hamisa Jane Hassan
Istituto Superiore di Sanità
Dipartimento di Ematologia, Oncologia e Medicina Molecolare
Reparto Metodologia Trasfusionali
Viale Regina Elena, 299
00161 Roma,
Italy
E-mail: j.hassan@iss.it

Giuseppe Aprili
Dipartimento di Immunoematologia e Medicina Trasfusionale
Azienda Ospedaliera di Verona
Piazzale A. Stefani, 1
37126 Verona,
Italy
E-mail: giuseppe.aprili@simti.it

H. Okazaki

Table 15 Summary of adverse events in 2003 and 2004

	Year	2003	2004	Total
Infections	No. of reports	256	293	549
	HBV	12	20	32
	HCV	0	0	0
	HIV	1	0	1
(confirmed)	HEV	0	2	2
	HGV	1	0	1
	HPV/B19	1	0	1
	Bacteria	1[a]	0	0
HTR	No. of reports	25	28	53
NHTR	No. of reports	1307	1609	2916
	Urticaria	554	563	1117
	Anaphylactoid or anaphylaxis	336	461	797
	Hypotension	38	81	119
	Dyspnea	68	151	219
	Febrile reactions	219	191	410
	TRALI[b]	25	40	65
	Others	63	110	173
	Withdrawn	4	12	16
TA-GvHD[c]	No. of reports	15	9	24
Others		3	4	7

[a]The bag was contaminated by different bacterial species from one detected from the patient.
[b]TRALI and possible TRALI.
[c]None of GvHD was confirmed.
HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus; HGV, hepatitis G virus; HIV, human immunodeficiency virus; HPV, human papilloma virus; TA-GvHD, transfusion-associated graft-vs.-host disease; TRALI, transfusion-related acute lung injury.

Question 1

The Japanese Red Cross (JRC) has had an established haemovigilance system since 1993.

Question 2

The reporting system from physicians in charge is based on voluntary reporting. However, the JRC established a nation-wide medical representative network in 1992 that provides information on the proper use of blood products, receives technical requests or claims, and prompts physicians to report infections/adverse effects of transfusion. In addition to our haemovigilance system, the Japanese Ministry of Health, Labour and Welfare (MHLW) also encourages physicians to report severe and/or previously unrecognized adverse effects, either through the JRC and/or to the MHLW directly, by the Law for the Stable Supply of Safe Blood Products as well as the amendments of Pharmaceutical Affairs Law enforced in July 2003. In 2004, 1943 cases were reported to the JRC, as described in detail in Table 15, and 45 cases of adverse effects and 25 cases of suspected infections were reported directly to the MHLW.

Question 3

The JRC haemovigilance system does not include misuse of blood products or incidents and accidents occurring in the hospitals, of which the local hospital should be in charge.

Question 4

In general, physicians in charge are reluctant to report subtle events, such as local urticaria or slight fever. They tend to report moderate to severe cases that are suspected to be relevant to transfusion. The JRC must report new and/or severe adverse events to the MHLW, according to the above amendments of Pharmaceutical Affairs Law.

Question 5

The number of reports on adverse events is increasing year by year. In 2003, 1606 reports were collected and 1943 were

collected in 2004. A summary of the last 2 years is presented in Table 15.

Question 6
Not applicable.

Hitoshi Okazaki
Deputy General Manager
Research and Development Department
Central Blood Institute
The Japanese Red Cross Society Blood Service Headquarters
2-4-1-B14 Shiba-koen, Minato-ku, Tokyo 105-0011, Japan
E-mail: okazaki@bs.jrc.or.jp

J. C. Faber

Question 1
A haemovigilance system has been established in Luxembourg since January 1996.

Question 2
For the moment, it is voluntary, but with the transposition of the European Blood Directive, 2002/98/EC, the notification of serious adverse events and serious adverse reactions, in donors and recipients, will become mandatory.

Question 3
The primary focus is the reporting of serious adverse events (AE) and adverse reactions (AR).

Question 4
Serious AE and AR, in donors and in recipients, as required in Blood Directive 2002/98/EC, need to be reported.

Question 5
See Table 16.

Table 16 Results from haemovigilance in Luxembourg (1996–2004)

1996	Three reports; distribution of blood products (in units-bags): RBCs, 19 432; PLTs, 5204; FFP, 3270 and 843 autologous
1997	Nine reports; distribution of blood products (in units-bags): RBCs, 19 318; PLTs, 6430; FFP, 3595 and 869 autologuous
1998	Six reports; distribution of blood products (in units-bags): RBCs, 19 495; PLTs, 5736; FFP, 3366 and 918 autologuous
1999	Six reports; distribution of blood products (in units-bags): RBCs, 19 272; PLTs, 1528* (*change from single standard PLT to pools of filtered PLTs prepared from five buffy-coats); FFP, 3070 and 894 autologuous → incidence: 24/100 000 BC
2000	Four reports: incidence 16/100 000 BC issued
2001	Three reports: incidence 12/100 000 BC issued
2002	Five reports (all regarding RBC transfusions; all with low severity grades [four out of five were fever and/or chills] and all with low imputability scores); incidence 20/100 000 BC issued
2003	Nine reports (all regarding RBC transfusions; all with low severity grades [eight out of nine were fever and/or chills] and all with low imputability scores): incidence 35.2/100 000 BC issued
2004	Six reports (all regarding RBC transfusions; all with low severity grades except one related to ABO incompatibility – IBCT): incidence 22.72/100 000 BC issued

FFP, fresh-frozen plasma; IBCT, incorrect blood component/product transfused; PLTs, platelets; RBC, red blood cells.

Question 6
Yes, we will adapt our haemovigilance programme in November 2005 according to 2002/98/EC and 2005/nn/EC (the forthcoming Commission Directive on traceability and notification of serious AE and AR, in donors and in recipients).

Jean-Claude Faber
Medical director of the Luxembourg Red Cross Blood Service
E-mail: transfusion@croix-rouge.lu

Simon Benson

Question 1
The New Zealand Blood Service (NZBS) introduced a national haemovigilance programme on 1 May 2005. This followed a 4-month pilot programme at three North Island hospitals. The programme is modelled on similar schemes in the UK and Eire, and aims to capture data on the prevalence of all types of transfusion-related adverse events, not only so-called transfusion reactions.

Question 2
Participation in the NZBS Haemovigilance Programme is voluntary, although actively encouraged.

The programme appears to have gained acceptance within the New Zealand transfusion sector, with 19 of the country's 21 District Health Boards represented in the reports received during the first 3 months of activity.

Question 3
The NZBS has adopted the Council of Europe definition for haemovigilance (i.e. '... the detection, gathering and analysis of information regarding untoward and unexpected effects of blood transfusion ...') [1].

The programme is primarily aimed at collecting data on transfusion-related adverse events, including transfusion reactions. The NZBS also collects a wide range of data, which are considered under the umbrella of haemovigilance. These include data on the number of donations collected, number of components transfused, wastage and outdating of components, bacterial monitoring of platelets, reporting of adverse reactions to fractionated products, donor-related incidents, and donor infectious disease epidemiology, amongst others.

The process of drawing these activities into the formal haemovigilance programme, together with other associated activities, for example sample and request form errors, blood bank errors and near misses, is currently underway.

Question 4

The haemovigilance programme requires all transfusion-related adverse events to be reported. Thirteen categories of event have been chosen which capture data on incorrect blood components or products transfused, immune and cardiovascular complications of transfusion, transfusion-transmitted infections and events caused by specific equipment or components.

Each reported incident is further categorized into serious or non-serious events, with serious events requiring further discussion with a NZBS Transfusion Medicine Specialist.

Question 5

Since the start of the pilot, which ran from 1 January 2005 to the end of July 2005, 140 events have been entered into the haemovigilance database, representing submissions from 25 hospitals.

Not unexpectedly, the majority of events are non-haemolytic transfusion reactions or allergic reactions (59·3% and 28·6% respectively). Other types of events reported include incorrect blood component/product transfused (IBCT) (4·3%), transfusion-associated circulatory overload (TACO) (3·6%) and possible transfusion-related acute lung injury (TRALI) (2·1%).

Because of the relative newness of the programme, data are limited. Reporting should improve as hospitals become familiar with the programme and those involved with the transfusion process become aware of its existence and importance. Similarly, determination of the incidence and frequency of adverse events will be unreliable until levels of reporting are increased.

Question 6

Not applicable to New Zealand.

Reference

1 Council of Europe Publishing: Haemovigilance, Chapter 30; in Council of Europe (eds): *Guide to the Preparation, Use and Quality Assurance of Blood Components*, 11th edn. Strasbourg, Council of Europe Publishing, 2005:225–232

Simon Benson
Clinical Support Officer
New Zealand Blood Service
71 Great South Road
EPSOM
Auckland
New Zealand
E-mail: simon.benson@nzblood.co.nz

Bjarte G. Solheim

Question 1

A haemovigilance system has been in place in Norway since 2004.

Question 2

Reporting of serious adverse events to the National Health Authorities has been obligatory for many years. Reporting to the haemovigilance system is voluntary.

Question 3

The main purpose of haemovigilance is to report events and reactions related to transfusions in patients and to donation in blood donors.

Question 4

All types of events and reactions are to be reported.

Question 5

Results for 2004 are provided in Tables 17 and 18. The low frequency of adverse events observed with plasma is attributed to 100% use of solvent detergent-treated plasma (Octaplas).

Question 6

In Norway, the haemovigilance programme was adapted to that of European Union Blood Directive on 1 January 2005.

Bjarte G. Solheim
Professor, MD, PhD, MHA
Institute of Immunology
Rikshsopitalet University Hospital
NO-0027 Oslo
Norway
E-mail: bjarte.solheim@rikshospitalet.no

Table 17 Norway 2004, all reports

	Transfusion failures			ABO major incompatibility		Clinical outcomes or morbidity			Component transfused				Imputability			Reports
		Wrong transfusion														
Reported events	None	Wrong component	Wrong patient	No	Yes	Death	Major symptom	Mild or no symptom	Red cells	Platelet	Plasma	Other mixed	Possible dubious	Likely probably	Certain proven	Total number
No symptoms		4	9	10	3			13	11	1	1			1	12	13
Allergic	43			43			2	41	21	21	1		14	28	1	43
Anaphylactic																
TRALI	1			1			1		1					1		1
AHTR		4	4	4	4	1	4	3	7		1			3	5	8
DHTR																
PTP																
TACO	2			2			2		2				1	1		2
GVHD																
FNHTR	174			174				174	157	16	1		93	81		174
TTI																
Total number	220	8	13	234	7	1	9	231	199	38	4	0	108	115	18	241

AHTR, acute haemolytic reaction;DHTR, delayed haemolytic transfusion reaction; FNHTR, febrile non-haemolytic transfusion reaction; GvHD, graft-vs.-host disease; PTP, post transfusion purpura; TACO, transfusion-associated circulatory overload; TRALI, transfusion-associated acute lung injury; and TTI, transfusion transmitted infection.

 Vox Sanguinis (2006) **90**, 207–241

Table 18 Norway 2004, serious hazards

	Transfusion failures			ABO major incompatibility		Clinical outcomes or morbidity			Component transfused				Imputability			Reports
		Wrong transfusion														
Reported events	None	Wrong component	Wrong patient	No	Yes	Death	Major symptom	Mild or no symptom	Red cells	Platelet	Plasma	Other mixed	Possible dubious	Likely probably	Certain proven	Total number
No symptoms		4	9	10	3			13	11	1	1			1	12	13
Allergic	3			3			2	1	2		1		1	2		3
Anaphylactic																
TRALI	1			1			1		1					1		1
AHTR		4	4	4	4	1	4	3	7		1			3	5	8
DHTR																
PTP																
TACO	2			2			2		2				1	1		2
GVHD																
TTI																
Total number	6	8	13	20	7	1	9	17	23	1	3		2	8	17	27

AHTR, acute haemolytic reaction; DHTR, delayed haemolytic transfusion reaction; FNHTR, febrile non-haemolytic transfusion reaction; GvHD, graft-vs.-host disease; PTP, post transfusion purpura; TACO, transfusion-associated circulatory overload; TRALI, transfusion-associated acute lung injury; TTI, transfusion-transmitted infection.

M. Letowska

Question 1

The voluntary haemovigilance system was introduced in Poland about twenty years ago. Hospitals report serious adverse reactions to the Polish Blood Transfusion Service-BTS (regional blood centers and Institute of Haematology and Blood Transfusion). Each adverse reaction is analysed by the BTS. All necessary tests except microbiological ones, are performed by BTS labs. Annual reports are published in Polish Excerpta Transfusionica.

Question 2

In Poland, participation in the haemovigilance system is obligatory according to the Law on Public Blood Service of 1997.

Question 3

Reporting on transfusion related adverse events and reactions also has other aims such as:

- improvement of transfusion quality in clinical wards;
- improvement of pretransfusion testing performance by laboratory personnel (this goal is also reached by additional training of physicians, nurses and laboratory staff).

Every severe adverse event or reaction is carefully analysed by specialists. According to the Public Blood Service Law, regional blood centres supervise both blood transfusions and pretransfusion testing in hospitals. Blood transfusion personnel are obliged to carry out proecures according to the Ministry of Health Regulation issued in 2005 and to use the Report of Adverse Events and Reactions form based on one published by the European Haemovigilance Network. This Report will be in use after 1 January 2006.

Question 4

According to the definition of adverse events published in the Directive 2002/98/ EC, every serious adverse event must be reported. According to the Council of Europe recommendations, near-miss events should also be reported.

Question 5

Data for 2003 and 2004, collected by 21 regional blood centres, are presented in Tables 19–24. The classification system of adverse reactions, according to severity as well as imputability, still needs improvement. The personnel involved in the documentation of adverse events and reactions will be trained to achieve a uniform system of qualification. Such training is necessary because discrepancies still exist in the classification criteria of haemolytic reactions, as a result of blood incompatibility. In some regional centres, a reaction occurring directly after transfusion, but which is not too dramatic, is classified as a 'sign without vital risk'. In our

Table 20 Severity of adverse reactions in 2003

Grade	Description	%
0	No sign	6·2
1	Signs without vital risk	82·6
2	Signs with vital risk	10·1
3	Long-term morbidity	0·5
4	Death	0·6

Table 21 Imputability in 2003

Grade	Imputability scale	%
0	Excluded/unlikely	8·1
1	Possible	45·9
2	Probable	32·9
3	Certain	13·1

Table 19 Transfusion adverse reactions in recipients registered in 2003

	Blood component transfused		
Adverse reaction	Red cell concentrate	Platelet concentrate	FFP
Haemolytic reaction caused by ABO incompatibility	4	1	0[a]
Haemolytic reaction caused by other antibodies	16	0	0
Bacterial infection	5	3	0
TRALI	3	0	0
Allergy/anaphylaxis	143	46	47
Febrile non-haemolytic	448	53	16
Others (cardiovascular, respiratory, vasovagal)	160	6	4

[a]ABO-incompatible fresh-frozen plasma (FFP) transfused to one patient; adverse reactions not observed.
TRALI, transfusion-associated acute lung injury.

Table 22 Transfusion adverse reactions in recipients registered in 2004

	Blood component transfused		
Adverse reaction	Red cell concentrate	Platelet concentrate	FFP
Haemolytic reaction caused by ABO incompatibility	7	0	0[a]
Haemolytic reaction caused by other antibodies	10	0	0
Bacterial infection	13	0	0
TRALI[b]	14	0	1
Allergy/anaphylaxis	97	34	28
Febrile non-haemolytic	390	36	5
Others (cardiovascular, respiratory, vasovagal)	174	38	33

[a]ABO incompatible fresh-frozen plasma (FFP) transfused to three patients.
[b]Twelve out of 15 cases – probable.
TRALI, transfusion-associated acute lung injury.

Table 23 Severity of adverse reactions in 2004

Score	Description	%
1	Signs without vital risk	93·3
2	Signs with vital risk	6·5
3	Long-term morbidity	0·1
4	Death	0·1

Table 24 Imputability in 2004

Imputability scale	%
0 Excluded/unlikely	22
1 Possible	14
2 Probable, but other causes are present	33
3 Probable, other causes excluded	22
4 Certain	9

opinion, however, every clinical sign of incompatible red cell concentrate transfusion should be classified as being a vital risk for the patient.

Question 6

After the new European Union Blood Directive has been implemented, the Polish haemovigilance programme will be adapted accordingly.

Reference

1 Blood Transfusion in Europe: *The White Book 2005*. Ph Rouger (ed). EuroNet-TMS 2005

Magdalena Letowska (E-mail: letowska@ihit.waw.pl)
Professor Halina Seyfried (E-mail: h.seyfried@ihit.waw.pl)
Institute of Haematology and Blood Transfusion
00-957 Warsaw, Chocimska 5
Poland

E. Selivanov & T. Danilova

Question 1

A haemovigilance system was set up in Russia before 1999 and it is in action at present.

Question 2

In our country, this system is a legal obligation for all blood banks and hospitals. All documents listed are approved by the Russian Ministry of Health.

Question 3

The main purpose of the haemovigilance system is prophylaxis of the post-transfusion complications, which include: regulations for examination of donors and the testing of donor blood; blood collection; the processing of blood components and blood products; organization of transfusion therapy in hospitals; regulations for transfusion of blood components and blood products; and misuse of blood products. The actual problem is ensuring the infection safety of blood transfusion.

Question 4

Hospitals must report all events and post-transfusion complications connected with the use of blood, blood components and preparations.

Question 5

At present, in Russia all donor blood collected is tested for: ABO blood group, Rh(D) type, hepatitis B surface antigen (HBsAg), syphilis, antibody to hepatitis C virus (anti-HCV), antibodies to human immunodeficiency virus-1/2 (anti-HIV-1/2), and alanine aminotransferase (ALT). Donor blood is rejected and discarded when the results of testing show the presence of infectious agents. During blood collection, the control of blood sterility is carried out according to existing normative documents. About 5% of donor blood was discarded in 2004, mostly because of HBsAg (15·5%), anti-HCV (23·5%), syphilis (9%) and anti-HIV (1%). The Russian research Institute of Haematology and Transfusiology performs a regular annual analysis of the cases reported of post-transfusion complications. In 1997–2004, 122 cases of severe post-transfusion complications were reported in Russia: ABO incompatibility, 59; Rh incompatibility, 19; transfusion of haemolysed red blood cells (RBC), 20; anaphylactic shock, 8; transfusion-transmitted hepatitis and HIV, 7, other causes, 9. However, we are not sure that all causes of severe post-transfusion complications were registered.

E. Selivanov
T. Danilova
Russian Research Institute of Haematology and Transfusiology,
St Petersburg, Russia
E-mail: haematology@atlant.ru

I. Snopek

Question 1

A set of guidelines, regulations and principles relating to quality and safety for donor selection, blood collection, testing, processing, storage, distribution, reporting and usage of blood and blood components intended for transfusion since 1999 were prepared and issued by the Ministry of Health of the Slovak Republic:

- Methodical Regulation on basic technical procedures in immunohaematology/issued in October 2000/;
- Methodical Directive 74 on preventing the transmission of infectious diseases by transfusion of blood and blood components/issued in October 2002/;

- Methodical Directive 75 on preventing, reporting and analysing adverse transfusion events/issued in October 2002/;
- Methodical Directive 81 for providing correct indications of blood medicaments/issued in November 2004/; and
- Public Notice 333: Requirements for good practice in preparing blood components/issued in August 2005/.

All of the documents referred to above aim to increase blood safety at a European level and they include the reporting of all adverse events and reactions in order to prevent the occurence or recurrence of unexpected or undesirable effects resulting from the therapeutic use of labile blood products.

Question 2

In the Slovak Republic it is legally obligatory to follow all of the above-mentioned documents of the Ministry of Health.

Question 3

Reporting the misuse of blood and blood products is not included in our system of haemovigilance.

Question 4

Any serious adverse events/accidents and errors related to the collecting, testing, processing, storage and distribution of blood and blood components, which may have an influence on their quality and safety, as well as any serious adverse reactions observed during or after transfusion, which may be attributed to the quality and the safety of blood and blood components, are notified to the competent authority. The Slovak Haemovigilance System is operated by the Expert for Transfusion Medicine by the Ministry of Health.

Question 5

In 2004 in Slovak Republic (with ≈ 5·4 million inhabitants) 137 375 units of blood and blood components were collected from voluntary and non-remunerated blood donors. Forty-two hepatitis B surface antigen (HBsAg)-positive donors, 24 donors positive for antibodies to hepatitis C virus (anti-HCV) and 10 donors positive for syphilis were excluded from donation in 2004. We have not found human immunodeficiency virus (HIV)-repeat reactive or HIV-positive donors. A total of 116 420 red cell units, 50 683 plasma units, 15 619 units of whole blood and 16 459 units of platelets were transfused in 2004 in the Slovak Republic.

In 2004 we identified:

- one haemolytic reaction after a transfusion of whole blood and one haemolytic reaction after a transfusion of red cells (in both cases the blood component was administered to the wrong patient);
- 388 light febrile non-haemolytic transfusion reactions; and
- 288 other complications, such as transfusion-transmitted bacterial infection, hypotension and hypocalcaemia (Data from The State Institute of Health Information and Statistics.)

Question 6

I am sure that immediately after the implementation of the new European Union Blood Directive in November 2005, our country will adopt the haemovigilance programme.

Ivan Snopek
Department of Transfusiology
Hospital
Rastislavova 2237
95501 Topoľčany
Slovak Republic
E-mail: ivan.snopek@hospitalto.sk

T. Nel

Question 1

The Haemovigilance Programme for South Africa was established at a meeting of the Medical and Administrative Directors' Advisory Committee for Blood Transfusion in South Africa on 2 November 2000. At that stage the decision was to start with a basic haemovigilance programme. The Serious Hazards of Transfusion (SHOT) programme of the United Kingdom was used as a reference for defining the type of reactions that would be reported to the programme.

The programme started with the retrospective collection of data for serious transfusion reactions for the year 2000. Data were collected in terms of the following serious reactions:

- acute haemolytic reactions (including anaphylaxis);
- delayed haemolytic reactions;
- incorrect blood products transfused;
- transfusion-transmitted infections;
- transfusion-associated graft-vs.-host disease;
- transfusion-related acute lung injury; and
- post-transfusion purpura.

Until 2004, the programme was managed by means of a questionnaire that was sent to the various blood transfusion services once a year. This information was then collated and published in an annual report. The reason for this approach was the limited recourses available to run the programme. In 2004 a half-day position was approved to help with the management of the programme. This allowed for the collection of information closer to the time of the reaction. It further created more awareness on the reporting of reactions.

Compared with other international haemovigilance programmes, the system in South Africa is still in its infancy. Steps have been taken to try and move the programme to the next level. These include: motivation to establish the programme at arms length from the operations of the blood transfusion services; and establishing a seat for the programme on the National Blood Council, which is a body that advises the Minister of Health on blood transfusion.

Question 2

The act that governs blood transfusion, currently namely the Human Tissue Act, requires that blood prescribers must report all untoward reactions to the blood transfusion services. While this is the case, the haemovigilance programme was established as a voluntary reporting system and in the communication about the programme this is how it is portrayed.

The new Health Act was published in 2004, but the chapter pertaining to Blood Transfusion was excluded from it. This chapter, however, only refers to the fact that the Minister of Health can put in place systems that will further ensure the safety of the blood supply. The regulations pertaining to this chapter of the new Health Act are not yet available for comment. It is hoped that a voluntary approach will be decided upon by the Minister of Health and that this is reflected in the new regulations for the practice of blood transfusion in South Africa.

Question 3

Serious transfusion-related adverse events and reactions are the main purpose of the current haemovigilance programme. The scope of the programme has not been expanded to include non-serious events and reactions. Other aspects, such as the misuse of blood products, have been included in the motivation that was submitted in order to improve the status of the current South African programme.

Question 4

Currently, the South African Haemovigilance system still only requires the following reactions to be reported to the programme:

- acute haemolytic reactions (including anaphylaxis);
- delayed haemolytic reactions;
- incorrect blood products transfused;
- transfusion-transmitted infections;
- transfusion-associated graft-vs.-host disease;
- transfusion-related acute lung injury; and
- post-transfusion purpura.

Question 5

In 2003 and 2004, 880 880 and 845 907 blood products were transfused respectively. The reactions reported for the last 2 years are given in Table 25, which gives a reporting rate of 9·5 per 100 000 products transfused for 2003 and a rate of 8·9 per 100 000 products transfused for 2004. The transfusion-transmitted infections that were recorded are not confirmed. The organisms that were implicated in these cases are listed in Table 26.

Question 6

As South Africa is not part of the European Union, this is not applicable. However, the Directives of the European Union are monitored and used as guidance. The aim is to broadly follow these so that participation on an international level can be achieved in future.

Table 25 Reactions for 2003 and 2004

Reaction	2003	2004
Acute haemolytic reactions	20	49
Delayed haemolytic reactions	4	1
Incorrect blood product transfused	57	19
Transfusion-transmissible infections	3	4
Transfusion-related acute lung injury	0	2
Transfusion-associated graft-vs.-host disease	0	0
Post-transfusion purpura	0	0
Total	84	75

Table 26 Organisms implicated for 2003 and 2004

Organism	2003	2004
Bacteria	1	1
Human immunodeficiency virus	2	1
Hepatitis B virus	0	2
Hepatitis C virus	0	0
Protozoa (malaria)	0	0
Total	3	4

Teresa Nel
South African Haemovigilance Programme
PO Box 28126
Danhof 9310
South Africa
E-mail: teresa.nel@pathcare.co.za

M. P. Martín

Question 1

Based on the agreement signed between the Spanish Ministry of Health, the Spanish Blood Transfusion Association (SETS: *Sociedad Española de Transfusión Sanguínea*) and the Spanish Haematology and Hemotherapy Association (AEHH: *Asociación Española de Hematología y Hemoterapia*), the Spanish programme of haemovigilance (PEHV: *Programa Estatal de Hemovigilancia*) has been running since the beginning of 2004 as a pilot project. At present, the system is structured on three levels: the hospital (reporting transfusion-related events) and blood establishment (reporting blood products donation- or preparation-related events) level; the autonomous region co-ordination level; and the State level. At the hospital level, the specialist in haematology and haemotherapy in charge of the hospital blood bank co-ordinates the system. In most of the 17 autonomous regions (which have been delegated control of health organization in

their territories), there is already a haemovigilance specialist responsible for combining efforts regionally. Finally, the PEHV co-ordinates the State haemovigilance system. The main objectives of the PEHV are to prevent the recurrence of adverse events and incorporate an early reporting system through a solid communication structure.

The first meeting of the haemovigilance autonomous region co-ordinators took place in December 2004, and the first official haemovigilance report, corresponding to 2004, has been presented at the SETS annual meeting (June 2005) and will soon be published and accessible on web pages and official association journals.

Although great advances have been made, thanks mostly to the efforts of those reporting in hospitals, blood transfusion establishments and autonomous regions, work still remains to be carried out in order to firmly establish a solid system of communication between hospitals, regional competent authorities and the State haemovigilance office.

Also, as a pilot project, the construction of the system has been under constant review with the aim of establishing the most efficient and reliable haemovigilance system possible.

Question 2

While in most of the Spanish autonomous regions participation in the pilot programme is voluntary, some have adopted legal measures which make participation of the hospitals obligatory. Once the European Union (EU) directive and its corresponding transposition into Spanish law become effective, participation of all the autonomous regions, ensuring that a system of serious adverse events reporting is in place, will be mandatory.

Question 3

Currently, the reporting of the misuse of blood products is not included specifically in the haemovigilance system. However, in 2004 some reports of this kind were communicated through the document 'Incorrect Blood Components Transfused'. In addition, hospital transfusion committees look after the correct use of blood products, and the haemovigilance system, stimulating the work of them, will certainly assist in this regard.

Question 4

Increased security of blood transfusion, by communicating all transfusion-related events since blood donation to bedside transfusion, is the main purpose of the PEHV. In that sense, not only transfusion-related events or reactions are reported, but also events related to the preparation or donation of blood products. The list of adverse events reported at the PEHV is as follows:

- donation-related event;
- blood components preparation-related event;
- incorrect blood component transfused;
- haemolytic reaction;
- allergic/anaphylactic reactions;
- hypotensive or febrile non-haemolytic reactions;
- transfusion-related acute lung injury (TRALI);
- transfusion acute circulatory overload;
- transfusion-associated graft-vs.-host disease;
- post-transfusion purpura (PTP);
- post-transfusion viral infection;
- bacterial contamination;
- haemosiderosis; and
- near-miss event.

Question 5

The data included in the 2004 report are summarized as follows.

(1) A total of 1325 adverse events were reported to the PEHV in 2004. Of these, 921 were febrile or allergic reactions, 104 were near-miss events, 86 were unclassifiable events, 75 were cases of incorrect administration of blood components, 38 were delayed haemolytic transfusion reactions, 31 were cases of transfusion-related acute lung injury (TRALI), 19 were notifications of transfusion-associated circulatory overload (TACO), 17 were alloimmunization, 21 were studies for suspected viral infection, 12 were studies for suspected bacterial contamination and one was a case of haemosiderosis.

(2) Regarding the imputability and severity of cases notified, imputability in most cases reported was > 1, and only 6% of the events were found to be unrelated to transfusion after study (e.g. viral or bacterial contamination). A total of 11% of reports were described as serious adverse events. Seven patients died, probably or possibly as a result of transfusion, five of them after TRALI.

(3) Encouragingly, 104 cases of near-miss events were reported. Cases of incorrect blood component/product transfused and near-miss events occurred mostly where blood was prescribed or transfused (72%) rather than in the hospital blood bank laboratory (28%).

(4) A total of 1212 events related to donation were reported. Of these, only 6% were considered serious. A total of 2591 events related to the preparation of blood components were notified, with only 3·6% of these classified as having a severity of ≥ 2. Analysis of the reported events related to donation and preparation of blood components showed that it is necessary to define the cases that have to be notified.

Question 6

The PEHV pilot project was conceived on the basis of the terms of haemovigilance in the EU Directive, so no major changes will be necessary. The PEHV and autonomous regions will continue in order to ensure that any serious adverse events, especially those regarding the quality or safety of blood components, are notified to the relevant authorities.

Table 27 Reports received 2002/2003

Codes	2002	2003	Total	RBC	FFP	PLTs	Auto	[a]
FNHTR	96	165	261	202	8	39	5	7
Allergic TR	52	74	126	55	22	45		4
Anaphylactic TR	10	10	20	3	7	7		3
Suspected bacterial contamination	9	3	12	9		3		
HTR	4	4	8	8				
TRALI	3	3	6		3	1		2
TACO	8	24	32	28	2	1		1
Near miss	30	24	54					
IBPT	7	6	13	8	2	1	1	1[b]
Hypotensive TR		9	9	7			1	1
CJD investigations[c]	16	15	31					
Others	36	131	167					
Total	271	468	739					

[a]Multiple products.

[b]Donor mix-up.

[c]Every time a Creutzfeldt–Jacob disease (CJD) case becomes known, we determine whether or not the person was a blood donor.

FFP, fresh-frozen plasma (quarantine or solvent–detergent); FNHTR, febrile non-haemolytic transfusion reaction; HTR, haemolytic transfusion reaction; IBPT, incorrect blood product transfused; PLTs, platelets (apheresis and buffy coat); RBC, red blood cells (100% leukodepleted); TR, transfusion reaction; TACO, transfusion-associated circulatory overload; TRALI, transfusion-related acute lung injury.

Dra. María Paz Martín
Programa Estatal de Hemovigilancia
Despacho 724
Ministerio de Sanidad y Consumo
Paseo del Prado 18–20
Madrid 28015
E-mail: mpmartin@msc.es

M. Senn

Question 1

Based on the Law on Therapeutic Products (LTP), Swissmedic, the Swiss Agency for Therapeutic Products, took responsibility for the haemovigilance system in 2002. The haemovigilance system covers the full process – beginning at donor selection right through to evaluating the clinical effects of transfusion.

Question 2

The law states clearly that all adverse events must be reported. In addition, the reporting of errors and near misses is requested with the sole purpose of recognizing critical weak points in the transfusion chain. The legal responsibilities in cases of malpractice are divided between the cantons and the federal Swissmedic. The blood centres – independent or hospital based – operate under a Swissmedic authorisation. Therefore, Swissmedic is also responsible for taking appropriate actions when serious incidents occur. The Swiss hospitals operate under the surveillance of the cantons. Therefore, the cantons are responsible for taking action in regard to medical malpractice aspects. This allows Swissmedic, despite having an obligatory haemovigilance system, to operate it with a no-blame culture in regard to medical practice. We consider the no-blame culture for medical practice a very important aspect of our system.

Question 3

The LTP stipulates the use of medicinal products according to intended purpose and with moderation. Relating to blood components, the law implies the adherence to guidelines on the clinical use of blood. The indication to transfuse must be carefully evaluated, risks and benefits should always be taken into consideration when prescribing blood products, and emphasis must be placed to prescribe the specific blood component needed to treat a defined deficiency. The aim is to ensure that transfusions are appropriate according to current medical consensus. Furthermore, Swiss law requires institutions, which transfuse blood components, to establish a quality system for the administration of blood products according to the current state of the art. Obviously, this quality system is closely tied with haemovigilance.

Question 4

Every time a blood component might have caused an adverse event it should be reported. The only adverse events exempt from this are urticaria as the sole symptom covering less than one-third of the body surface and fever below 38 °C and less

Table 28 Serious events 2002/2003 with certain or probable correlation with transfusion

		Total	IBPT	HTR	Ana.	Hypo.	TACO	TRALI	Bact.	PTP
Deaths	RBC	3					3			
	FFP									
	PLTs	1							1	
Life-threatening	RBC	7	1	1	1	1	3			
	FFP	7			5			2		
	PLTs	3			1 (1[a])					1
	Multiple components	2			1	1				
Total		23	1	1	9	2	6	2	1	1

[a]Onc classification not certain.

Ana., anaphylactic transfusion reaction; Bact., bacterial contamination; FFP, fresh-frozen plasma (quarantine or solvent–detergent); FNHTR, febrile non-haemolytic transfusion reaction; HTR, haemolytic transfusion reaction; Hypo., hypotensive transfusion reaction; IBPT, incorrect blood product transfused; PLTs, platelets (apheresis and buffy coat); PTP, post-transfusion purpura; RBC, red blood cells (100% leucodepleted); TACO, transfusion-associated circulatory overload; TR, transfusion reaction; TRALI, transfusion-related acute lung injury.

No viral transmission become known during 2002/2003.

than 1 °C increment. Additionally, incidents occurring during the production process of blood components must be reported, such as: all safety risks to blood donors; all mismatches involving donors and donations; wrongful release and mislabelling; defective materials or reagents; and erroneous test results. All events are classified according to defined criteria. Reports of high quality are a prerequisite for proper assessment. Therefore, we redesigned our reporting form asking for more clinical information and results of laboratory investigations.

Question 5

See Tables 27 and 28.

Question 6

Switzerland does not belong to the European Union (EU). Nevertheless, we shall adapt our system to the EU Blood Directive in the future.

Marianne Senn
Head Hemovigilance
Swissmedic, Swiss Agency for Therapeutic Products
Hallerstrasse 7
3000 Berne
Switzerland
E-mail: Marianne.senn@swissmedic.ch

D. Stainsby, H. Cohen & H. Jones

Question 1

The Serious Hazards of Transfusion (SHOT) Scheme is currently the haemovigilance system in the United Kingdom and was established in 1996. SHOT now has 8 years of analysed data and has contributed to demonstrable improvements in blood transfusion safety [1].

Question 2

Participation in SHOT has been voluntary since its inception, but has been strongly encouraged by the UK Department of Health [2]. The reporting of serious adverse reactions and adverse events related to transfusion will become legally obligatory in the UK in November 2005 with implementation of the European Union (EU) Blood Directive.

Question 3

SHOT does not include reports of inappropriate transfusion of blood components, except where this has occurred as a result of error (e.g. an erroneous blood count report from a sample that was unsuitable or from the wrong patient). We consider clinical audit to be a better tool than critical incident reporting for evaluation of compliance with published guidelines on the use of blood. SHOT does receive reports of mishandling of blood components (e.g. inadvertent transfusion of blood that has exceeded its expiry date or has been out of temperature control).

Question 4

Categories of adverse events reported to SHOT are:

- incorrect blood component transfused (IBCT), where a patient was transfused with a blood component that did not meet the appropriate requirements or was intended for another patient;
- near miss;
- acute transfusion reaction (ATR);
- delayed transfusion reaction (DTR);
- transfusion-related acute lung injury (TRALI);
- transfusion-associated graft-vs.-host disease (TA-GvHD);
- post-transfusion purpura (PTP);
- transfusion-transmitted infection (TTI); and
- adverse events associated with autologous predonation and reinfusion of autologous blood.

Table 29 Findings for 2003 and 2004

	2003	2004
Total reports (excluding near miss)	457	540
IBCT	348 (of which 33 were ABO-incompatible transfusions)	439 (of which 23 were ABO-incompatible transfusions)
Near miss	906	1076
ATR	39 (6 AHTRs, 33 severe allergic/anaphylactic)	34 (4 AHTRs, 28 severe allergic/anaphylactic, 4 others)
DTR	25	43
TRALI	36	23
TA-GvHD	0	0
PTP	1	0
TTI	8 (2 HBV, 1 HIV, 1 HAV, 1 malaria, 3 bacterial contamination of platelets)	1 (HEV)

AHTR, acute haemolytic transfusion reaction; ATR, acute transfusion reaction; DTR, delayed transfusion reaction; HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus; HGV, hepatitis G virus; HIV, human immunodeficiency virus; HPV, human papilloma virus; IBCT, incorrect blood component transfused; TA-GvHD, transfusion-associated graft-vs.-host disease; TRALI, transfusion-related acute lung injury.

Question 5

A complete analysis of SHOT data, together with the recommendations of the Steering Group, is published annually, [3] and is also available on the SHOT website [4]. The findings for 2003 and 2004 are summarised in Table 29.

Question 6

The EU Directive will have a significant impact on haemovigilance in the UK. The Department of Health has appointed, as the Competent Authority, the Medicines and Healthcare Products Regulatory Agency (MHRA). An electronic reporting system is being developed to capture data for MHRA and also for SHOT, and a working relationship is evolving.

The scope of the Directive excludes bedside 'no-harm' errors, detailed analysis of which has enabled understanding of the root causes of avoidable and potentially serious adverse reactions. The Department of Health has stated that whilst MHRA fulfils the legislative requirements of the Directive, the integrity of SHOT should be preserved. We are therefore optimistic that these events will continue to be reported to SHOT and that the continuity and validity of SHOT data will be maintained.

References

1 Stainsby D, Williamson L, Jones H, Cohen H: 6 years of SHOT reporting – its influence on UK blood safety. *Transfus Apheresis Sci* 2004; **31**:123–131

2 UK Department of Health: *Health Service Circular: Better Blood Transfusion – Appropriate Use of Blood*. http://www.dh.gov.uk/PublicationsAndStatistics/LettersAndCirculars/fs/en

3 Stainsby D *et al.* on behalf of the SHOT Steering Group: SHOT Annual Report 2003. ISBN 0 9532 789 6 4

4 www.shotuk.org

Dorothy Stainsby
SHOT Office
Manchester Blood Centre
Plymouth Grove
Manchester M13 9LL
UK
E-mail: dorothy.stainsby@nbs.nhs.uk
Hannah Cohen
Hilary Jones

N. Blumberg

Question 1

There is no formal haemovigilance system in the USA. In part this is a result of the absence of a national health system, and the fact that oversight of transfusion medicine is divided into a state level (regulation of medical practice and monitoring public health, and sometimes regulation of blood centres and transfusion services) and a federal level (regulation of blood centres, transfusion services and monitoring of public health). The model of oversight that has been ascendant in the USA for the last two decades is the administrative/legal/regulatory model rather than the medical/scientifically driven model. Evidence for this is replacement of physician leadership in many regional blood centres by those with primarily business or other non-scientific training. The regulatory model focuses on achieving perfection, sometimes punishing or levying fines on deviations from perfection, and does not focus on clinical outcomes. The haemovigilance or public health model recognizes the scientific and clinical realities that perfection is not achievable, that regulations are often semi-arbitrary, and that clinical outcomes are the most important measure of success. In haemovigilance one seeks to detect adverse events for the purpose of improving clinical practice. However, this monitoring is carried out with the understanding that adverse events are frequently a result of

biological or clinical variables out of our immediate control. This is virtually the opposite of the assumptions of the regulatory model now operating in the USA.

Emphasis in the USA has focused on 'quality programmes', emphasizing monitoring technical details, such as minor record keeping or manufacturing variations of little scientific or clinical utility. This 'manufacturing model' is, in my opinion, simply the wrong model. Unlike inorganic drug molecules (penicillin) and purified or manufactured biological agents (insulin), blood components such as red cell concentrates are irreducibly complex, variable and unpredictably dangerous. Thus, focusing on manufacturing controls and variability is extremely unlikely to provide a better or a safer product. We should consider instead devoting personnel to monitoring transfusion clinical outcomes and training our clinicians and nurses to recognize transfusion complications.

Blood centres now devote increasing numbers of personnel to compliance, and send large numbers of weekly product recall letters to transfusion services such as my own. To pick extreme examples, one might receive a recall of a red cell unit from months or years ago because (1) the donor was underage or (2) a donor screener has been found to be using a thermometer improperly and all products from donors examined by that screener must be 'recalled'. Other than generating a mountain of paperwork, this is an utter waste of time and activity. It is unfortunate that an erroneous paradigm for improving transfusion efficacy and safety has been chosen for the USA, but the simple reality is that we devote millions of dollars to activities that yield meaningless data and bog down hundreds or thousands of personnel in clinically irrelevant activities [1]. Similar objections have recently been raised in Europe to the Good Clinical Practice guideline for clinical research [2]. These approaches may look and feel good, but I would suggest that they do little or nothing to advance the goals of improved public health or clinical outcomes. These dollars and personnel would be more productively spent on clinical outcomes monitoring, such as haemovigilance, or on research, which has languished in many American blood centres since the ascendancy of the manufacturing/pharmaceutical model.

Question 2

Adverse events thought to occur as a result of transfusion in our hospital, if serious, are legally required to be reported to the New York State Department of Public Health [3] and the Food and Drug Administration (FDA) of the USA. Fatalities have been reportable to the FDA for decades and clinician scholars have access to these data through the Freedom of Information Act [4]. These are regulatory rather than clinical databases, not readily available for general inspection, although research findings from each have been employed to further public health and scientific understanding [3,5].

Question 3

As mentioned, the vast majority of required reporting to the Food and Drug Administration relates to records improperly filled out or not signed, water baths not monitored, laboratory or nursing errors of little clinical consequence, and other minutiae. Reporting of deaths and serious complications to both the FDA and state Department of Public Health are required in New York State, but because of varying compliance, are of unknown accuracy and quality. Most hospitals do not have full-time, highly motivated and/or expert physician coverage of transfusion services in our country, and attention to these functions is highly variable and usually left to technical personnel with varying degrees of interest and expertise in transfusion medicine.

Haemovigilance is a subspecialty term for public health and clinical outcomes monitoring, of the sort that is carried out in all US hospitals for infection-control purposes. There are several challenges to haemovigilance monitoring that probably affect even those countries with sound data-collection systems and medically/scientifically driven leadership. First, these systems are usually built on the infectious disease model of 'one pathogen, one sick patient'. This is a potential problem when many of the most serious side-effects of blood transfusion (acute lung injury, multi-organ failure, postoperative infection, postoperative tumour recurrence) are multifactorial in origin, heavily dependent on the patient's underlying condition, distant in time from the transfusion and of poorly defined pathogenesis. Only common infectious diseases that manifest within days, or errors in blood administration, are likely to be easily detected or tracked by haemovigilance systems.

Some of these problems are insuperable, and others need to be addressed by improved clinical outcomes monitoring that await better information technology and clinical databases. The current systems are good at tracking common, usually not very serious, events, but less good at tracking rare, complex, serious but delayed events. How much money to spend on clinical investigation versus haemovigilance is one issue. Another is how much effort to exert on regulatory compliance vs. haemovigilance, particularly in countries such as the USA, where the former activities have exceeded the latter, in both personnel and dollars, by several orders of magnitude.

Question 4

Required reports include everything along the spectrum from 'staff failed to note that the water bath was 0·1 °C beyond the acceptable range' to 'patient died of a ABO haemolytic reaction caused by an error in identification'.

Question 5

I am not aware of any reports from our state or federal regulatory agencies, or departments of public health, in the last 2 years.

Question 6

Does not apply.

References

1 Blumberg N: The costs and consequences of management fads and politically driven regulatory oversight – The case of blood transfusion. *Arch Pathol Lab Med* 1999; **123**:580–584

2 Grimes DA, Hubacher D, Nanda K, Schulz KF, Moher D, Altman DG: The Good Clinical Practice guideline: a bronze standard for clinical research. *Lancet* 2005; **366**:172–174

3 Linden JV, Wagner K, Voytovich AE, Sheehan J: Transfusion errors in New York State: an analysis of 10 years' experience. *Transfusion* 2000; **40**:1207–1213

4 Honig CL, Bove JR: Transfusion-associated fatalities: review of Bureau of Biologics reports 1976–1978. *Transfusion* 1980; **20**:653–561

5 Sazama K: Reports of 355 transfusion-associated deaths: 1976 through 1985. *Transfusion* 1990; **30**:583–590

Neil Blumberg
Professor of Pathology & Laboratory Medicine
Director, Clinical
Laboratories & Transfusion Medicine/Blood Bank
University of Rochester Medical Center
Box 608
601 Elmwood Avenue
Rochester, NY 14642
USA
E-mail: neil_blumberg@urmc.rochester.edu

M. M. Braun, M. A. Malarkey & J. S. Epstein

Question 1

A centralized, national haemovigilance system for blood and blood components does not exist in the USA. Instead, a well-established network of organizations works co-operatively to monitor blood safety, availability and clinical use. The Department of Health and Human Services (DHHS) provides leadership and co-ordination for this federal effort through collaboration with the Department of Veterans Affairs (VA) and the Department of Defense (DoD), as well as individual states. Agencies of the DHHS involved in safety monitoring include the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), the Centers for Medicare and Medicaid Services (CMS) and the National Institutes of Health (NIH). The National Heart, Lung, and Blood Institute (NHLBI) of the NIH funds research on the safety and adequacy of the blood supply, and the CDC engages in targeted surveillance to identify risks of transfusion. The CDC has a number of surveillance systems, including active monitoring for blood-borne infections in persons with haemophilia.

Blood industry trade organizations and blood establishments additionally are engaged in gathering safety data, assessing risks, as well as monitoring and maintaining the blood supply. These organizations include the AABB, of which nearly all blood collection and manufacturing establishments are members; America's Blood Centers, which includes collaboration among large community-based blood collectors; and the American National Red Cross.

Questions 2 and 4

The FDA has the lead responsibility for the safety of the US blood supply by regulating blood and blood components for transfusion or for further manufacturing (e.g. to make plasma derivatives). The FDA works closely with other parts of the DHHS to identify and respond to potential threats to blood safety; to develop standards for product safety, purity and potency; to monitor blood supplies; and to help industry promote an adequate supply of blood and blood products. The FDA gathers blood safety data through both mandatory and voluntary reporting systems. Most safety reporting in the USA is passive (adverse event reports submitted at the initiative of the reporter), rather than active (patients actively monitored for adverse events that are in turn reported). Reporting to the FDA is required for blood and blood components when a fatal adverse event occurs related to donation or transfusion (Title 21 Code of Federal Regulations 606·170(b)). For non-fatal adverse events, the blood collection and transfusion facilities are required to conduct investigations and maintain records; these reports may be reviewed in periodic FDA establishment inspections, but routine submission of reports to the FDA is not required. A proposed rule, published by the FDA on 14 March 2003, would require the reporting of non-fatal serious adverse events to the FDA within 45 calendar days [1]. The FDA also receives voluntary reports of medical errors and adverse events related to blood components under a reporting system called 'MedWatch.' Any person or organization can report incidents to the FDA through this system (http://www.fda.gov/medwatch/index.html). Blood collection establishments and transfusion services must also report to the FDA biological product deviations involving events that represent deviations from current good manufacturing practice, applicable regulations and standards, or established specifications that may affect the safety, purity, or potency of distributed products (Title 21 Code of Federal Regulations 606·171). Unexpected or unforeseeable events that may affect the safety, purity or potency of a distributed product must also be reported to the FDA. Most reported deviations are associated with postdonation information, but the FDA also receives reports associated with donor suitability determinations. These reports include, for example, failure to defer for geographical exposure to malaria or variant Creutzfeldt-Jakob disease (vCJD), tattoo and postdonation illness. The FDA posts annual summaries of biological product deviation reports, received each fiscal year, at http://www.fda.gov/cber/biodev/biodev.htm.

The FDA also collects safety data related to the use of medical devices (e.g. donor screening tests, cell separators, etc.) that are involved in the collection and processing of blood and blood components. User facilities (e.g. blood collection establishments, hospital transfusion services, donor testing laboratories, etc.) are required to report suspected medical device related deaths to both the FDA and the device manufacturers. User facilities are required to report medical device related serious injuries to the manufacturer. If the medical device manufacturer is unknown, the user facility must submit the report of the serious injury to the FDA (Title 21 Code of Federal Regulations Part 803).

Question 3

The misuse of blood components is not subject to haemovigilance reporting to FDA. However, the FDA may receive information about misuse through reports of fatalities, biological product deviations or unexpected or unforeseen events, or device reports. In addition, the CDC and NHLBI support research on the risks associated with blood transfusion, including studies related to clinical use of blood. The CMS gathers data on medical errors and complications of treatment in hospitals.

Reference

1 Safety reporting requirements for human drug and biological products proposed rule. *Federal Register* March 14 2003; **68**:12405–12497

M. Miles Braun
Mary A. Malarkey
Jay S. Epstein
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852–1448
USA
E-mail: epsteinj@cber.fda.gov

J. E. Menitove & K. S. Lipton

Question 1

The United States Food and Drug Administration (FDA) requires hospital transfusion services to report all transfusion-related fatalities. Donor centres must report all donation-related fatalities. Currently, no centralized agency in the USA monitors, receives reports, or conducts trend analyses of non-fatal transfusion-related adverse events.

Question 2

Transfusion- and donation-related fatalities must be reported to the FDA. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO), whose accreditation is required for government-related reimbursement for hospital charges, mandates reporting of sentinel events (e.g. a haemolytic transfusion reaction involving administration of a blood component with a major blood group incompatibility). In addition, the College of American Pathologists' accreditation check list requires the transfusion service director to have protocols for evaluating adverse effects of transfusion. However, there is no requirement to forward this information to a centralized agency.

Question 3

While there is no formal haemovigilance programme in the USA, several obligatory and voluntary reporting requirements exist. For example, the Centers for Disease Prevention and Control (CDC) collects data about human immunodeficiency virus (HIV) infected persons, conducts the reporting of viral hepatitis cases, and gathers uniform data about health outcomes in people with congenital blood clotting disorders. The FDA, in addition to mandating reports of fatal events, requires licensed and registered blood establishment and transfusion services to file biological product deviation reports when a break in current Good Manufacturing Practice (cGMP) affects the safety, purity, or potency of a blood product. Periodically, the FDA presents this information in various formats. Manufacturers must submit medical device reports involving deaths and serious injuries or illnesses connected with the use of medical devices for patient treatment or diagnosis. The National Heart Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) currently sponsors the Retrovirus Epidemiology Donor Study (REDS) that conducts epidemiologial and etiological investigations of transfusion transmitted viral infections and now investigates transfusion transmission of non viral agents, and other aspects of blood supply safety in the USA and internationally. Specimen repositories have been established at the NIH Clinical Center, by REDS and the Retrovirus Epidemiology Donor Study Allogeneic Donor and Recipient RADAR programme (seven blood centres and eight collaborating hospitals). NHLBI funding supports research involving transfusion related acute lung injury (TRALI), the optimal platelet dose, and other transfusion medicine research. The outcomes of these investigations are reported in peer review journals and at professional meetings. The Institute of Medicine, also, has issued reports and recommendations about medical errors. A recently enacted law in the USA, The Patient Safety and Quality Improvement Act, provides for the establishment of a non governmental patient safety organization to collect voluntary error reports for those providing health care, to analyse the data, and to recommend steps for improvement. Presumably, some adverse transfusion events will be included in this analysis.

The Association of State and Territorial Health Officers, and the Council of State and Territorial Epidemiogist, evaluate

disease outbreaks and routes of transmission, including blood transfusion.

Question 4

In the USA, mandatory adverse reporting of transfusion events involves those resulting in fatalities; transmission of diseases such as hepatitis and HIV; deviations from cGMPs that affect the safety, purity, or potency of a blood product; and deaths and serious injuries associated with medical devices.

Question 5

According to the US FDA, TRALI is the leading cause of transfusion-related fatalities (30%), followed by haemolytic transfusion reactions (16%) and bacterial contamination (16%) (L. Holness 2004) (www.fda.gov/ohrms/dockets/ac/04/briefings/2004-4057b1.htm). Most of the errors reported to the Joint Commission related to communication, training, and patient assessment issues. (http://www.jcaho.org/accredited+organizations/sentinel+event/se_pp.htm)

Question 6

Not applicable.

Jay E. Menitove
Executive Director and Medical Director
Community Blood Center of Greater Kansas City
4040 Main Street
Kansas City, Missouri 64111
USA
E-mail: jem@cbckc.org

Karen Shoos Lipton
AABB
8101 Glenbrook Road
Bethesda, MD 20814-2749
USA
E-mail: karen@aabb.org