afssaps

Agence française
de sécurité sanitaire
des produits de santé

France
Annual Haemovigilance report 2009
Summary

French Agency for the safety of health products

FOREWORD

Article L1221-13, modified by order n°2005-1087 dated 1 September 2005, states that "Haemovigilance covers all the procedures for the monitoring and assessment of incidents, as well as adverse reactions affecting donors or recipients of labile blood products. It covers the entire transfusion chain, from the collection of the labile blood products to the follow-up of their recipients. Haemovigilance also includes the epidemiological follow-up of donors".

Article R1221-27 of the French Public Health Code states that “the French Health Products Safety Agency (Afssaps) must draw up an annual haemovigilance summary report. This report is sent to both the Minister for Health and the European Commission (EC) no later than 30 June of the following year." This report is adopted by the French National Haemovigilance Commission.

1. Highlights of 2009

1.1. General comments

1. Regulatory context
On a regulatory level, year 2009 was marked by:
- the publication of 9 decisions by the director general, including 6 relating to the task forces and their missions
- opinions and recommendations regarding the use of methylene blue virus-inactivated Fresh Frozen Plasma:
. Procedure for the investigation of serious allergic reactions (grades 3 and 4) during transfusion involving VIP-MB (05/06/09).
. Warning dated 02/06/2009 regarding the use of methylene blue virus-inactivated Fresh Frozen Plasma
- The introduction of the platform for the new version, V2, of the e-FIT application, in the 4th quarter of 2009 including 6 user training sessions (BE HVC, CHU HVC and RHC).

2. Transfusion activity
- 2,979,117 LBPs were dispensed per 538,506 patients (52% women and 48% men) in 2009: 99.2% of these LBPs were traced.

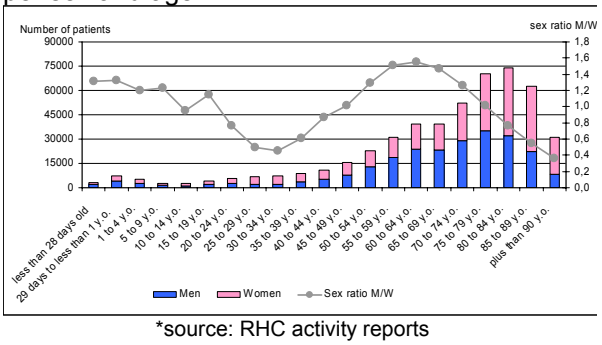
- Approximately 1,741,633 donors in 2009 (51% women and 49% men) provided 3,071,238 samples, i.e. 1.8 donations per donor. They constituted 4.1% of the population aged between 18 and 69 and 34% were less than 30 years old. Samples of whole blood constituted 81% of donations, the remaining 19% being aphaeresis.

1.2. Transfusion activity: general data

1.2.1. Number of patients transfused

In 2009, the number of transfused patients was estimated to be 538,506: 52% were women, 48% men.
82% of the transfused patients were more than 55 years old and 66% were more than 65 years old.

Distribution of the number of transfused patients per sex and age*



*source: RHC activity reports

Ratio of transfused patients per age group and sex *

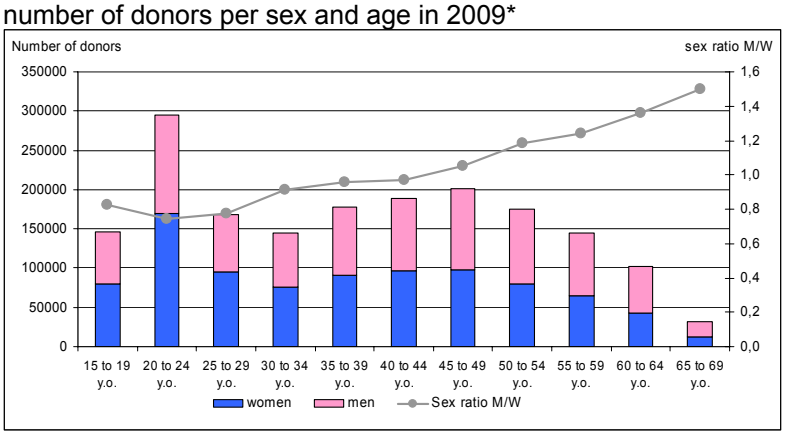
	Less than 1 year old	1-19 y.o.	20-54 y.o.	55 y.o. and over
Men	15,5	1,1	2,6	24,7
Women	12,1	1,0	3,0	21,1
Total	13,9	1,0	2,8	22,7

* Number of patients per 1,000 inhabitants

1.2.2. Number of donors and donations

The number of donors rose to 1,773,374 in 2009. They constituted 4.1% of the population between 18 and 69 years old. The donors were equally spread over both sexes. The sex ratio was 1 but varied greatly according to age. 34% of donors were less than 30 years old. These donors provided 3,071,238 samples, i.e. 1.7 donations per donor. Samples of whole blood constituted 81% of donations, the remaining 19% being aphaeresis.

Distribution of the number of donors per sex and age in 2009*



*source: RHC activity reports

1.2.3. Release/issue of labile blood products (LBPs)

● Distribution/issue: all products

In 2009, 2,979,117 LBPs were distributed, 79% red blood cells (RBC), 9% platelets and 12% plasmas. Homologous products constituted the vast majority of this number. The figure given for autologous LBPs was the number of samples taken in the event of a scheduled autologous transfusion package (including autologous red blood cells and fresh frozen plasma)

Homologous and autologous LBPs

LBP*	Quantity (%)
Homologous	2,975,147 (99.9%)
Autologous**	3,970 (0.1%)
Total	2,979,117 (100.0%)

* Source: EFS and CTSA ** package

Issue of LBPs in 2009 per type of product

Type of LBP*	Quantity (%)
HOMOLOGOUS	
RBC	2,339,834 (78.5%)
PCM (total)	76,649 (2.6%)
including storage sol.	51,869 (1.7%)
including Intercept	11,586 (0.4%)
APC (total)	186,752 (6.3%)
including storage sol.	56,706 (1.9%)
including Intercept	10,181 (0.3%)
PLASMA (total)	371,658 (12.5%)
including VIP-SD	142,533 (4.8%)
including quarantined FFPs	1,378 (0%)
including Intercept-VIP	22,933 (0.8%)
including VIP-MB	204,814 (6.9%)
AGC	254 (0%)
AUTOLOGOUS	
Autologous packages**	3 970 (0,1%)
Total	2 979 117 (100%)

* Source: EFS and CTSA ** package

● Product destruction

- The number of homologous LBPs destroyed was 44,940, i.e. a rate of destruction of 1.5%.
- The number of autologous LBPs destroyed was 1,106 (data source: RHC activity report), i.e. a rate of destruction of 20%. This same source gave the number of transfused autologous products as 4,313: 2,674 RBC, 1,637 plasmas and 2 APC.

In 2009, the Afssaps haemovigilance unit received 10,018 declarations, i.e. 7,808 RARs, 475 DSARs, 440 serious adverse events and 1,295 reports of PDI.

1.3. Recipient adverse events (RAR)

According to the French Public Health Code, a recipient adverse reaction (RAR) is a harmful reaction affecting a recipient, related or likely to be related to the administration of a labile blood product

1.3.1. The number of declarations and their frequency

In 2009, the number of RAR declarations, including all grades, levels of imputability and enquiries, stood at 7,808, i.e. a frequency of 2.6 per 1,000 distributed LBPs.

- RAR declarations – all LBPs

Distribution of 7,808 RARs declared in 2009 per grade[1] and imputability[2], irrespective of the level of enquiry

Imputability*	Per level of severity				
	Grade 1	Grade 2	Grade 3	Grade 4	Total & %
Imputability 0	518	24	54	8	604 (7.7%)
Imputability 1	1,007	10	42	12	1,071 (13.7%)
Imputability 2	2,113	143	99	8	2,363 (30.3%)
Imputability 3	1,740	652	160	3	2,555 (32.7%)
Imputability 4	116	1 057	41	1	1,215 (15.6%)
Total & %	5,494 (70.4%)	1,886 (24.2%)	396 (5.1%)	32 (0.4%)	7,808 (100%)
Number of RARs per 1,000 LBPs	1.84	0.63	0.13	0.01	2.62

- RAR declarations with autologous LBPs

Two RARs relating to the transfusion of autologous RBC were reported in 2009, with the following diagnoses: one bacterial infection of grade 1 and imputability 0 (and enquiry closed), one FNHTR of grade 1 and imputability 3 (and enquiry closed). This case is presumably an error as the RBC involved was autologous but the transfusion was declared to be homologous.

1.3.2. Confirmed cases of imputability 2 to 4

Of the 7,808 RARs declared in 2009, 5,902 were of imputability 2 to 4, enquiry closed. This level of declarations of imputability 2 to 4 was the highest ever reached since the introduction of haemovigilance, under the law dated the 4th January 1993. However, as a percentage of the number of LBPs, it constituted 2.0 RARs per 1,000 LBPs.

As for the previous years, 2009 saw variable levels of imputability per diagnosis: 87% of cases of imputability 4 involved appearances of irregular antibodies, 34% of cases of imputability 3 allergies and 45% of cases of imputability FNHTR.

[1] Grade 4: death of the recipient.
Grade 3: immediate danger of death. (Clinical or biological manifestations presented by the recipient during or after the transfusion which were immediately life-threatening and which required intensive care).
Grade 2: long-term morbidity. (Examples: Positive post-transfusion serology with a negative or unknown pre-transfusion serology; appearance of irregular anti-erythrocyte antibodies; appearance of anti-HLA antibodies).
Grade 1: absence of immediate or long-term danger of death. (Adverse effect with minor symptoms. This therefore covers all transfusion RARs which are not grades 2, 3 or 4.

[2] The imputability levels are classified according to the following criteria:
Imputability 4: Certain: The tests prove that the adverse event was caused by the transfusion.
Imputability 3: Likely: the adverse event does not appear to be accounted for by an intercurrent cause, and diagnostic information remains suggesting the adverse effect was caused by the transfusion.
Imputability 2: Possible: the adverse effect could be accounted for either by the transfusion or an intercurrent cause without it being possible to decide at the current stage of the investigation.
Imputability 1: Doubtful: the adverse event does not seem to be fully accounted for by the administration of the LBP, without it being possible to totally exclude this possibility.
Imputability 0: Excluded: it was proven that the LBP was not involved in the occurrence of the adverse effect.

Distribution per diagnosis of adverse events of imputability 2 to 4 in 2009

Diagnoses	Imputability score, N (%)			Total
	Imputability 2	Imputability 3	Imputability 4	
appearance of irregular antibodies	114 (5.1%)	632 (25.5%)	1,054 (87.1%)	1,800 (30.5%)
FNHTR	1,000 (45.1%)	506 (20.4%)	2 (0.2%)	1,508 (25.6%)
allergy	464 (20,9%)	847 (34.2%)	51 (4.2%)	1,362 (23.1%)
immunological incompatibility	82 (3.7%)	182 (7.4%)	52 (4.3%)	316 (5.4%)
including ABO with RBC	3 (0.1%)	2 (0.1%)	6 (0.5%)	11 (0.2%)
TACO	83 (3.7%)	161 (6.5%)	23 (1.9%)	267 (4.5%)
TRALI	13 (0.6%)	15 (0.6%)	14 (1.2%)	42 (0.7%)
bacterial infection	4 (0.2%)	2 (0.1%)	4 (0.3%)	10 (0.2%)
viral infection		2 (0.1%)	1 (0.1%)	3 (0.1%)
other (immediate or delayed effects)	32 (1.4%)	27 (1.1%)	7 (0.6%)	66 (1.1%)
unknown[3]	424 (19.1%)	102 (4.1%)	2 (0.2%)	528 (8.9%)
Total	2 216 (100%)	2 476 (100%)	1,210 (100%)	5,902 (100%)

● Distribution per immediate and delayed diagnosis:

- The immediate reactions (appearance within 8 days) included:

* 1,508 febrile non-haemolytic transfusion reactions (FNHTR), i.e. 25.6% of all RARs
* 1,362 allergies, i.e. 23.1% of RARs
* 528 RARs of unknown aetiology, i.e. 8.9% of RARs, including 80% of possible imputability (imputability 2)
* 316 immunological incompatibilities, including 11 in the ABO system after a RBC transfusion
* 267 TACOs, i.e. 4.5% of the RARs
* 42 TRALI
* 10 suspected bacterial infections, including 7 transfusion-transmitted bacterial infections (TTBI). For these 7 cases of TTBI (enquiries closed), the LBP cultures proved positive.

In 6 cases, the same microorganism was identified in the LBP cultures and the recipient haemocultures (imputability 3 and 4). In one case, the haemoculture remained negative with imputability of 2 for the transfusion (taking into account the type of microorganism identified in the LBP and the clinical condition of the recipient). Furthermore, the investigation made it possible to demonstrate in one case the presence in the female donor of the microorganism responsible for the TTBI (Staphylcoccus aereus).

The distribution of the microorganisms identified in these 7 cases was as follows: 2 Bacillus, including 1 Bacillus Cereus, 1 Escherichia Coli, 1 Klebsiella oxytoca, 1 Klebsiella pneumoniae, 2 Staphylococcus aureus.

- The delayed adverse reactions (appearance after more than 8 days) included:

* 1,800 appearances of irregular antibodies. The principal specific types of antibodies were, in descending order: anti-JK1 (Jka), anti-RH3 (E), anti-KEL1 (K), anti-FY1 (Fya), anti-LU1 (Lua)…
* 3 post-transfusion viral infections: 1 HCV of grade 2 and imputability 3 with a transfusion in 1985, 1 CMV of grade 2 and imputability 3 and one parvovirus of grade 2 and imputability 4.
* 1 haemosiderosis
* 1 post-transfusion purpura

Number of diagnoses per 10,000 LBPs distributed per inter-region of imputability 2 to 4 that occurred in 2009

Diagnoses	Total	Inter-region						Total	
	Nbr of RARs	Ile-de-France	North East	North West	South East	South West	DOM-TOM	Average	Standard deviation
appearance of irregular antibodies	1,800	5.11	7.55	5.03	7.36	4.65	2.65	6.06	1.40
febrile non-haemolytic transfusion reaction	1,508	2.41	3.77	5.56	7.60	6.28	3.64	5.08	2.05
allergy	1,362	5.35	5.25	4.26	3.53	5.10	1.49	4.59	0.78
Immunological incompatibility*	316	0.50	0.87	1.82	1.22	1.03	0.17	1.06	0.49

* including ABO	11	0.00	0.01	0.09	0.06	0.02	0.00	0.04	0.04
TACO	267	0.81	0.92	0.99	1.02	0.70	0.66	0.90	0.13
TRALI	42	0.16	0.10	0.31	0.12	0.02	0.00	0.14	0.11
bacterial infection	10	0.03	0.01	0.02	0.01	0.12	0.00	0.03	0.05
viral infection	3	0.02	0.00	0.00	0.03	0.00	0.00	0.01	0.01
purpura	2	0.00	0.00	0.02	0.01	0.00	0.00	0.01	0.01
haemosiderosis	1	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.01
other (immediate and delayed effects)	63	0.31	0.16	0.09	0.09	0.51	0.33	0.21	0.18
unknown	528	1.07	1.89	2.24	2.00	1.76	0.66	1.78	0.44
Total	5,902	15.80	20.52	20.35	22.99	20.17	9.60	19.88	2.60

(1) Standard deviation excl. DOM-TOM

● Per diagnosis and per type of product (only the LBP declared as being the most likely to have caused the AE is taken into account)

Average number of diagnoses per 10,000 units of LBP distributed of imputability 2 to 4 that occurred in 2009

Diagnoses	RBC	APC	PCM	VIP	FFPs	All LBPs
appearance of irregular antibodies	7.05	3.80	8.87	0,08	7,26	6,04
FNHTR	5.48	8.51	6.26	0.41	0.00	5.06
allergy	1.60	39.73	9.65	4.56	0.00	4.57
immunological incompatibility	0.70	6.05	4.83	0.03	0.00	1.06
including ABO	0.03	0.21	0.13	0.00	0.00	0.04
TACO	1.06	0.48	0.39	0.14	0.00	0.90
TRALI	0.11	0.64	0.13	0.05	0.00	0.14
bacterial infection	0.01	0.32	0.26	0.00	0.00	0.03
viral infection	0.01	0.00	0.00	0.00	0.00	0.01
other (immediate or delayed effects)	0.19	0.86	0.39	0.08	0.00	0.22
unknown	1.46	7.12	4.57	0.19	0.00	1.77
Total	17.68	67.52	35.36	5.54	7.26	19.81

● Death

Eight deaths (8 cases of imputability 2 to 4) were identified in 2009 in France, corresponding to enquiries conducted and closed. They involved 3 women and 5 men, aged from 41 to 89 years old. 4 of these 8 cases were of certain or probable imputability.

The 4 cases of imputability 3 and 4 involved:

- A "TRALI" diagnosis: a 74-year old woman transfused at day hospital for chemotherapy-induced anaemia following treatment for myelodysplastic syndrome. 40 mins after the transfusion of 2 RBCs (both 27 days old), she suffered a brutal desaturation to 80% with respiratory distress and acute pulmonary oedema. The X-ray image showed 2 white lungs: there was no underlying heart condition.
The patient was hospitalised but her respiratory symptoms worsened and she died shortly afterwards. The immunological tests performed were negative.
The TF experts confirmed the diagnosis of TRALI: the imputability to the transfusion was probable, graded 3.

- One diagnosis of "Allergy": 74-year old man with myelodysplastic syndrome (type-II RAEB) discovered two months before the RAE. Hospitalisation for asthenia, dyspnoea with the slightest exertion and pain in the left side; anaemia and thrombopenia. A transfusion of an APC and 3 RBCs was scheduled. In the minutes that followed the start of the transfusion of a TSol APC, the patient suffered anaphylactic shock and a Quincke's oedema. In spite of the attempts to resuscitate him, the patient died. The imputability was graded 3.

- One diagnosis of "immunological incompatibility" (JK1): a 50-year-old man, hospitalised for treatment of post-traumatic haemorrhagic shock with a haematoma on the left thigh and immediate generalised jaundice. Profound anaemia and haemostasis problems on non-weaned chronic alcoholic ground justified the prescription of LBP. Faced with the relative inefficacy of the transfusion and in the absence of an external haemorrhage, the hypothesis of acute haemolysis was raised and this was confirmed by the detection of the anti-JK1 antibody the day before the patient's death. In spite of the subsequent use of pheno-compatible transfusions, the patient died on the 7th day of hospitalisation.

The enquiry conducted found the notion of transfusion of RBC 8 months before the patient's death, in another facility in the same region. The imputability was graded 3.

- One 'Post-transfusion purpura" diagnosis: an 81-year-old woman, hospitalised for treatment of a haemorrhagic shock on a digestive haemorrhage that occurred during treatment with anticoagulants (aortic valve). Progressive appearance after transfusion of 17 RBCs of a thrombopenia, resistant to platelet transfusions. Death on the 15th day of hospitalisation. The assessment conducted revealed class I anti-HLA and IIB IIIa anti-GP antibodies. The imputability was graded 4, i.e. certain.

1.4. Serious adverse events (SAE)

"A serious adverse events is an incident related to the collection of blood, the biological qualification of donations, preparation, storage, distribution, issue or use of labile blood products, due to an accident or error, likely to affect the safety or quality of this product and cause serious adverse events, i.e. adverse reactions resulting in death or danger of death, resulting in disability or incapacity, or provoking or prolonging hospitalisation or any other morbid condition."

In 2009, 440 SAEs were declared, i.e.:
- 176 incidents with transfusion of LBP without SAE (ratio of 5.9 per 100,000 distributed LBPs)
- 33 incidents with transfusion of LBP that caused an SAE of a grade higher than or equal to 1 (ratio of 1.1 per 100,000 distributed LBPs)
- 231 serious incidents with transfusion (ratio of 7.8 per 100,000 distributed LBPs)

1.4.1. SAEs with transfusion of LBP declared on the AR as grade 0 without clinical or biological manifestation

The declarations (N=176) principally covered SAEs that occurred in HFs (68%), both the HF and BE (13%) and BE (7%) and 82% of cases involved RBCs, 11% platelets and 5% plasmas.

Distribution of the 176 SAEs declared in the RARFs as grade 0 in 2009 per type of LBP

Type of LBP	Number of grade 0 and %	Number of grade 0 per 100,000 distributed LBPs*	Reminder of the number of distributed LBPs
RBC	145 (82.4%)	6.2	2,343,804
APC	17 (9.7%)	9.1	186,752
PCM	3 (1.7%)	3.9	76,649
VIP	8 (4.5%)	2.2	370,280
FFPs	0		1,378
Others	3 (1.7%)		254
Total	176 (100.%)	5.9	2,979,117

1.4.2. SAEs with transfusion of LBP that caused an RAE of a grade higher than or equal to 1

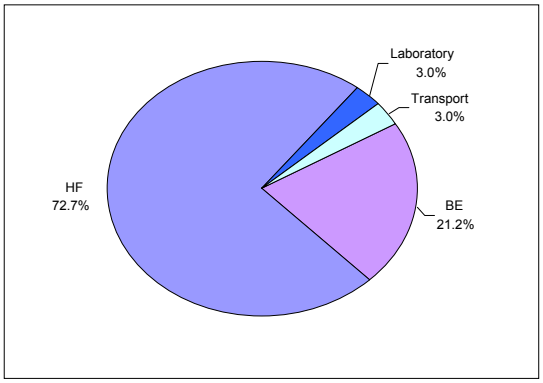
In 2009, 33 incidents were associated with an RAE of grade ≥ 1, of which 73% occurred in HFs. 21 were of grade 1, 5 grade 2, 5 others grade 3 and 2 grade 4.

73% of the anomalies or errors principally occurred in HFs.

Distribution per grade of the SAEs associated with RARs

Total number	Grade 1	Grade 2	Grade 3	Grade 4
33	21	5	5	2
100.0%	63.6%	15.2%	15.2%	6.1%

Distribution per site of dysfunction of the SAEs with transfusion of LBP that caused an RAR



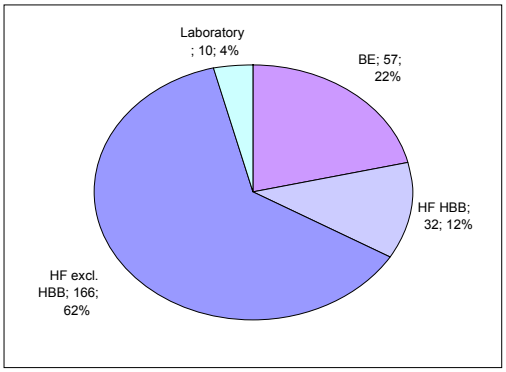
1.4.3. SAEs without transfusion of LBP

An SAE with transfusion of LBP is an incident that occurred during a stage of the transfusion chain, which may compromise the quality of the products and which, thanks to its detection, did not go as far as transfusion.
In 2009, 231 incidents without transfusion were declared, including 195 reported as being potentially serious and 28 classified as incidents of a repetitive nature.

74% of the declarations of SAEs without transfusion involved HFs (including banks).

The principle causes of declaration were patient identification errors (61%), "procedural non-compliance" (9%), prescription, sampling, receipt and transport anomalies (7%), LBP storage system failures (5%), blood group mismatches (3%)...

Sites of dysfunction of the SAEs without transfusion of LBP



1.5. Serious adverse reactions in donors (DSAR)

A donor serious adverse event is defined as any harmful reaction suffered by a blood donor, related or likely to be related to the sampling of blood and liable to result in death or danger of death, result in disability or incapacity, provoke or prolong hospitalisation or any other morbid condition.

1.5.1. The number of declarations and their frequency

In 2009, 475 DSARs were declared (irrespective of the level of imputability) per 3,071,238 donations made, i.e. 15.5 DSARs per 100,000 donations.

Distribution of DSARs per grade and per imputability

Imputability	Grade 2	Grade 3	Grade 4	NS	Total
NE – Non-assessable	5 (1.4%)	2 (1.8%)	0	0	7 (1.5%)
0 – excluded	7 (1.9%)	4 (3.6%)	0	1 (50%)	12 (2.5%)
1 – possible	56 (15.5%)	27 (24.5%)	0	0	83 (17.5%)
2 -probable	120 (33.1%)	50 (45.5%)	0	0	170 (35.8%)
3 – certain	174 (48.1%)	27 (24.5%)	1 (100%)	1 (50%)	203 (42.7%)
Total	362 (100%)	110 (100%)	1 (100%)	2 (100%)	475 (100%)

79% of the 475 recorded declarations had a level of imputability of probable or certain.
In 65% of the declarations, the event occurred during a donation of whole blood and in 35% during a donation of aphaere SARs.
The ratio of declared DSARs appeared 2 times higher for aphaere SARs procedures than for donations of whole blood (29.0 per 100,000 aphaere SARs donations versus 12.3 per 100,000 donations of whole blood).

1.5.2. The principal characteristics of the DSARs of imputability NE and 1 to 3

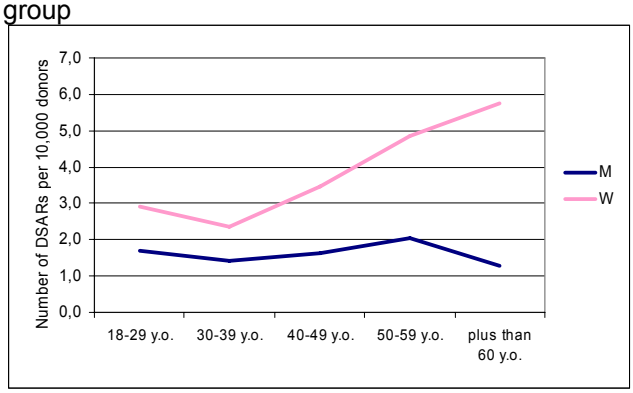
The tables and figures, below, specify the principal characteristics of the 463 DSARs (475-12=463) of imputability different from "0" (imputability: NE, 1, 2 and 3):

● According to donor age and sex
The ratio of DSARs per 10,000 female donors appeared to increase with age, rising from 2.9 in donors between the ages of 18 and 29 to 5.8 in those over the age of 60.
The ratio for male donors appeared more stable, varying between 1.5 and 2.1 per 10,000 donors.

Distribution of the number of DSARs according to sex and age

DSAR	M	W	NS	Total	%
18-29 y.o.	45	100		145	31.3%
30-39 y.o.	22	39	1	62	13.4%
40-49 y.o.	32	67		99	21.4%
50-59 y.o.	36	70		106	22.9%
Over 60y.o.	10	32		42	9.1%
NS	5	3	1	9	1.9%
Total	150	311	2	463	100%
%	32.4%	67.2%	0.4%	100%	

Ratio of DSARs per 10,000 donors per sex and age group



● According to the level of severity and collection method

77% of DSARs were declared as grade 2 (external consultation required), 23% as grade 3 (AR requiring hospitalisation) and 0.2% as grade 4 (death[20]).
The severity was not specified on 0.2% of the forms.
* In September 2009, a plasmaphaeresis procedure caused a cardiac arrest and the subsequent death of the female donor, in spite of the measures taken to resuscitate her. The enquiry is in progress. However, a set of measures aiming to increase the safety of donors faced with this type of risk has been drawn up and has begun to be implemented.

Distribution of DSARs per grade and type of donation

Type of donation	grade 2	grade 3	grade 4	NS	Total	Ratio per 10,000 collections
Whole blood	236 (78.1%)	66 (21.9%)	0	0	302 (100%)	12.1
Aphaeresis	119 (73.9%)	40 (24.8%)	1 (0.6%)	1 (0.6%)	161 (100%)	27.9
Including: Plasmapha eresis	92 (70.2%)	37 (28.2%)	1* (0.8%)	1 (0.8%)	131 (100%)	NS
Intermittent flow plateletpha eresis	4 (80%)	1 (20%)	0	0	5 (100%)	NS
Continuous flow plateletpha eresis	9 (90%)	1 (10%)	0	0	10 (100%)	NS
Combined Aphaeresis	14 (93.3%)	1 (6.7%)	0	0	15 (100%)	NS
Total	355 (76.7%)	106 (22.9%)	1 (0.2%)	1 (0.2%)	463 (100%)	15.1

● According to the clinical signs

Among the 463 DSARs, the most-frequently reported topical manifestations were: haematomas (51%), inflammatory reactions (9%) and nerve injuries (5%).

Topical clinical manifestations of the DSARs according to the type of donation

Topical clinical manifestations	Whole blood	Plasma phaeresis	Intermittent flow platelet phaeresis	Continuous flow platelet phaeresis	Combined Aphaeresis	Total	Percentage
Haematoma	65	43	2	6	7	123	50.8%
Allergic reaction	2	1	0	0	0	3	1.2%
Inflammatory reaction	14	3	1	2	1	21	8.7%
Puncture site infection	5	0	0	1	0	6	2.5%
Arterial injury	6	1	0	0	0	7	2.9%
Nerve injury	9	0	1	1	0	11	4.5%
Others	48	16	1	3	3	71	29.3%
Total	149	64	5	13	11	242	100.0%

Generalised manifestations were more frequent than topical manifestations; the most common were vasovagal attacks, loss of consciousness and extremely low blood pressure.

Generalised clinical manifestations according to the type of donation

Generalised clinical manifestations	Whole blood	Plasma phaeresis	Intermit tent flow platelet phaeresis	Continuous flow platelet phaeresis	Combined Aphaeresis	Total	Percenta ge
Vasovagal attack	129	58	2	1	6	196	34.5%
Loss of consciousness	116	47	1	1	1	166	29.2%
Major hypotension	38	27	0	0	1	66	11.6%
Tetany attack	12	6	0	1	0	19	3.3%
Convulsions	14	5	1	0	0	20	3.5%
Fit of angina, MI, arrhythmia	5	3	0	0	0	8	1.4%
Generalised allergic reaction	0	0	0	1	2	3	0.5%
Other	48	27	0	1	4	80	14.1%
Total	362	173	4	5	14	558	100%

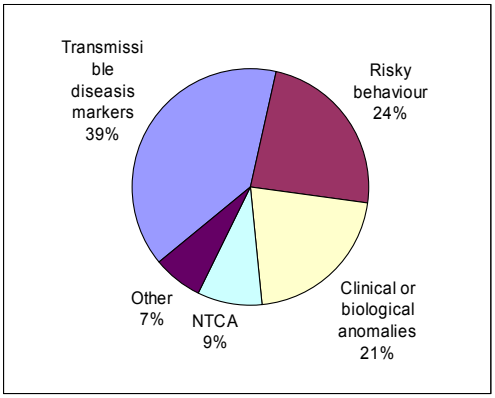
Note: a single DSAR form can include 0, 1 or several topical or generalised signs.

1.6. Post-donation information (PDI)

PDI is defined as any information provided after a donation likely to cast doubt on the quality and safety of the products from the donation. Their declaration to Afssaps was introduced in October 2002 and only applies to donations used to create LBPs having left the BE.
Given the "LBPs having left BE" criterion and the logistics of the storage of products at the BE, the number of PDIs declared to Afssaps was lower than the number of declarations/reports listed by the EFS (source – EFS: PDI received from Afssaps represented around 10% of the PDI recorded by the BE).

1,295 PDIs were declared in 2009. The information covered, in descending order: transmissible disease markers, risky donor behaviour, clinical or biological anomalies and non-conventional transmissible agent transmission risks.

The distribution of PDI declaration causes.

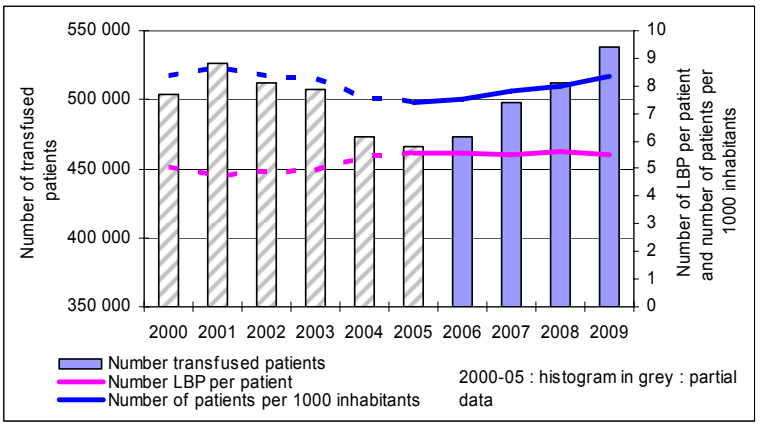


2. Major trends 2000-2009

2.1. Transfusion activity

Consumption of LBPs has continued to increase since 2000 at a rhythm of +1.2% per year. The progression has been greater for VIP (+14%) and PCM (+8%) than for the other products, particularly RBCs. This change should be partially linked to the slight growth in the number of patients.
Since 2006, there has been an increase in the number of transfused patients. The blue curve in the same figure representing the number of transfused patients per 1,000 inhabitants has also increased in the same way since 2006.
However, the number of LBPs per transfused patient has been stable since 2006.

Evolution of the number of transfused patients, the ratio of patients per 1,000 inhabitants and of the number of LBPs distributed per transfused patient

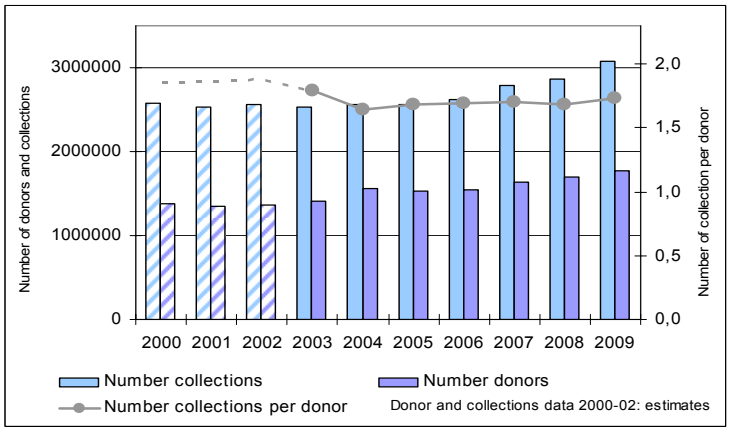


Sources: EFS, CTSA and RHC Activity Report

Number of donors and donations

Since 2003, the number of donors and donations has increased, respectively by 3.7% and 3.3% per year. The number of donations per donor has remained around 1.7.

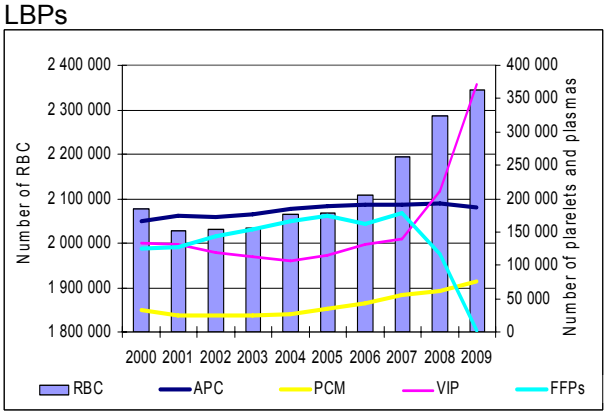
Evolution of the number of donors and donations



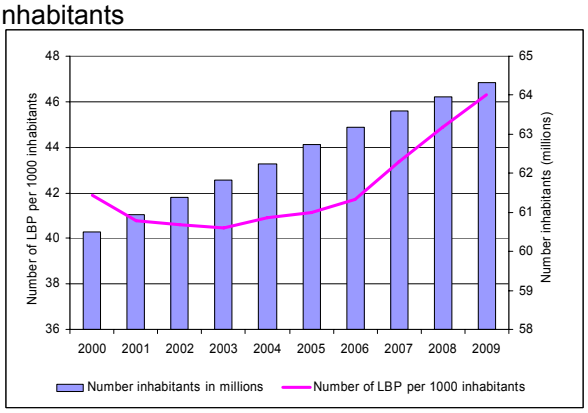
Sources: EFS and CTSA

The rate of use of LBPs per 1,000 inhabitants has also grown by 1.0% per year since 2000.

Evolution of the consumption of different types of LBPs



Evolution of the rate of use of LBPs per 1,000 inhabitants

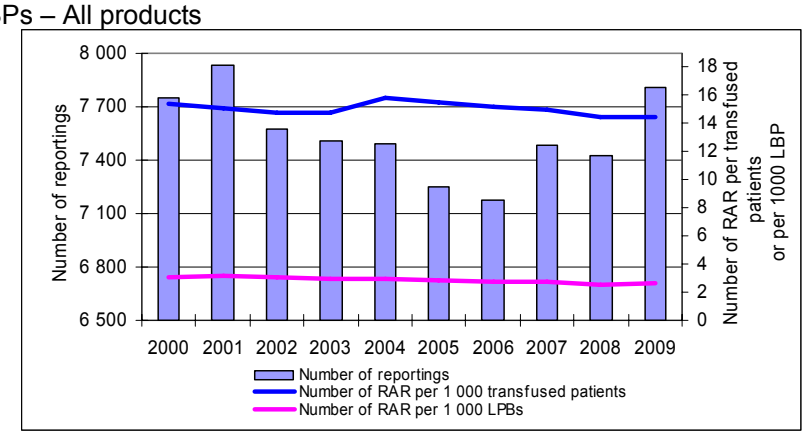


2.2. Recipient adverse reactions (RAR)

2.2.1. The number of reportings and their frequency

Having fallen from 2000 to 2006, the number of RAR declaration has increased since 2006 by nearly 2% per year. However, this number in relation to 1,000 distributed LBPs has, conversely, followed a downward trend since 2001 (3.1 in 2000, 3.2 in 2001 and 2.6 in 2009).

Evolution of the number of RAR declarations, ratio of declared RARs per 1,000 transfused patients and per 1,000 LBPs – All products



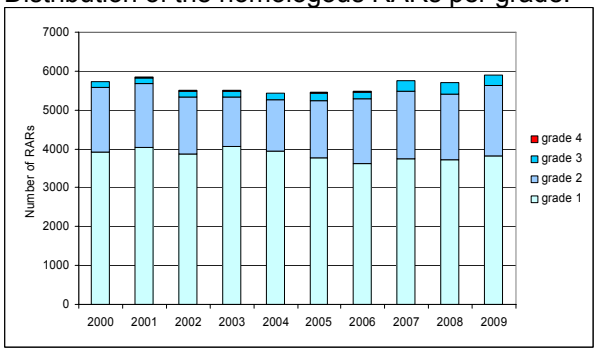
2.2.2. Confirmed cases of imputability 2 to 4

2.2.2.1. According to the level of severity and in the event of transfusion

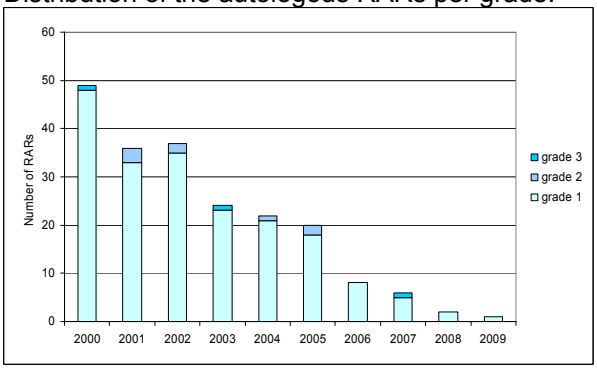
The distribution per grade of the homologous RARs of imputability 2 to 4 varied only a little over the past 10 years.

95% of the RARs declared with autologous LBPs were benign (grade 1). Indeed, over this period, 8 grade-2 RARs and 3 grade-3 RARs were reported.

Distribution of the homologous RARs per grade.



Distribution of the autologous RARs per grade.



2.2.2.2. According to diagnosis

Principal diagnoses of the RARs and their evolution over the last 10 years:

- increase in the frequency of declarations of:
. TACOs (4% of diagnoses): growth of 5% per year
. allo-immunisations (26% of diagnoses over the period): average growth of 3% per year
. "unknown" aetiologies (10% of diagnoses): average growth of 10% per year
. TRALI (data available since 2003: i.e. 1% of diagnoses between 2003 and 2009 and average growth of 29% per year over this period)

- almost stable frequency of declaration of:
. FNHTRs (26% of diagnoses)
. allergic-type reactions (25% of diagnoses)
. immunological incompatibilities (5% of diagnoses)

- reduction in the frequency of declaration of bacterial infections (less than 0.3% of diagnoses): reduction of -0.6% per year.

Evolution of the number of grade 1 to 4 and imputability 2 to 4 RARs, enquiry closed, over the 2000-09 period

Diagnosis	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2000-09
appearance of irregular antibodies	1,426	1,427	1,349	1,201	1,266	1,430	1,627	1,732	1,686	1,800	5.69
FNHTR	1,768	1,854	1,817	1,762	1,068	1,003	1,202	1,439	1,501	1,508	5.68
allergy	1,364	1,400	1,379	1,545	1,598	1,443	1,319	1,375	1,337	1,362	5.37

immunological incompatibility	353	305	259	257	292	288	258	284	238	316	1.08
including ABO	28	20	21	12	17	14	12	11	13	11	0.06
TACO	174	180	168	209	191	208	219	253	277	267	0.82
viral infection	219	189	100	54	44	24	15	8	3	3	0.25
TRALI	1	1	9	18	24	34	37	47	54	42	0.10
bacterial infection	40	21	16	35	13	6	8	11	9	10	0.06
other (immediate or delayed)	72	80	54	58	59	38	53	50	52	66	0.22
Unknown	363	424	387	394	901	1005	745	565	552	528	2.23
Total	5,780	5,881	5,538	5,533	5,456	5,479	5,483	5,764	5,709	5,902	21.51

2.2.2.3. The most serious and most certain RARs (grades 3-4 and imputability 3-4)

We recorded on average 145 RARs of grade 3-4 and imputability 3-4 per year from 2000 to 2009 (62% with RBCs, 26% with APCs, 4% with PCMs, 8% with plasmas).

Confirmed RARs of grade 3-4 and imputability 3-4 – according to the type of products

Type of LBP	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
RBC	66	62	85	85	78	81	92	111	133	107
APC	24	31	35	36	38	42	32	49	40	51
PCM/SPC	6	2	0	3	1	3	2	12	13	9
VIP	1	2	0	0	0	2	1	4	14	16
FFPs	8	5	9	9	8	3	7	19	4	0
Others	0	1	0	0	1	0	0	2	0	2
Total	105	103	129	133	126	131	134	197	204	185
Per 100,000 distributed LBPs	4,1	4,1	5,2	5,3	4,9	5,1	5,1	7,2	7,1	6,2

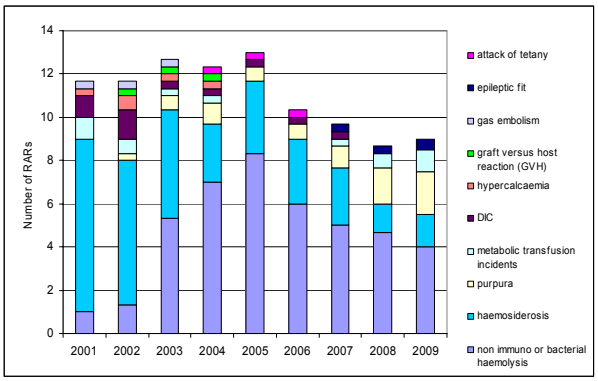
2.2.2.4. Rarest RARs

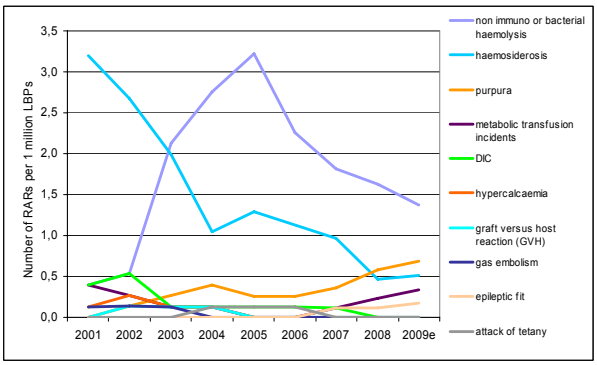
● The rarest RARs: the criterion adopted was the occurrence of "less than 5 diagnoses of this type declared per year", i.e. an incidence of less than 2 per million transfused LBPs.

● The diagnoses in question were as follows:
(N=cumulated number between 2000 and 2009, inc=incidence per million transfused LBPs over the same period)
- non-immune or post-septicaemic haemolysis N=47 inc=1.7
- haemosiderosis N=41 inc=1.6
- purpura N=8 inc=0.3
- transfusion-related metabolic accidents N=6 inc=0.3
- DIC N=5 inc=0.2
- hypercalcaemia N=2 inc=0.1
- graft versus host reaction (GVH) N=1, inc=0.04; ditto for the following 3 types of RAE:
- gas embolism
- epileptic fit
- tetany attack
- confirmed viral, parasitic or other infections

Evolution of confirmed rare effects of grade 1 to 4 and imputability 2 to 4 per date of occurrence*

Evolution of incidence of confirmed rare effects of grade 1 to 4 and imputability 2 to 4 per date of occurrence



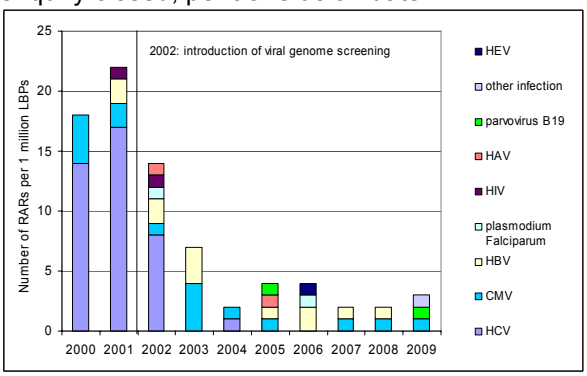


* Due to the low number of cases observed and, for certain years, the complete lack of cases, the above evolution uses moving 3-year averages

For these infections, please note that between 2000 and 2009, for 26 million transfused LBPs, there were:

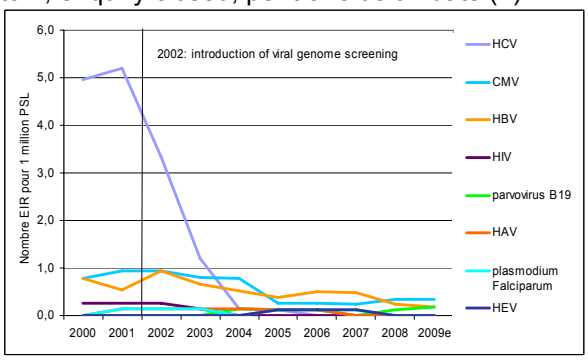
. 40 declarations of HVC infection (none since 2004)
. 16 declarations of CMV (average of 1 to 2 per year)
. 2 declarations of HIV infection (none since 2002)
. 2 declarations of Parvovirus B19 virus (in 2005 and in 2009)
. 2 declarations of HVA infection (in 2002 and 2005)
. 2 declarations of malaria (none since 2006)
. 1 declaration of HEV infection (in 2006)

Evolution of the number of viral, parasitic or other infections of grade 1 to 4 and imputability 2 to 4, enquiry closed, per transfusion date



(1) 2009: 3 declarations of viral infections with RBC: 1 B19 parvovirus (grade 2, imputability 4), 1 CMV (grade 2, imputability 3) and one other CMV infection (grade 1, imputability 2 – with intercurrent pathology): E-coli urinary tract infection)

Evolution of the incidence of viral, parasitic or other infections of grade 1 to 4 and imputability 2 to 4, enquiry closed, per transfusion date (1)



(1) number per 1 million LBPs – moving average over 3 years

2.3. Serious adverse events (SAE)

Serious adverse events (SAE)

- The declaration of SAEs of grade 0 began in November 2002. The number of declarations has progressively increased, 138 in 2003 and 197 in 2008, before falling to 176 in 2009. The rate of occurrence per 100,000 distributed LBPs was on average 6.0 between 2003 and 2009.
- The declaration of SAEs without transfusion began in May 2007. Over the 1st eight months of declaration, 47 SAEs were declared, then 124 SAEs in 2008 and 231 in 2009, i.e. an increase of 86% between 2008 and 2009. The rate of occurrence was 3.4 SAEs per 100,000 distributed in 2008 and 7.8 in 2009.

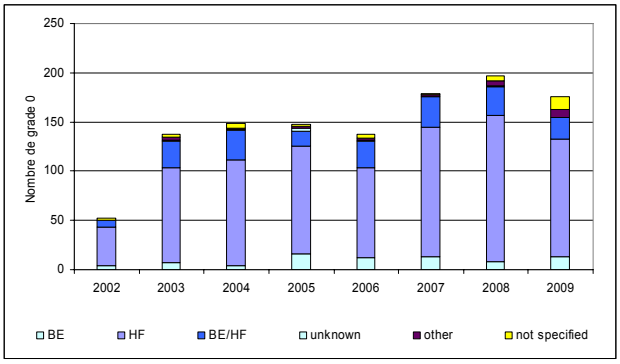
● SAEs with transfusion of LBP without RAR

Healthcare facilities remained the principal site of dysfunction over the 8 years

Evolution of SAEs declared on the RARF as grade 0 according to site of dysfunction

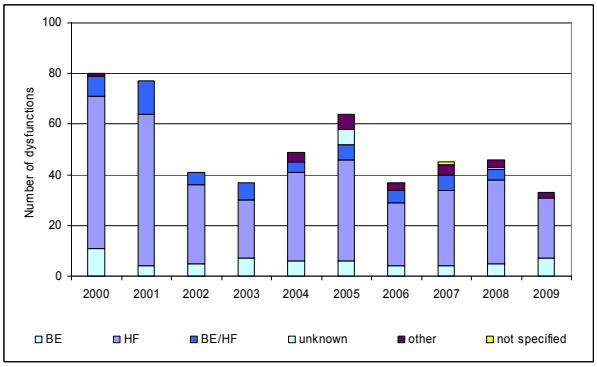
● SAEs with transfusion of LBP that caused an RAR (grade higher than or equal to 1)

On average, 51 SAEs were declared between 2000 and 2009. During this period, 70.9% occurred in HFs, 11.4% both at the BE and HF, 11.6% in BE



and 6.1% on other sites.

Evolution of SAEs associated with RARs of a grade higher than or equal to 1 according to dysfunction site

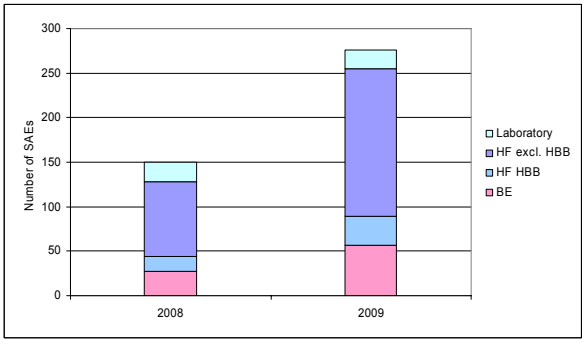


● SAEs without transfusion of LBP

This chapter covers the declarations from 2008 and 2009: the SI declaration system was introduced in May 2007 (47 SAEs over 8 months of declaration). Accordingly, 124 SAEs were declared in 2008 and 231 in 2009, i.e. an increase of 86%. Of these, those identified in HFs increased from 101 to 198, i.e. an increase of 75%.

83% of the 355 SAEs declared between 2008 and 2009 were estimated to be potentially serious, 15% of a repetitive nature, 54% resulted in preventive measures and 86% corrective measures.

Sites of dysfunction of the SAEs without transfusion of LBP



Severity of SI and accompanying measures

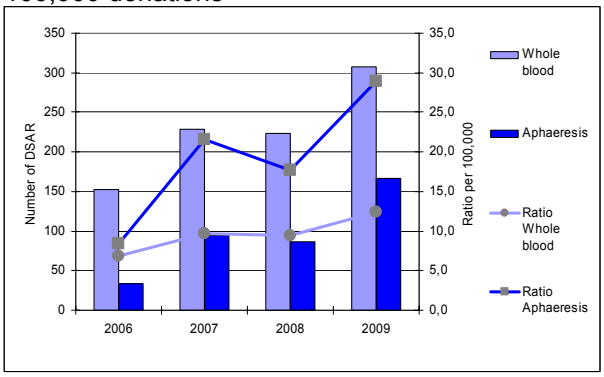
	2008	2009	2008-09
Potential severity	100 (80.6%)	195 (84.4%)	295 (83.1%)
Repetitive incident	24 (19.4%)	28 (12.1%)	52 (14.6%)
Preventive measure	78 (62.9%)	113 (48.9%)	191 (53.8%)
Corrective measure	106 (85.5%)	199 (86.1%)	305 (85.9%)
Total SAEs	124 (100%)	231 (100%)	355 (100%)

2.4. Donor serious adverse reactions (DSAR)

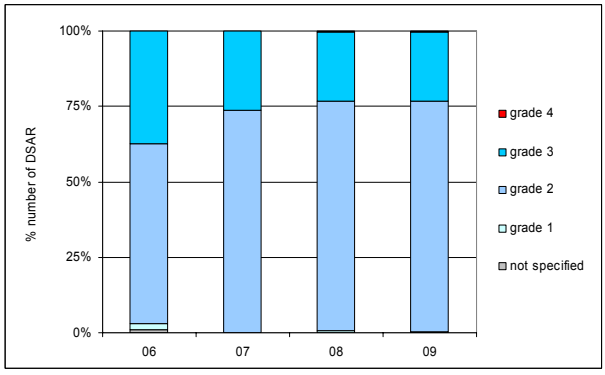
In 2006, DSAR declaration was introduced by Afssaps on an experimental basis. Between 2006 and 2009, the number of declarations more than doubled, increasing from 188 forms in 2006 to 475 forms in 2009. This shows a rate of declaration increasing from 7.2 to 15.5 declarations per 100,000 samples over the same period (all grades and levels of imputability and enquiry).

However, the rate would appear to have been 2 times higher for DSARS occurring during Aphaeresis samples than for DSARs observed during sampling of whole blood.

Evolution of the number and ratio of DSARs per 100,000 donations



Evolution of the distribution per grade of DSAR declarations



● Principal characteristics of the DSARs declared with imputability NE and 1 to 3 (2007-09)
Between 2007 and 2009, 1,084 DSARs were declared with imputability of NE and 1 to 3. We observed that:
- 84% of DSARs were of probable or certain imputability.
- 76% grade 2 and 24% grade 3. However, there was a grade 4 of certain imputability in 2009 (see chapter 2.5);
- 69% involved donations of whole blood, 31% Aphaeresis donations;
- 75% involved no subsequent complications and 25% caused genuine subsequent complications;
- 76% occurred after donation and 23% during donation: in 1% of the declarations this information was not specified.

Distribution of DSARs per grade and type of donation – Combined total 2007-09

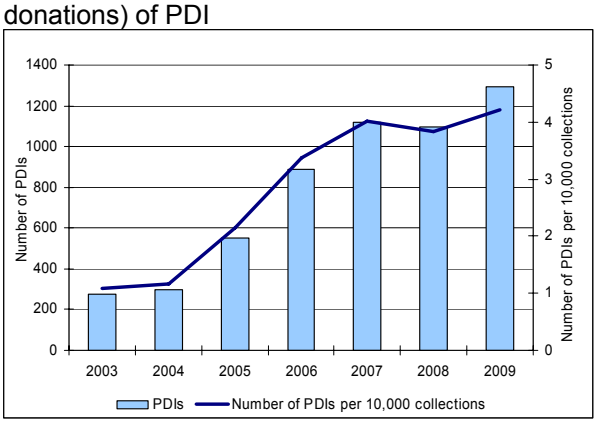
Type of donation	grade 1	grade 2	grade 3	grade 4	NS	Total
Whole blood	2 (0.3%)	565 (75.8%)	178 (23.9%)	(0%)	0	745 (100%)
Plasmaphaeresis	0	174 (71.9%)	66 (27.3%)	1 (0.4%)	1* (0.4%)	242 (100%)
Intermittent flow plateletphaere SAEs	0	16 (84.2%)	3 (15.8%)	(0%)	0	19 (100%)
Continuous flow plateletphaere SAEs	0	39 (81.3%)	9 (18.8%)	(0%)	0	48 (100%)
Combined Aphaeresis	0	26 (86.7%)	4 (13.3%)	(0%)	0	30 (100%)
Total	2 (0.2%)	820 (75.6%)	260 (24%)	1 (0.1%)	1 (0.1%)	1084 (100%)

* 2009 case: see chapter 3.3

2.5. Post-donation information (PDI)

The number of PDI declarations has multiplied by 5 since 2003, reaching 1,295 in 2009. The rate of declaration during the last 4 years was 3.9 per 10,000 samples.
PDI has been declared to Afssaps since October 2002, but only for products having left the EFS after donation.
Their number multiplied by 5 between 2002 and 2009, with a slight decrease in declarations in 2008.

Evolution of the number and ratio (per 10,000 donations) of PDI



3. Prospects

● 2010 shall be devoted to the revision of the regulations covering serious adverse reactions affecting blood donors and serious adverse events: this revision follows the changes to haemovigilance, in both medical and IT terms.

● In March 2010, direct accessibility for declarants to the DSAR forms, as well as the SI forms via e-FIT shall offer the haemovigilance network the possibility of better responsiveness, via the simultaneous communication of the information to all the relevant participants.

● Under the aegis of the National Haemovigilance Commission, a multi-disciplinary task force is being formed to deal with adverse reactions affecting blood product donors.