afssaps

Agence française
de sécurité sanitaire
des produits de santé

Annual haemovigilance report 2008

Haemovigilance report 2008 Table of contents

Foreword

In compliance with Article R1221-27 of the Public health code (PHC), “the French Agency for the safety of health products establishes annually a summary report concerning haemovigilance. This report is sent to the minister in charge of health as well as to the European commission (EC) at the latest by the 30 June of the following year. "

The main objectives of this report are as follows:
- provide national data on the notifications of adverse events associated with transfusions that occurred during the year 2008,
- analyse the temporal evolution of the frequency of events during the 2000-2008 period (globally and by diagnostic),
- identify the questions requiring further study.

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Created by the Law n°. 93-5 of 4 January 1993 concerning safety in blood and medicinal product transfusion matters, “haemovigilance preserves today its essential characteristics that have contributed to its strength and are still perfectly topical” (Jean Marimbert, Director General of the Afssaps, Address to VIIIth National Haemovigilance and Transfusion Safety Congress in Perpignan on the 21 November 2008).

Among the basic characteristics of haemovigilance in France, two have been internationally recognised: its organisation and notification system.

This organisation is based on a well structured local level network – the haemovigilance correspondents of health establishments (HE HVC), and blood transfusion sites; at a regional level – haemovigilance correspondents of Blood establishments (BE HVC) and regional haemovigilance coordinators (RHC); the national – haemovigilance unit of the Etablissement français du sang (EFS) and the haemovigilance cell of the Armed Forces Blood/Transfusion Centre (CTSA); the entire network is led and coordinated by the haemovigilance unit of the Afssaps.

These different levels constantly work on the improvement of transfusion safety, in compliance with regulations and good practice. Accordingly:

- The meetings of the sub-commissions in charge of transfusion safety and haemovigilance (sCSTH) and the Transfusion safety and haemovigilance committees (CSTH) allow the various participants to monitor transfusion safety and exchange their experiences with respect to the training of participants and to the function of the network.

- The organisation of regular seminars bringing together at the Afssaps all the RHCs, the haemovigilance unit, representatives of other directorates and departments of the Afssaps involved in the management of labile blood products (LBP) or vigilances, participants from the EFS, ministry directorates and other partner institutions, is also a major management tool in the haemovigilance network.

- The meetings of the National Computerisation of Traceability Committee (CNIT) of labile blood products, as well as of the two technical groups have as an objective since 1999 the harmonisation of regional computerisation of traceability projects, in particular regional data exchange contracts, etc.

This organisation has also been designed to be sensitive and collect all adverse events, not just serious strong attribution events (reported every year in the annual report), but also “weak signals” and “background noises”, such as mild adverse events or with low attribution to transfusion, from which pertinent information must be extracted with the objective of applying appropriate measures.

In summary, the Afssaps has today a database concerning receiver adverse reactions (RAR) of almost 102,000 files recorded between 1994 and 2008. This database receives regular

methodological improvements (from the computer management of files with GIFIT since 1996 to e-fit[1] since 2004 and soon e-fit2 expected for 2010).

Furthermore:

- Since 2007, the experts of the work groups of the National Haemovigilance Commission (NHC) analyse the information compiled in e-fit (in particular bacterial contaminations, pulmonary lesions, allergy, serious transfusion chain incidents, etc.) and assess the results.

- In 2008 for the 1st time, a work symposium bringing together the RHCs and the haemovigilance correspondents of the BE was organised, under the aegis of the haemovigilance unit of the Afssaps and the Vigilance Section of the EFS, in order to harmonise all the efforts, in particular to improve the notification of transfusion-related incidents and adverse reactions. As the efficacy of haemovigilance is strongly dependent on the quality of the data compiled and its interest resides in the possibility of proposing local, regional and national preventive and corrective measures.

It is important to remember that the data compiled in this report reflect the notifications by the haemovigilance correspondents of receiver adverse reactions (RAR), donor serious adverse reactions (DSAR), serious adverse events/incidents of the transfusion chain (SAE) and post-donation information (PDI) to the Afssaps (in compliance with article R1221-29 of the PHC) and compilations of transfusion vigilance and activity data set up by the Afssaps since 1999. The information provided is as complete as possible, and relatively detailed. This very large database obtained from multiple sources cannot be devoid of defects, due to the difficulty and time required to obtain certain information, thus errors in the notifications, irreducible variability between declaring parties or between regions, etc. are possible (though rare). These difficulties, which only very marginally affect the data presented in this report, must nonetheless be taken into account to interpret certain of the results presented in this report.

[1] *e-fit is the name of the computer application that allows declaring electronically and feeding the national haemovigilance database of receiver adverse reactions.*

1. Introduction

1.1. The new texts published in 2008

2008 was marked by the publication of four decisions of the Director General of the Afssaps:

- Decision of 19 February 2008 fixing the standard template for annual summary report of adverse reactions and events envisaged in article R. 1211-45 of the public health code (biological products)

- Decision DG no. 2008-52 of 3 March 2008 modifying the technical directive n°. 2 bis of the French blood agency of 24 November 1997 concerning the conditions for the implantation of the computerisation of the traceability of labile blood products, taken in application of article R. 666-12-11 of the public health code (new product codes)

- Decision of 10 April 2008 modifying the decision of 28 February 2006 fixing the form and content of the questionnaire filled-in by blood donation candidates in application of article R. 1221-5 of the public health code

- Decision DG no. 2008-325 of 26 December 2008 modifying the technical directive n°. 2 bis of the French Blood Agency of 24 November 1997 concerning the conditions for the implantation of the computerisation of the traceability of labile blood products, taken in application of article R. 666-12-11 of the public health code (Annex I Codification of blood transfusion establishment sites, Annex II Codification of therapeutic labile blood products)

The main national and community texts concerning haemovigilance that appeared before 2008 may be consulted at the Internet site of the Afssaps at the following address: www.afssaps.sante.fr

1.2. News in 2008

2008 was also marked by the generalisation of the haemovigilance notifications following three decisions of the Director General of the Afssaps published in 2007 concerning the content and modes of transmission of the notification form for adverse reactions occurring in a receiver of labile blood product (RARF), of the notification form for serious adverse reaction occurring in a blood donor (DARF) and the notification form for serious adverse events of the transfusion chain (SAEF).

Furthermore in 2008, the National Haemovigilance Commission (CNH), organised in 2007:

- adopted for the 1st time the summary report 2007 established by the Afssaps concerning haemovigilance in compliance with article R. 1221-28 of the public health code,

- created three new theme groups, in charge of working on the most frequent and most serious adverse events: allergy, pulmonary oedema (Transfusion related acute lung injury or TRALI, volemic overloads) and the root causes of transfusion chain incidents,

- accompanied two existing work groups on their work: Transfusion transmitted bacterial infection (TTBI) and National haemovigilance network (NHVN).

1.3. Organisation of haemovigilance

The organisation of haemovigilance in 2008 has not changed compared to that of 2007, thus this chapter covers the main descriptions of the report from last year, updating it with recent number data.

1.3.1. Actors

According to Decree n°. 2006-99 dated 1 February 2006 concerning the French Blood Establisment (Etablissement Français du Sang EFS) and haemovigilance and modifying the public health code (Art. R1221-24), the national haemovigilance system includes:

- the French Agency for the safety of health products (Afssaps);

- the National haemovigilance commission (CNH);

- the regional haemovigilance coordinators (RHC) mentioned in article R1221-32;

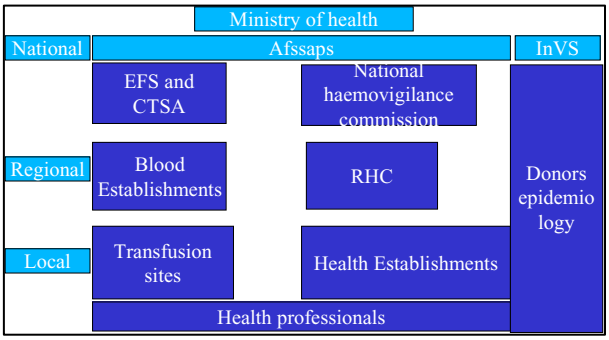
- the Etablissement Français du Sang (EFS) and the Armed Forces Blood Transfusion Centre (CTSA);

- the Institut de veille sanitaire (InVS);

- the health establishments (ES) and armed forces hospitals (haemovigilance correspondents (HVC), transfusion and haemovigilance safety committee (CSTH) or establishment medical commission sub-commission);

- any health professional.

Diagram 1. The 3 haemovigilance organisational levels



In 2008, the haemovigilance network included:

- 1405 haemovigilance correspondents (HVC) and 1521 transfusion health establishment (incomplete data)*

- 18 referring haemovigilance correspondents from the BE and 140 persons certified by the latter on the distribution sites (site correspondents), 3 members of the Vigilance section of the French Blood Establishment (EFS) and 1 member of the haemovigilance cell of the Armed Forces Transfusion Centre (CTSA)

- 29 regional haemovigilance coordinators (RHC)

- the InVS for the epidemiology of blood donors

- the haemovigilance unit of the Afssaps

**Furthermore, 3120 haemovigilance correspondents were listed in non-transfusing health establishments.*

1.3.2. Regulatory roles of each actor

- French healthcare products safety agency Afssaps (Article R1221-25 of the PHC)

The Afssaps ensures the implementation of haemovigilance. It defines the orientations, leads and coordinates the actions of the various participants and monitors the compliance with the monitoring procedures. If applicable, it takes the appropriate measures to guarantee transfusion safety or refers to the competent authorities.

- National haemovigilance commission NHVC (Article R1221-28 of the PHC)

Based within the Afssaps, the NHC has four main missions:

1º Provide an opinion on the assessment of the information compiled

2° Propose the performance of investigations and studies and evaluate the results

3° Provide an opinion to the Director General of the Agency on the measures taken or to be taken to prevent the occurrence or repetition of any incident or adverse event

4° Adopt the annual haemovigilance report

- Regional haemovigilance coordinators RHVCs (Article R1221-32 of the PHC)

Working for the regional director of health and social affairs (DRASS), the RHC is in charge of:

1º Following the implementation of the haemovigilance provisions, Afssaps decisions and actions undertaken by the Transfusion and Haemovigilance Safety Committees (CSTH) or the Sub-commissions concerning haemovigilance and transfusion safety (for the sake of simplicity, these 2 forms of committee/sub-commission will be designated by the same acronym: CSTH);

2º Maintain direct relationships with each of the HVC of the region, monitor with them the quality and reliability of the information compiled and be informed of any difficulties the HVC may encounter in the exercise of their mission;

3º Inform the regional prefect and the Afssaps of its activity, especially via an annual activity report;

4º Propose, if applicable, to the Agency the adoption of any measure likely to improve the quality, reliability and coherence of the haemovigilance system;

5º Inform without delay the regional prefect and the Agency of any difficulty likely to compromise transfusion safety and simultaneously inform the EFS;

6º Propose, if applicable, to the departmental prefect the measures to be taken in view of the notification forms.

- Haemovigilance correspondents of blood transfusion establishments HVC (Article R1221-39 of the PHC)

The BE HVC is in charge of the following:

1º The compilation and storage of information, monitoring their quality and reliability;

2º The notification of any adverse reaction occurring in a blood donor and any adverse reaction occurring in a LBP recipient as well as any serious adverse event;

3º The communication of the information to the Afssaps, InVS and the RHC;

4º The information of the HE on the usage of LBP distributed or issued by their referring BE;

5º Reporting to the Afssaps and to the RHC any difficulty likely to compromise transfusion safety;

6º Investigations to be undertaken in case of emergency following undesirable reactions or serious adverse events. In such cases, it informs the Afssaps immediately, which decides on the continuation or interruption of these investigations as well as the RHC.

- Haemovigilance correspondents of health establishments HVC (Article R1221-43 of the PHC)

The HE HVC is in charge of the following:

1º The notification of any adverse reaction occurring in a labile blood product recipient as well as any serious adverse event;

2º The compilation and storage of information, monitoring their quality and reliability;

3º The communication to the Afssaps and RHC of the information requested;

4º The transmission to the referring BE of the information;

5º Reporting to the Afssaps and to the RHC any difficulty likely to compromise transfusion safety;

6º Investigations to be undertaken in case of emergency following undesirable reactions occurring in LBP recipients or serious adverse events. In such cases, it informs the RHC immediately, which decides on the continuation or interruption of these investigations as well as the Afssaps.

- Transfusion safety and haemovigilance committee (CSTH) and sub-commission in charge of transfusion safety and haemovigilance (sCSTH) – Article R1221-45 of the PHC

The mission of the sCSTH and the CSTH is to contribute to the improvement of the safety, through their studies and proposals, of patients transfused in health establishments, inter-hospital syndicates and health cooperation groups where they are organised.

This committee or subcommission monitors the implementation of the haemovigilance rules and procedures envisaged in this section. They are especially in charge of the coordination of company haemovigilance actions within each of the establishments mentioned in the previous paragraph.

Accordingly, these organisations:

1º Verify with the departments responsible the presence in the medical record mentioned in article R. 1112-2 of documents concerning transfusions and, if applicable, a copy of the notification form for an adverse reaction occurring in a recipient;

2º Are consulted for any question concerning the collaboration of haemovigilance correspondents of the blood transfusion establishment and the health establishment, of the inter-hospital syndicate and the health cooperation group, and more generally of any questions concerning the information transmission circuits, in order to improve the efficacy of the haemovigilance.

3º Are kept informed of the function conditions of blood banks;

4º Are warned of serious adverse events that occur in the health establishment, the inter-hospital syndicate or the health cooperation group, as well as the adverse reactions that occurred in recipients and conceive any measure intended to remedy it;

5º Present to the establishment medical commission, medical commission or medical conference, a transfusion safety training programme intended for the personnel concerned;

6º Transmit to the establishment medical commission, the medical commission or medical conference an annual activity report.

2,260 CSTH/sCSTH meetings were held in 2008, the RHC participated in 70.4% of these meetings. The subjects were related to: consumption of labile blood products (LBP), destruction of LBP, traceability, adverse reactions occurring in recipients, serious transfusion chain incidents, transfusion procedures, transfusion dossier and training... The management of blood banks was also discussed.

1.3.3. Other actions of the network

The RHC give opinion during the blood bank authorisation procedures within the framework of their missions. They also lead the regional haemovigilance network (regional meetings, training actions, adjustment and distribution of adverse event exploration procedures, coordination of regional computerisation of LBP traceability projects, etc.).

Furthermore, numerous actors of the network participate in studies performed by learned societies, Afssaps working groups and the scientific exploitation of haemovigilance data.

1.4. Process

1.4.1. Notifications

The haemovigilance field, initially centred on the adverse reactions occurring in LBP recipients, has expanded with time, especially on the occasion of the transposition of the European directives, to adverse reactions occurring in donors (DSAR), to post-donation information (PDI) and finally to the very important upstream field of pre-transfusion safety (SAE).

While any adverse event that occurs in a LBP recipient must be declared, irrespective of its severity, only the serious adverse reactions occurring in blood donors and the serious events of the transfusion chain must be reported. The definitions and degrees of severity are provided in an annex.

Two steps in the notification process are distinguished:

- the reporting of the reaction or event by the health professional who observes it to the haemovigilance correspondent (HVC) of the HE or BE concerned
- the actual notification, carried out by the HVC after having carried out the required investigations and examinations.

The donor and recipient adverse reaction forms, as well as those concerning serious transfusion chain events must be sent simultaneously to the Afssaps and the RHC. The EFS and CTSA are each sent the notification forms of the events that concern them.

1.4.2. Notifications deadlines

1) Transfusion chain incidents

1.a) Serious adverse event of the transfusion chain (SAE):

✓Reporting procedures: **Immediately and at the latest within eight hours**

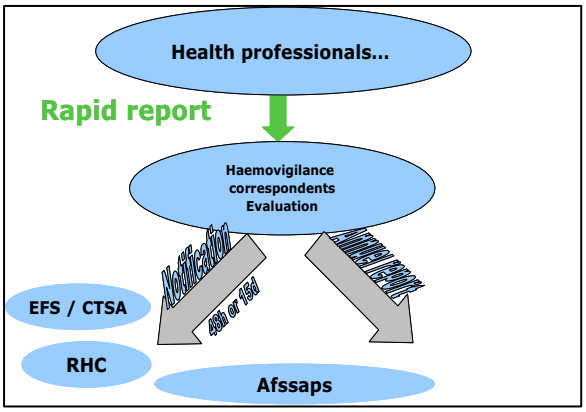
✓Notification procedures:

The HVC concerned can declare the SAE either in immediate notification using the Serious adverse event form (SAEF) or in differed notification in the annual report of SAE that occurred in their establishments. The choice of the notification mode for each SAE is made by the HVC, which carried out the required investigations and examinations, as a function criteria concerning the future of the LBP, process step, repetitive character and existence or not of a warning system:

- Notification deadline:

• So-called immediate notification: **maximum delay of fifteen days to transmit the notification form**. However, in case of event likely to have an impact on transfusion safety or supply in LBP, in each case where a SAE must be made public or when the HVC deems it necessary, the notification takes place as soon as possible and at the latest within 48 working hours following the occurrence of the incident.

Diagram 2. Reporting and notification of transfusion chain incidents



- Decision of the Director General of the Afssaps dated 7 May 2007 setting the transmission form, content and procedures of the notification form for serious adverse event

• Notification in the annual report: notification of all SAE whether they were declared immediately or not; report drafted each year and attached to the annual activity report of the BE and CTSA and to the annual activity report of the CSTH of the HE.

1.b) Post-donation information (PDI):

The notification of certain information concerning the donor obtained after the donation (PDI) is not regulated and is subject to an agreement between the Afssaps, the EFS and the CTSA. The recommended delay ranges between 48h and 15 days after obtaining the information. The notification to the Afssaps is only carried out if the LBP distributed from the donations in cause have left the BE.

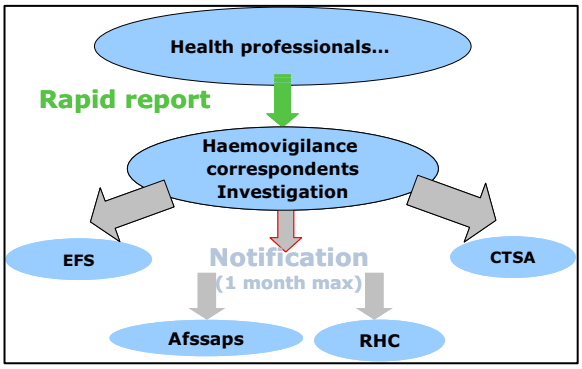
2) Donor serious adverse reaction (DSAR)

✓Reporting procedures: **Immediately and at the latest within eight hours**

✓Notification procedures: **maximum delay one month** to finish the investigations and transmit the notification form. The notification takes place immediately when the HVC of the BE deems it necessary or in certain cases envisaged by the regulations.

✓An assessment of all the serious adverse reactions that occurred in a blood donor is established each year and attached to the annual activity report of the BE

Diagram 3. Reporting and notification of donor serious adverse reactions



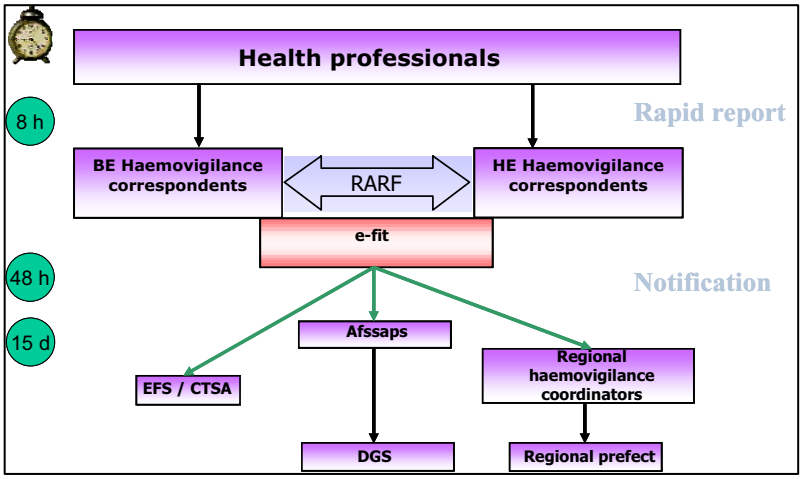
Decision of the Director General of the Afssaps dated 7 May 2007 setting the transmission form, content and procedures of the notification form for serious adverse event occurring in a donor.

3) Recipient adverse reation (RAR)

Diagram 4. Notification of Recipient adverse reations

✓Reporting procedures: **Immediately and at the latest within eight hours**

✓Notification procedures: **delay of 15 days to enter the notification in the e-fit application.** This timeline is brought to 48 hours when the form is referred to as "reported", i.e. in the following cases:



Decision of the Director General of the Afssaps dated 5 January 2007 setting the transmission form, content and procedures of the notification form for serious adverse event occurring in a recipient of a labile blood product.

RARF: RAR form

- adverse reaction likely to involve the safety of at least another recipient, irrespective of the grade
- adverse reaction of grade 2, 3 or 4 excluding grade 2 adverse reactions with appearances of irregular anti-erythrocyte antibodies,
- suspicion of bacterial incident, irrespective of the grade;
- ABO incompatibility, irrespective of the grade

1.4.3. Traceability

The public health code makes obligatory the compilation, filing and exchange of information concerning the dispensing of LBP and allowing their traceability from donor to recipient by the BE and HE. The respect of the anonymity of the donor, under the responsibility of the BE, as well as the medical secrecy concerning the recipient are guaranteed.

The traceability data are reported for each transfusion HE in the annual activity report of the RHC. The Afssaps compiles these data in a national base.

1.4.4. Annual report

The Afssaps establishes annually a summary report concerning to all the notifications concerning the events that occurred in the year concerned. This document also contains an analysis of the evolving tendencies (since 2000) of the main indicators found in the report. This eventually allows a review of the data in previous reports to take into account information obtained after they were written.

This report concerns the year 2008.

2. 2008 data

2.1. Methodology reminder

2.1.1. Data sources

Reminder:

The Afssaps is responsible for the compilation of haemovigilance data. To do this it bases itself firstly on the notifications of HVC on electronic support (e-fit concerning RAR) or not (concerning SAE and DSAR), and secondly on the activity reports of the RHCs. It also has the reports from the CSTHs.

In total, the data taken into account in this report originate from several sources:

• RAR: notifications of HVC,of HE and BE in the “e-fit” database

• DSAR: HVC of BE notifications

• SAE: HVC of HE and BE notifications

• PDI: HVC of BE notifications

•Transfusion activity national data: EFS and CTSA (number of LBP distributed (i.e. billed), donations and donors)

•Transfusion activity regional data: RHC (number of LBP distributed, issued, transfused, destroyed, traced, number of sites and their activities in terms of collection, preparation, distribution). The RHC report is prepared from the data provided by the HE and BE haemovigilance correspondents. The data certified by the HE can differ from that of BE especially due to the absence of link between the HE and the LBP billed and the type of LBP transfused. Furthermore, certain data concerning the HE are sometimes obtained from the BE.

Warning:

•The regional data are grouped by inter-regions in order to obtain sufficiently large sample sizes for statistical comparison (see annex 8.3).

• For the data that may be obtained from several sources, differences (often minimal) may appear depending on the source used.

• Concerning the exhaustiveness of the data, two major types of difficulties have been identified: 1) missing data, when the items requested are never filled in, 2) incomplete data, when the information or values are partially filled in.

• All of the databases were frozen on the 28 February 2009.

Furthermore, concerning the “transfused patients” data, they should be considered with caution due to the existence of multiple entries and missing data. The 2008 annual report of the RHC Conference, concerning 25 regions, evaluated the margin of error as approximately 5% of the data reported.

Finally, compared with the data from previous reports, the 2008 report includes new data that allows establishing the distribution of patients and donors per sex and age group. However, it should be noted that for certain regions, the information communicated are incomplete and non-homogeneous. Certain regional data per sex are missing and others are filled in with age groups different from those requested. An estimate of the missing or incomplete values was performed under these conditions taking into account the typology of the regions for which the information exists (standardisation method). This estimate concerned approximately 15% of patients and 11% of donors.

2.1.2. Validation of the data

Note: The validation system of the RAR forms data in 2008 remained the same as that of 2007, therefore this chapter is also identical to that described in the previous report.

1. Notification of RAR declared via e-fit

The HVCs possess, on the e-fit on-line notification site, an automatic treatment of a certain number of incoherencies (in particular the existence of multiple entries, date and choice of diagnosis incoherencies, etc.) and a guide for filling-in the RAR form.

Each form must be seen by the 2 haemovigilance correspondents (HVC) concerned (of the HE and the BE), irrespective of who created it. The form is referred to as “validated” if the 2 HVCs consider that it is coherent and its data reliable. If applicable, a completed standard questionnaire (for example: ABO, TTBI, TRALI questionnaire) or any other useful document (copy of operative records, diagrams, in-house investigations, etc.) may be attached to the RAR form in e-fit.

The role of the regional haemovigilance coordinator (RHC) is to analyse the form and request any additional information required before affixing a visa to the form which certifies the quality of the data it contains.

It is important to highlight the fact that a notification form has been validated by the HVCs, or even with a visa put up by the RHC does not mean that the investigation on the declared reaction is closed. In theory, any form can be modified if new information is available later.

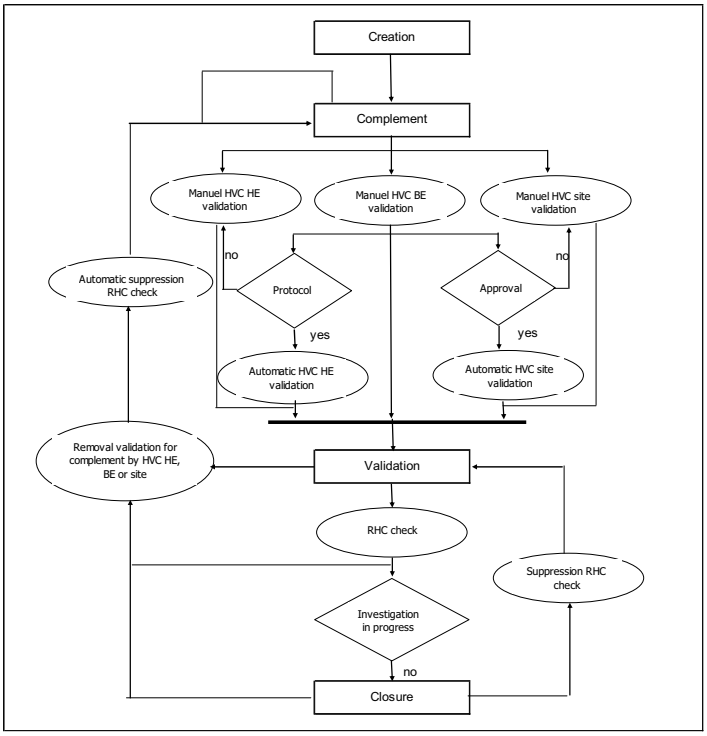
Table 1: The different status of a RARF as a function of its progress in the “e-fit” process

Form status	Description of the status
Initial entry	When the RAR form has been entered and saved
Complement in progress	When one of the correspondents has saved a modification of one of the items of the RAR
Individual validation	When the RARF has been validated by one or two correspondents
Validated	When the RARF has been validated by the three correspondents HE, transfusion site and BE
Seen	When the RARF has been seen by the RHC
Checked (visa)	When the RARF has been checked by the RHC
Invalidated, complements in progress	When one of the correspondents has invalidated the RARF to make modifications.
Closed	The closure is an automatic treatment, performed in differed time (batch) once the RARF has been validated and checked and that the investigation is no longer ongoing. At this stage of the process, the information of the RARF may be considered as stable.

The follow-up of forms, performed daily by the haemovigilance unit of the Afssaps, also participates in the improvement of data quality. Certain forms, especially the so-called "signaled” have a special follow-up.

The follow-up of certain diagnoses (TTBI, TRALI, volemic overload, allergies, etc.) depends on the ad-hoc work groups.

Diagram 5. Logical diagram of the saving of RAR in e-fit from creation to closure



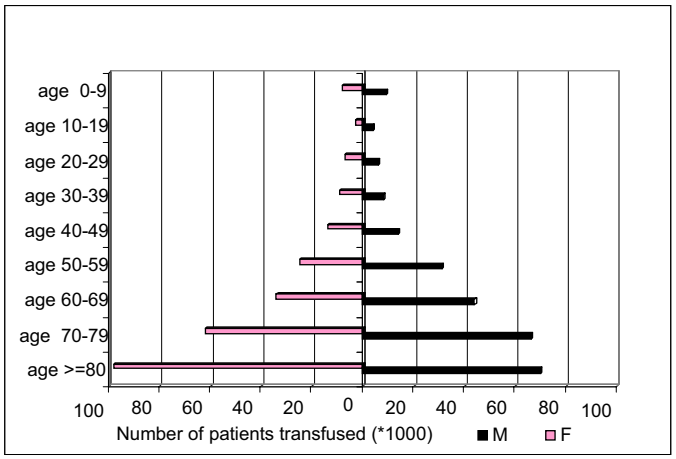
2. The paper notification (SARF, PDI, DSARF)

These notifications, as well as any documentation associated, are sent to the Haemovigilance unit of the Afssaps (fax, post, electronic mail, etc.), the addresses and numbers are found on the web site of the Agency (www.afssaps.sante.fr

2.2. Transfusion activity: general information

2.2.1. Number of patients

Figure 1. Age pyramid of patients transfused in 2008



In 2008, the number of patients transfused was estimated* at approximately 512,300 (table 2):

50.9% are women, 49.1% men and 73% are aged over 60 years.

**See chapter 2.1.1.*

There are 8 transfused patients per 1000 inhabitants, and each patient received on average 5.5 LBP. As shown in table 3, the number of patients transfused per 1000 inhabitants and the number of LBPs per patient transfused vary little from one inter-region to another (standard deviation of 0.43 and 0.36, respectively, excluding DOM-TOM).

Table 2. Number of patients transfused and number of inhabitants in the 6 inter-regions

Inter-regions	Patients transfused (estimate)	Population*
South West	73 900 (14.4%)	8 354 000 (13.2%)
South East	125 200 (24.4%)	15 042 000 (23.7%)
North West	98 700 (19.3%)	12 341 000 (19.5%)
North East	115 400 (22.5%)	14 224 000 (22.4%)
Ile-de-France	88 900 (17.4%)	11 577 000 (18.3%)
DOM-TOM	10 200 (2%)	1 854 000 (2.9%)
Total	512 300 (100%)	63 392 000 (100%)

** Source INSEE: Population of estimates on the 1st January 2007*

Table 3. Ratio of patients transfused per 1000 inhabitants and mean number of LPBs per patient transfused in the 6 inter-regions

Inter-regions	Number of patients transfused per 1000 inhabitants	Number of LBP per patient transfused
South West	8.8	5.4
South East	8.3	5.3
North West	8.0	5.2
North East	8.1	5.6
Ile-de-France	7.7	6.1
DOM-TOM	5.5	5.6
Total	8.1*	5.5**

*Standard deviation except DOM-TOM: * 0.43. ** 0.36*

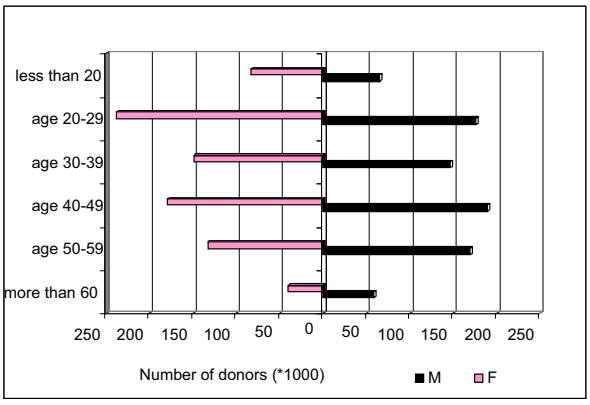
2.2.2. Number of donors and donations

The number of donors* was approximately 1,635,875 in 2008, of which 24.7 % are new donors. They represented 4.1 % of the population between 18 and 65 years and allowed obtaining 2,869,647 collections (2,377,570 in total blood and 492,077 in aphaeresis).

The donors are distributed almost evenly between the two sexes (50.4% women). More than a third is under 30 years, as shown in figure 2.

**See chapter 2.1.1.*

Figure 2. Age pyramid of patients transfused in 2008



2.2.3. Number of labile blood products distributed (LBP)

In 2008, 2,870,835 LBPs were distributed. Approximately 80% are packed red blood cell (PRBC), 9% platelets and 11% plasma. Table 4 shows the distribution in volume and percentage and table 5 its distribution by inter-region, with the number of LBPs and the number of LBPs per 100,000 inhabitants for each region. The number of LBP per 100,000 inhabitants varies very slightly from one inter-region to another, apart from the DOM-TOM.

Table 4. Distribution of LBP in 2008 per type of product

Type of LBP*	Quantity (%)
PRBC	2 287 350 (79.7%)
APC	192 784 (6.7%)
PCM	62 139 (2.2%)
VIP	211 422 (7.4%)
FFPs	117 140 (4.1%)
Total	2 870 835 (100%)

** Source EFS and CTSA (LBP distributed)*

There is still a difference in the total of LBP declared nationally and regionally (tables 4 and 5, the national data come from the distribution/billing files for the EFS, while those of the RHC come from the BE distribution files).

Table 5. Number of LBP distributed in 2008, per inter-region and use rate per 100,000 inhabitants

Inter-regions	Total number of LBP*	Number of LBP per 100,000 inhabitants
South West	401 419	4 805
South East	664 145	4 415
North West	514 429	4 168
North East	650 542	4 574
Ile-de-France	544 432	4 703
DOM-TOM	56 723	3 059
Total	**2 831 690**	4 467**

** Source: Inter-regions RHCs (LBP distributed – LBP recovered)*

***Standard deviation: 250.6 except for DOM-TOM*

2.2.4. LBP transiting through the hospital blood banks

The 2008 data on LBPs transiting through the BHH was only available for 18 regions; those of the Alsace, Centre, Corsica, Franche-Comté, Ile-de-France, Normandy (Low-), Normandy (High-), Pays de la Loire regions are missing. Based on the 2007 report, we can estimate that the data available represent approximately 75% of the total of LBPs. These data indicated that 53.1% of LBPs transit through a distribution bank (83% of these LBPs are then issued* by the bank while 17% were distributed by the EFS). Table 6 gives the distribution of LBPs per HBB category.

**Distribution and issue: See definition in annex 8.3.5*

Table 6. Number of LBP transiting through the banks in 2008

Total LBP	Delivery banks	Relay Banks	Vital emergency banks	Vital emergency + Relay banks	NR
383 582	203 542	10 457	5 645	144 258	19 680
100.0%	53.1%	2.7%	1.5%	37.6%	5.1%

NR: not reported in the regional databases (more than 95 % due to a single region)

2.2.5. Traceability of LBP

The national traceability levels is at 98.9 % in 2008, and it is greater than 95% irrespective of the region (figure 3).

Figure 3. Traceability of products issued* in 2008

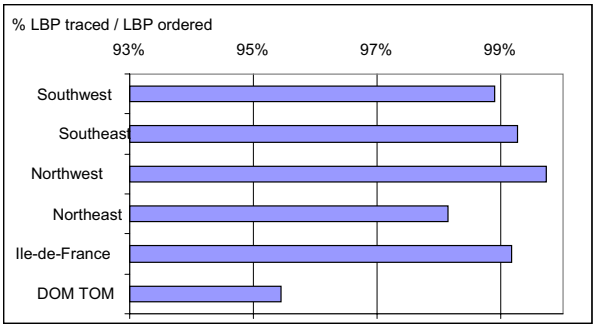
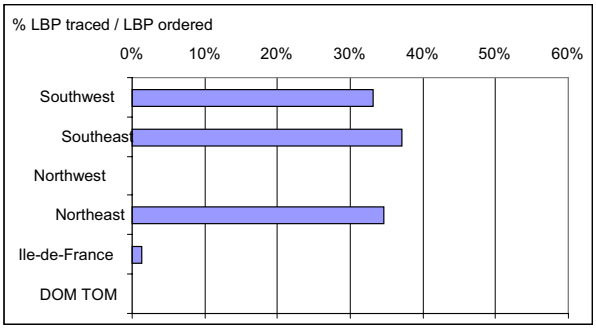


Figure 4. Computerisation of traceability data in 2008



**Distribution and issue: See definition in annex 8.3.5*

The traceability was performed using computerised procedures for only 21.7% of LBPs, essentially from three inter-regions. The electronic exchanges of traceability data between the HE and EFS comply with the AFNOR NF S97-530, NF S97-531, NF S97-532 and XP S97-536 specifications.

2.3. Recipient adverse reactions (RAR)

2.3.1. Definitions and number of notifications

Definition: According to the Public Health Code, a Recipient adverse reaction (RAR) is a harmful reaction occurring in a recipient, related or likely to be related to the administration of a labile blood product

Number: In 2008, the number of RAR notifications, including all degrees and levels of imputability, was of 7,298, i.e. 2.5 per 1,000 LBP transfused (table 7). Nearly 50% are high imputability (49.5% likely (3) and certain (4) imputability)), 29.3% possible imputability (2) and 21.2% excluded or doubtful imputability (0 and 1).

Table 7. Distribution of 7,298 RAR declared in 2008 per grade and imputability

	Severity (S); N; irrespective of the investigation level				
Imputability (I), N	S 1	S 2	S 3	S 4	Total
I 0	444	32	40	16	**532 (7.3%)**
I 1	942	13	48	10	**1 013 (13.9%)**
I 2	1 927	119	83	8	**2 137 (29.3%)**
I 3	1 648	547	152	2	**2 349 (32.2%)**
I 4	177	1034	53	3	**1 267 (17.4%)**
Total	**5 138 (70.4%)**	**1 745 (23.9%)**	**376 (5.2%)**	**39 (0.5%)**	**7 298 (100.0%)**
RAR/1000 LBP	1.79	0.61	0.13	0.01	2.54

The definition of the different levels of severity and imputability is given in annex 8.

Thirty nine notifications mention death (severity level 4), i.e. 1.4 per 100,000 LBP. However, it should be noted that for 2/3 of these deaths, the responsibility of the transfusion was excluded (imputability 0) or deemed doubtful (imputability 1) after investigation.

Warning: The following analysis will only concern reactions:

1 – imputability 2 to 4

2 – confirmed, i.e. with the mention "investigation final".

2.3.2. Grades 3 to 4 RAR

- **Deaths**

Table 8 specifies, per type of LBP*, the distribution of 12 deaths of imputability 2 to 4 for which the investigation is completed.

The death rate with platelets is 5 times greater than with the other types of products.

**1st LBP of the list of LBPs likely to have caused a RAR, or LBP suspected to be the cause of the adverse reaction.*

Table 8. Distribution of 12 deaths of imputability 2 to 4 with complete investigation according to the type of LBP transfused

Type of LBP	Number of RAR	RAR per 100.000 LBP
PRBC	7	0.31
APC	3	1.56
PCM	1	1.61
MB-VIP	1	0.30
Total	**12**	**0.42**

Five of the 12 deaths were declared with a high imputability score (3 or 4). Following the case analysis by the NHC expert groups, 2 of them were re-classified as imputability 2 (2 volemic overloads). The remaining 3 deaths concerned 1 TRALI, 1 allergy and 1 bacterial infection. These three cases are summarised below.

1) Allergy

38-years old man for whom the diagnosis, a very inflammatory form of MS (multiple sclerosis), had been set out and who was treated since 6 months by plasmapheresis (or plasma exchange) combining albumin and therapeutic plasma. During the twenty plasmapheresis sessions performed before the reaction, the patient had presented once a grade 1 allergy type adverse reaction with FFPs, and had already received MB-VIP, without allergic reaction. The circumstances of the death were the following: Approximately 1.5 hours after the start of the plasmapheresis (successively: 1 MB-VIP, 2 SD-VIP, 2 MB-VIP) the patient presented rapidly extensive cutaneous signs, followed by a drop in blood pressure, dyspnoea, desaturation, nausea and vomiting and finally convulsive seizure, ventricular fibrillation and circulatory arrest. The patient was taken over in intensive care where he died the next day.

This RAR was investigated by the Allergy WG. The imputability of the blood transfusion was deemed probable (imputability 3). Concerning specifically the MB-VIP, the group deemed the imputability as likely/possible (imputability 2).

2) Bacterial infection

74 years old man, followed for leukaemia, transfused with APC T-Sol indicated in the context of a thrombocytopoenia. Five minutes after the start of the transfusion, the first signs, shivering and fever, appeared. These signs evolved rapidly to a septic shock picture with diarrhoea and fever. In spite the transfer to intensive care, the patient died 48 h later in a multi-organ failure picture.
The microbiological investigations revealed the presence of Gram negative bacteria: Escherichia coli in the APC (direct examination and culture of the bag and neighbouring flange) and haemoculture in recipient.
The ascending investigation (questioning, donor collections and donation conditions) did not reveal the origin of the LBP contamination. The microbiological analysis of the plasma from the same donation was negative.
At the request of the expert group, a genotype comparison of the micro-organisms was performed which revealed the identity of the Escherichia coli strains found in the recipient, in the APC bag and the flange next to the APC bag. The clinical elements and the results of the microbiological investigations led the experts to propose an imputability score of 4 to this TTBI.

3) TRALI

64 years old man, followed for HIV infection and treated since 1 year for RAEB-2 (refractory anaemia with excess blasts-2) for which he was regularly transfused in day-hospital. This patient was hospitalised after falling at home and received 1 PCM in additive solution and 1 PRBC (Hb 7g/dl and platelets 30 g/l). From the end of the transfusion, he presented a fever at 39ºC then very rapidly (less than one hour) a sudden degradation of the clinical condition with respiratory distress, APO, desaturation and death in spite of the reanimation manoeuvres. Two of the PCM donors presented class I anti HLA AB, the cross match (flow cytometry cross-compatibility test) is positive between the donors and the patient.

The TRALI work group agrees with the diagnosis orientation and imputability.

- **Grade 3 RAR**

In 2008, 251 grade 3 adverse events were recorded: 187 (77.5%) imputability 3 or 4[2], and 64 (25.5%) imputability 2.

2 *See Annex 8.1.2 Table 26. Grade 3-4 and imputability 3-4 RAR as according to the type of products and diagnoses in 2008*

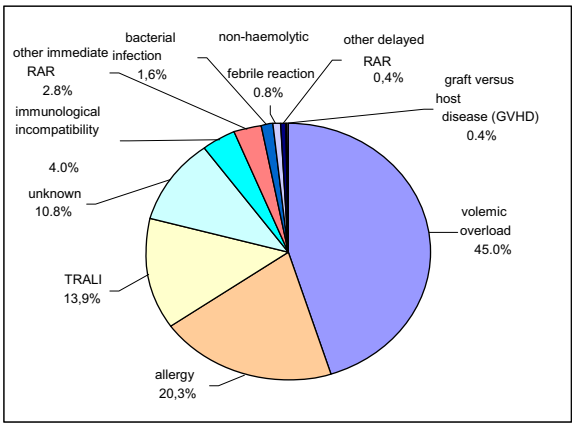
Like for the deaths, the number of grade 3 RAR per 100,000 LBP is highest with APC and PCM, i.e. 19 to 23 RAR per 100,000 platelets versus 7 RAR per 100,000 PRBC (table 9).

Table 9. Distribution of 251 RAR grade 3

Type of LBP	Number of RAR (%)	Number of RAR per 100,000 LBP
PRBC	173	7.56
APC	45	23.34
PCM/SPC	12	19.31
Plasma	21	6.39
Total	**251**	8.74

According to figure 5, 45% of these adverse events are associated with a diagnosis of volemic overload and 20.3% with an allergy. TRALI comes in 3rd position (13.9%). The diagnosis is unknown in 10.8% of cases.

Figure 5. Distribution per diagnosis of grade 3 RAR recorded in 2008



"Immunological incompatibilities" represent 4.0% of grade 3 RAR (i.e. 10 cases, including 3 ABO, 5 leuko-platelet, 1 MNS, 1 unlisted group).

- **Characteristics of patients concerned by grade 3 and 4 RAR**

Nearly half (49.4%) of the grade 3 or 4 adverse reactions declared in 2008 occurred in patients older than 70 years, and 27.8% in patients older than 80 years (figure 6).

The number of reactions per 10,000 patients transfused varies depending on the age. It reaches a peak (9.5 per 10,000) for the age group 20-29 years, then decreases regularly (4.4-4.5 per 10,000 in patients 70 years and older) (figure 7).

Figure 6. Number of grade 3 and 4 RAR per age group

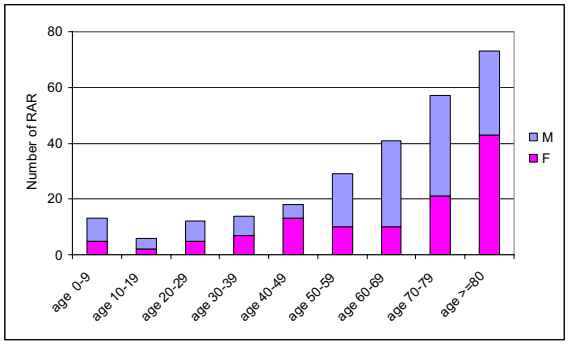


Figure 7. Number of grade 3 and 4 RAR per 10,000 patients transfused per age group

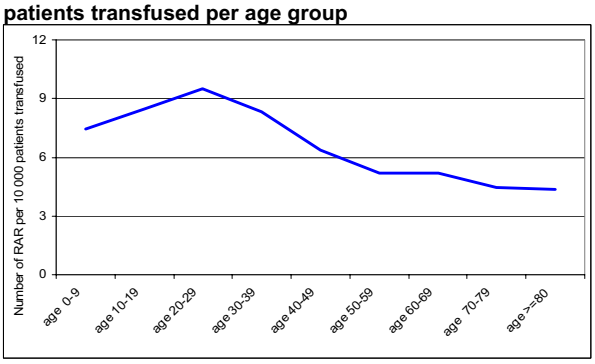
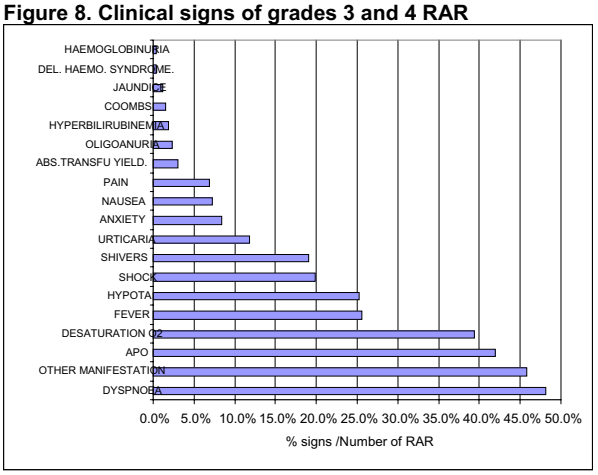


Figure 8 gives the hierarch of frequency of the clinical signs observed during grade 3 and 4 RAR; in decreasing order we find dyspnoea, APO, oxygen desaturation, fever, hypotension, shock, etc.

Figure 8. Clinical signs of grades 3 and 4 RAR



2.3.3. Grades 1 and 2 RAR

Table 10 presents the distribution per type of LBP of 5,231 grade 1-2 RAR recorded in 2008, as well as the rate per 100,000. The distribution per diagnosis (figure 9) is different from that of grade 3 adverse reactions, with only 2.8% volemic overloads (versus 45.0% for grade 3) and 27.7% of non-haemolytic febrile reactions (versus 0.8% for grade 3).

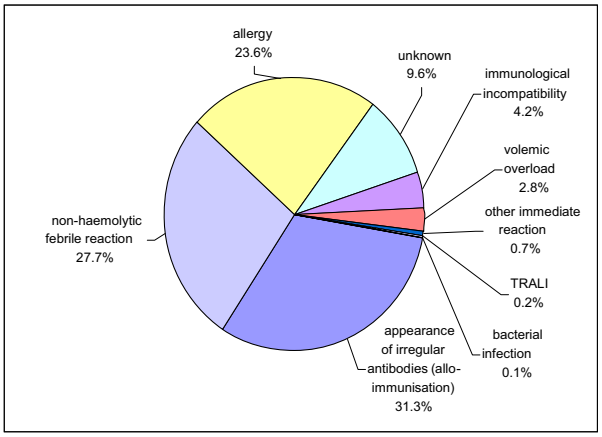
Table 10. Distribution of grades 1-2 adverse events recorded in 2008 (imputability 2 to 4) according to the LBP type*

Type of LBP	Number of RAR (%)	Number of RAR per 100,000 LBP
PRBC	3 665 (70.1%)	160.23
APC	1 209 (23.1%)	627.13
PCM	212 (4.1%)	341.17
VIP	62 (1.2%)	29.33
FFPs	73 (1.4%)	62.32
Other products **	10 (0.2%)	
Total	5 231 (100%)	182.21

** 1st line of the list of LBP likely to be at the origin of the notification, according to the RARF filling-in guide*

*** 4 with CGA, 1 total blood, 3 reconstituted blood, 2 NR*

Figure 9. Distribution per diagnosis of grades 1-2 adverse reactions in 2008 (imputability 2 to 4)



2.3.4. Global analysis per diagnosis of imputability 2 to 4 RAR

Table 11 presents the distribution of 5,494 adverse reactions according to the imputability score and the diagnosis:

- Distribution per imputability

The variability of the distribution of the imputability levels per diagnosis is high: more than 2/3 of the NHFR are imputability 2, while appearance of irregular antibodies, allergies, immunological incompatibilities, volemic overloads, TRALI and bacterial infections mostly have a high imputability (3 or 4).

Table 11. Distribution per diagnosis of imputability 2 to 4 adverse reactions in 2008

Diagnosis	Imputability score, N (%)			Total N (%)
	Imputability 2	Imputability 3	Imputability 4	
appearance of irregular antibodies	90 (4.5%)	522 (23.2%)	1023 (81.6%)	1635 (29.8%)
non-haemolytic febrile reaction	968 (48.7%)	476 (21.1%)	5 (0.4%)	1449 (26.4%)
allergy	361 (18.2%)	836 (37.1%)	89 (7.1%)	1286 (23.4%)
volemic overload	54 (2.7%)	164 (7.3%)	44 (3.5%)	262 (4.8%)
immunological incompatibility including ABO	47 (2.4%) 1 (0.1%)	126 (5.6%) 2 (0.1%)	56 (4.5%) 8 (0.6%)*	229 (4.2%) 11 (0.2%)*
TRALI	16 (0.8%)	15 (0.7%)	14 (1.1%)	45 (0.8%)
bacterial infection	2 (0.1%)	2 (0.1%)	5 (0.4%)	9 (0.2%)
haemosiderosis	(0%)	1 (0%)	1 (0.1%)	2 (0%)
viral infection	1 (0.1%)	1 (0%)		2 (0%)
purpura	1 (0.1%)			1 (0%)
graft versus host disease	1 (0.1%)			1 (0%)
other (immediate or delayed reactions)	20 (1%)	14 (0.6%)	6 (0.5%)	40 (0.7%)
unknown[3]	426 (21.4%)	97 (4.3%)	10 (0.8%)	533 (9.7%)
Total	**1 987 (100%)**	**2 254 (100%)**	**1 253 (100%)**	**5 494 (100%)**

** including 7 with PRBC*

- Distribution per diagnosis

7 out of 10 diagnosis are immediate reactions (appearance within 8 days), out of a total of 3,848 RAR, the following was observed:

- 1449 non haemolytic febrile reactions (NHFR), i.e. 26.4% of all RAR

- 1286 allergies, i.e. 23.4% of RAR

- 533 RAR of unknown aetiology, i.e. 9.7% of all RAR, of which 94.0% are mostly benign reactions (grade 1) and 79.9 % of possible imputability (imputability 2).

- 262 volemic overloads

- 229 immunological incompatibilities. 11 have been identified in the ABO system: 7 with a PRBC transfusion and 4 with platelet transfusion

- 45 TRALI

- 9 bacterial infections, including 8 with positive LBP culture[4]: 2 *Escherichia coli* one imputability 3 and the other imputability 4, 2 *Staphylococcus aureus* imputability 4, 2 Streptococcus imputability 4, 1 *Klebsiella pneumoniae* imputability 2 and 1 *Proteus mirabilis* imputability 3.

- 35 other immediate effects, including 32 unlisted or unspecified immediate effects

3 out of 10 reactions are of the delayed type (appearance after 8 days). Among the 1,646 delayed RAR, the following were recorded:

- 1635 appearances of irregular antibodies. The main specificities of these antibodies are the following in diminishing order: leuko-platelets, MNS, KEL, JK, RH, etc.

3 *Definition of an unknown diagnosis RAR according to the filling-in guide: RAR for which all the tests performed came back negative, RAR insufficiently recorded, tests performed do not allow reaching a conclusion or RAR for which it was impossible to decide between several diagnostic orientations.*

4 *In the 9th case, the PRBC transfusion caused a fever at 39.1ºC with positive Streptococcus bovis haemoculture in patient asymptomatic before transfusion and without intercurrent infectious pathology; the LBP culture was not performed.*

- 2 post-transfusion viral infections: 1 grade 2 HBV declared in 2008 – imputability 3 with PRBC transfused in 2007, 1 grade CMV and imputability 2 with PRBC transfused in 2008

- 2 haemosiderosis

- 7 other delayed effects (including 1 purpura, 1 graft versus host reaction)

- Distribution per inter-region

Table 12 indicates the number and rate of occurrence of RAR per 10,000 LBP by diagnosis and per inter-region.

Table 12. Distribution per inter-region and per diagnosis of imputability 2 to 4 adverse events in 2008

Diagnosis	Total no.	Number RAR per 10,000 LBP							
		Ile-de-France	North East	North West	South East	South West	DOM-TOM	Mean	Standard deviation*
appearance of irregular antibodies	1635	5.07	7.41	4.86	7.45	3.04	1.76	5.77	1.88
non-haemolytic febrile reaction	1449	2.68	3.24	5.83	7.63	6.23	6.17	5.12	2.09
allergy	1286	5.75	4.83	4.67	3.36	4.68	1.41	4.54	0.85
volemic overload	262	0.57	1.01	1.22	1.05	0.65	1.06	0.93	0.28
immunological incompatibility	229	0.55	0.77	1.05	0.92	0.82	0.18	0.81	0.19
including ABO	11	0.04	0.02	0.06	0.05	0.05	0.00	0.04	0.02
TRALI	45	0.17	0.15	0.35	0.05	0.07	0.18	0.16	0.12
bacterial infection	9	0.02	0.03	0.04	0.03	0.05	0.00	0.03	0.01
haemosiderosis	2	0.00	0.02	0.00	0.02	0.00	0.00	0.01	0.01
viral infection	2	0.00	0.00	0.00	0.00	0.05	0.00	0.01	0.02
purpura	1	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.01
graft versus host disease	1	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.01
other (immediate or delayed reactions)	40	0.07	0.06	0.12	0.20	0.30	0.18	0.14	0.10
unknown	533	1.29	1.88	2.02	2.32	1.87	1.41	1.88	0.38
Total	**5 494**	**16.16**	**19.43**	**20.16**	**23.04**	**17.76**	**12.34**	**19.40**	**2.59**

**Standard deviation except DOM-TOM*

2.3.5. Diagnoses per type of product

According to table 13, the most frequent diagnoses are the appearance of irregular antibodies (5.7 RAR per 10,000 units of LBP), NHFRs (5.1 per 10,000) and allergy (4.5 per 10,000). With respect to the products involved, the number of reactions per 10,000 units is much higher for platelets (65 RAR per 10,000) than for the other products.

Table 13. Mean number of diagnoses per 10,000 LBP of imputability 2 to 4 that occurred in 2008

Diagnosis	All LBP[5]	PRBC	APC	PCM	VIP	FFPs
appearance of irregular antibodies	5.70	6.39	4.41	13.20	0.09	0.26
non-haemolytic febrile reaction	5.05	5.41	7.99	8.21	0.14	0.26
allergy	4.48	1.50	39.99	7.40	3.03	4.87
volemic overload	0.91	1.08	0.41	0.32	0.14	0.09
immunological incompatibility	0.80	0.45	5.24	3.86	0.00	0.00
including ABO	0.04	0.03	0.21	0.00	0.00	0.00
TRALI	0.16	0.14	0.26	0.48	0.05	0.34
bacterial infection	0.03	0.01	0.26	0.16	0.00	0.00
haemosiderosis	0.01	0.00	0.00	0.00	0.00	0.00
viral infection	0.01	0.01	0.00	0.00	0.00	0.00
purpura	0.00	0.00	0.00	0.00	0.00	0.00
graft versus host disease	0.00	0.00	0.00	0.00	0.00	0.00
other (immediate or delayed reactions)	0.14	0.14	0.41	0.00	0.00	0.00
unknown	1.86	1.66	6.22	2.57	0.24	0.94
Total	**19.14**	**16.81**	**65.20**	**36.21**	**3.69**	**3.74**

2.4. Serious adverse event of the transfusion chain (SAE)

"A serious adverse event of the transfusion chains, is an incident related to the collection of blood, biological qualification of donation, preparation, storage, distribution, dispensing or use of the labile blood products, due to an accident or error, likely to affect the safety or quality of the product and result in serious adverse events, i.e. adverse events resulting in death or life-threatening, resulting in an invalidity or incapacity, or provoking or prolonging hospitalisation or any other morbid condition."

Whenever a SAE of the transfusion chain is associated with a grade ≥ 1 adverse reaction, the latter must be declared as any other RAR, via a RARF accompanied of a SAEF for analysis of the incident. However, since the decree n°. 2006-99 dated 1st February 2006 (articles R1221-22 and 23 and R1221-49), the transfusion chain SAE declared up to now in RARF grade 0 will be declared under SAE, as the RARF grade 0 is going to disappear. However, they continue to be declared on e-fit while waiting the implementation of the electronic-notification of all SAE.

Warning: This paragraph concerns the 360 SAE declared in 2008, whether associated with a RAR notification or not and whether the LBP was transfused or not.

2.4.1. SAE with or without transfused LBP

In 2008, 360 SAE were declared, i.e.:

- 196 events with transfusion of LBP without RAR
- 45 events with transfusion of LBP that caused a RAR grade higher than or equal to 1
- 119 serious adverse events without transfusion

In quantitative terms, the SAE declared are mainly related to failures in the acquisition and verification of the identity of patients as well as insufficient standardisation of the solutions that allows the identification of patients in the various phases of the care process (documents, entries, validations and verifications of identities in the computer systems specific to the establishments and in the interfaces with other computer systems, controls on the prescription of LBP and requests for biological tests and last pre-transfusion controls, etc.).

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5 *The differences observed between the column "All LBP" of table 13 and the column "Mean per inter-region" of table 12 are due to the differences in the number of LBPs used in different denominator and sources (see Chapter 2.1 and 2.2.3).*

Failures concerning the computer systems have also been indirectly detected, as well as transfusion delays especially as consequences in the patients (delay of prescription of LBP, delay in the distribution of LBP, failure of HE-BE communication).

2.4.2. SAE with transfusion of LBP without RAR

The SAE declared in grade 0 RARF are by definition dysfunctions that did not cause any clinical or biological manifestations, in spite of the inappropriate transfusion of a LBP. Even though declared as RARF, they are transfusion chain events in the same manner as those detected before transfusion.

- National data

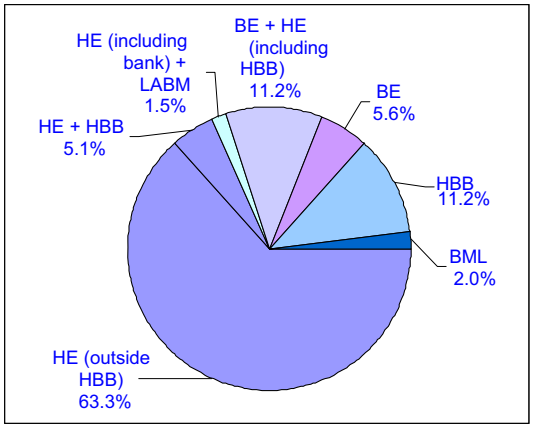
196 SAE without clinical or biological effect were declared in 2008, i.e. a rate of 6.8 per 100,000 LBP transfused (table 14).

Table 14. Distribution of 196 SAE declared in grade 0 RARF in 2008 per type of LBP

Type of LBP	2008	RAR per 100,000 LBP
PRBC	166 (84.7%)	7.2
APC	12 (6.1%)	6.2
PCM	7 (3.6%)	11.3
FFPs	5 (2.6%)	4.3
VIP-SD	4 (2.0%)	2.9
Other products	2 (1.0%)	
Total	**196 (100%)**	6.8

We can observe (figure 10) that it concerns mainly errors that occur in the HE (74%) or jointly in the HE and the BE (11%). They are mostly related to failures in the verification of the identity of patients especially during the last pre-transfusion controls.

Figure 10. Sites of dysfunction of the 196 SAE declared in grade 0 RARF in 2008



- Data per inter-region

The number of transfusion chain SAE without clinical or biological effect per 100,000 LBP is on average 6.9[6]. The heterogeneity between the inter-regions – the rates varying between 4.3 and 9.1 – is probably due, at least partly, to a lack of exhaustiveness of the notifications (table 15).

Table 15. Distribution per inter-region of SAE declared in RAR grade 0

Inter-regions	Number of grade 0	Grade 0 per 100,000 LBP
South West	23 (11.7%)	5.7
South East	52 (26.5%)	7.8
North West	22 (11.2%)	4.3
North East	59 (30.1%)	9.1
Ile-de-France	36 (18.4%)	6.6
DOM-TOM	4 (2%)	7.1
Total	**196 (100%)**	6.9*

** Standard deviation 1.66 for the 6 inter-regions and 1.85 apart DOM-TOM*

6 *The difference between the number of SAE per 100,000 LBP in table 15 (6.9) and that of table 14 (6.8) is due to the differences in the numbers of LBP used in different denominator and sources (see Chapter 2.1 and 2.2.3).*

2.4.3. SAE with transfusion of LBP that caused a RAR (grade higher than or equal to 1)

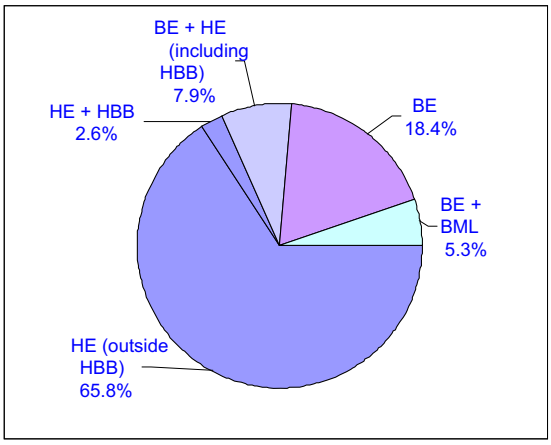
Forty five SAE were associated in 2008 with a RAR grade ≥ 1. Among these notifications, 38 were retained after investigation, the 7 others did not constitute SAE, as defined in the regulation (example delay of information of the HVC at the time of occurrence of RAR).

These 38 SAE are associated with grade 1 RAR for 50% of them (19/38), grade 2 for 26% (10/38) and grade 3 for 24% (9/38) (table 16); 68% (26/38) occurred in a HE (figure 11).

Table 16. Distribution of 38 serious adverse events of the transfusion chain, associated with a RAR of grade ≥ 1

Nature of SAE	N, grade gr			
	N	gr 1	gr 2	gr 3
Distribution error by bank	1	1		
Anti-D prevention fault	2		2	
Non-compliance transfusion protocol	12	3	7	2
LBP distributed error	1			1
Patient identity error	2	1		1
Patient transfused error	6	3	1	2
Transfusion after 6h	3	2		1
Unjustified (useless) transfusion	6	4		2
Transfusion interrupted (failure in patient treatment)	3	3		
Patient post-transfusion monitoring failure	1	1		
Anomaly LBP distribution circuit	1	1		
Total	38	19	10	9
%	100%	50%	26 %	24 %

Figure 11. Dysfunction sites of 38 serious adverse events of the transfusion chain, associated with a RAR of grade ≥ 1

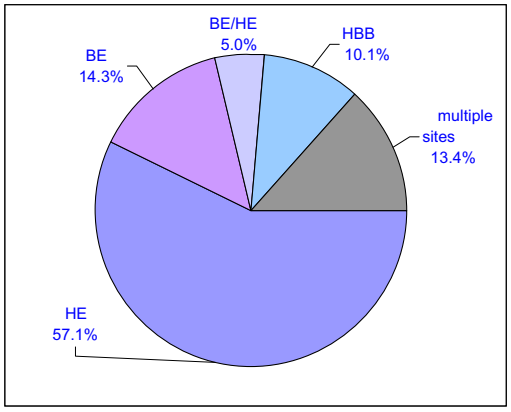


2.4.4. SAE without transfusion of LBP

Concerning the SAE without transfusion of LBP, 119 were declared in 2008. The majority (67%) occurred in a HE. Figure 12 details the distribution per site of occurrence.

These SAE are mainly related to failures in the acquisition of the identity of the patients and in the transfer of this identity on the LBP prescription documents and biological tests as well as on the biological test tubes.

Figure 12. Sites of dysfunction of 119 SAE without transfusion of LBP



2.5. Donor serious adverse reactions (DSAR)

In 2008, 321 DSAR were declared: 77% grade 2 (effects requiring medical consultation) and 23% grade 3 (effects requiring hospitalisation). The rate of DSAR per 10,000 collections is of 1.1.

Adverse reactions occurring in a donor are classified as serious if they meet the following criteria:

- grade 2: prescription of external consultation by the physician of the blood transfusion establishment,

- grade 3: hospitalisation of the donor.

2.6. Post-donation information (PDI)

PDIs are defined as any information provided after a donation by a donor or any other reliable source, and likely to threaten the quality and safety of the products issued from that donation. Their notification to the Afssaps was organised since October 2002 by an agreement between the EFS and the Afssaps without regulatory obligation and only concerns donations at the origin of LBP that have left the BE. Therefore, these notifications are always on a voluntary basis.

In 2008, 1,099 PDI were declared, i.e. 3.8 PDI per 10,000 collections.

3. Evolutions

3.1. Reminder of the main modifications that appeared on the RAR notification form since 2001:

- Year 2001: Notification of TRALI (implemented in September 2001)
- Year 2002: Grade 0: The grade 0 forms started to be sent to the Afssaps on November 2002
- Year 2003: Implementation of the additional grid “Bacterial incidents”
- Year 2004: Implementation of e-fit and a new electronic notification form including among the novelties the grade 0 item in isolated dysfunction without clinical or biological manifestation and among the diagnostic orientations: NHFR, pre-transfusion serologies, post-transfusion purpura, intercurrent pathologies and free text section,

  And new sections, such as additional bacteriological or immuno-haematological explorations, identification of antibodies, ABO/RH groups of LBP and ABO/RH of patient.
- Year 2005: New version of RARF completion guide, for which the main modifications are specifications concerning grade 0, pre-existing antibodies or of recent appearance, viral infection and RAR form numbering procedures.
- Year 2007: Update of RARF, distribution of SAEF guide and technical data sheet on non-haemolytic febrile reactions.
- Year 2008: Procedure of exploitation of serious allergic reactions (grades 3 and 4) during transfusion including MB-VIP

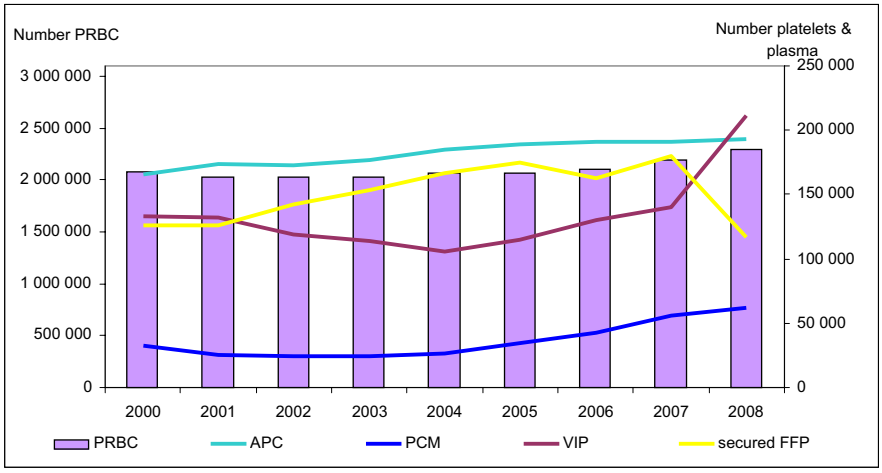
Warning: This analysis concerns the data from the 2000-2008 period (year of occurrence). Concerning the analysis of viral infections, which may be diagnosed several years after transfusion, the reference year will be the year of transfusion.

3.2. LBP consumption

The rate of LBP consumption growth is of 0.9% per year since 2000. However, the progression is greater for PCM than for the other products (figure 13).

The evolution curve for quarantine secured FFPs shows a break in 2008 because their distribution was stopped at the end of September. This product is now replaced by MB-VIP, which explains the increase of the VIP curve observed in 2008 (since mid-June 2008, see chapter 2.3.5).

Figure 13. Evolution of the consumption of different types of LBP

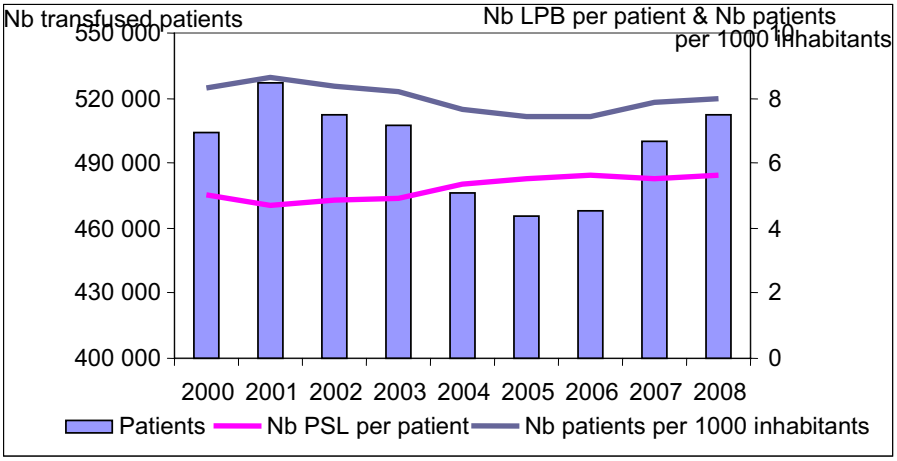


3.3. Recipients

The histogram of figure 14 shows a decrease in the number of patients transfused between 2001 and 2005-2006, followed by an increase in the next two years. According to the blue curve in the same figure, the ratio of patients transfused per 1000 inhabitants showed a concomitant decrease from 2001 to 2005, then tends to increase to reach 8.0 in 2008.

However, the number of LBP per patient transfused (pink curve in figure 14) continually increased since 2001 (4.7 in 2001 and 5.6 in 2008).

Figure 14. Evolution of the number of patients transfused, of ratio of patients transfused per 1000 inhabitants and of the number of LBP per patient transfused



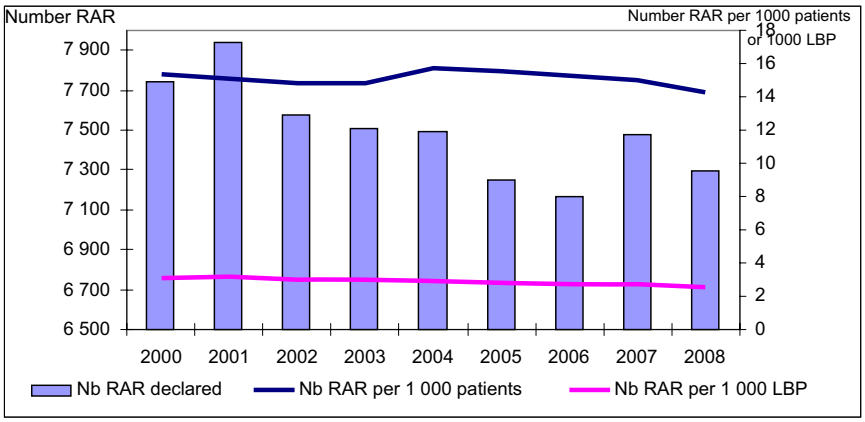
3.4. RAR

In 2008, the number of RAR[7] notifications decreased by 2.5% with respect to 2007 (7,298 versus 7,481 - figure 15), that of confirmed grade 1 to 4 and imputability 2 to 4 RAR showed a more marked decrease of minus 4.5% (5,494 versus 5,750).

On the long term, the number of RAR declared per 1000 LBP distributed also shows a tendency to decrease since 2001 and the RAR ratio per 1000 patients transfused decreases since 2004.

7 *Number of RAR notifications of all grade and imputability levels*

Figure 15. Evolution of the number of RAR notifications, ratio of declared RAR per 1000 patients transfused and per 1000 LBP distributed



According to table 17, the decrease concerns practically all the diagnoses and no increase that could have an epidemiological significance is observed.

Table 17. Evolution of the number of grade 1 to 4 and imputability 2 to 4 RAR, investigation completed over the 2000-08 period

	Year of occurrence									
Diagnosis	2000	2001	2002	2003	2004	2005	2006	2007	2008	2000-08 Nb. RAR per 10000 LBP
appearance of irregular antibodies	1 425	1 426	1 348	1 200	1 265	1 429	1 626	1 726	1 635	5,6
non-haemolytic febrile reaction	1 768	1 854	1 817	1 762	1 068	1 003	1 202	1 438	1 449	5,7
allergy	1 364	1 400	1 379	1 545	1 598	1 443	1 319	1 374	1 286	5,4
volemic overload	174	180	168	209	191	208	219	251	262	0,8
immunological incompatibility including ABO	353 28	305 20	259 21	257 12	292 17	288 14	258 12	283 14	229 11	1,1 0,1
TRALI	1	1	9	18	24	34	37	47	45	0,1
bacterial infection	40	21	16	35	13	6	8	11	9	0,1
haemosiderosis	7	7	10	3	2	3	5	1	2	0,0
viral infection	219	188	101	54	44	22	13	6	2	0,3
purpura				1	1	1		1	1	0,0
graft versus host disease				1					1	0,0
other (immediate or delayed reaction)	66	73	44	53	56	34	48	47	40	0,2
Unknown*	363	424	387	394	901	1 005	745	565	533	2,3
Total	**5 780**	**5 879**	**5 538**	**5 532**	**5 455**	**5 476**	**5 480**	**5 750**	**5 494**	**21,5**

** Unknown diagnoses represent a significant portion of all RAR, i.e. 6 to 18% depending on the year. The strong growth since 2004 should be put into perspective with the change in tool for the notification of RAR – e-fit – and its opening to a larger number of declaring persons. Furthermore, when the data from the old database GIFIT (year 2000 to 2004) was analysed, a large portion of the diagnoses were reclassified in NHRF when signs of shivering and/or fever were observed (ISBT consensus criteria, Vancouver August 2002).*

According to figure 16, 52 imputability 2 to 4[8] viral and parasitic infections have been notified in the e-fit database with a transfusion date after 2000 (18 HCV, 15 CMV, 11 HBV, 2 HIV, 2 HAV, 2 malaria, 1 parvovirus B19 and 1 HEV). The annual number of these contaminations has been decreasing since 2000 (10 in 2000 and 1 in 2008). This is essentially related to the evolution of biological qualification of donations techniques, with increasingly lower detection thresholds.

8 *30.8% of these infections (16/52) are imputability 3-4 : 4 HBV, 2 HCV, 2 HIV, 2 CMV, 2 HAV, 1 HEV, 1 HEV parvovirus and 2 malaria*

Figure 16. Evolution grade 1 to 4 and imputability 2 to 4 viral and parasitic infections, investigation completed per transfusion date[9]

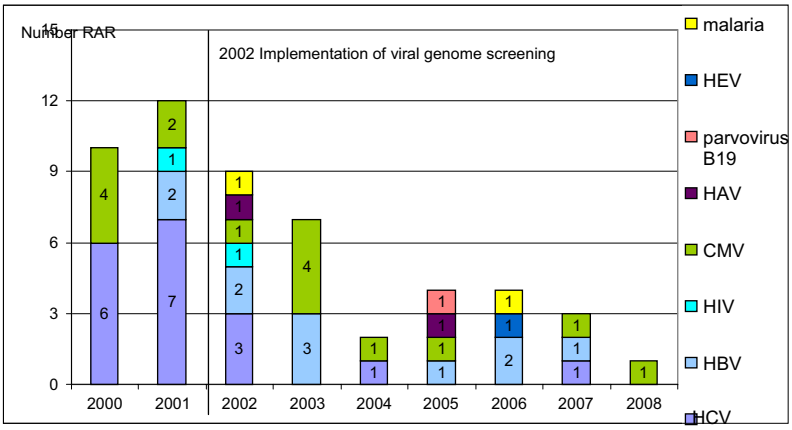


Table 18 shows that if the RAR related to PRBC transfusion are usually the largest group (67.5%), those related to platelets have a much higher incidence, i.e. a ratio of 82 RAE per 10,000 APC transfused and 40 RAE per 10,000 PCM transfused.

Table 18. Distribution of diagnoses of imputability 2 to 4 adverse reactions that occurred between 2000 and 2008, and % as a function of the type of LBP (1)

Mean number of diagnoses	Mean 2000-08	PRBC	APC	PCM	VIP	FFPs	Others (2)
non-haemolytic febrile reaction	1 485	81.2%	15.6%	1.8%	0.3%	0.7%	0.5%
appearance of irregular antibodies	1 453	92.7%	4.1%	2.5%	0.1%	0.3%	0.4%
allergy	1 412	28.0%	61.9%	3.5%	1.7%	4.8%	0.2%
immunological incompatibility	280	54.5%	39.1%	5.3%	0.3%	0.6%	0.2%
including ABO	17	67.1%	22.8%	2.0%	4.0%	3.4%	0.7%
volemic overload	207	92.3%	5.2%	0.5%	0.4%	1.3%	0.4%
viral infection	72	61.8%	0.5%	1.1%	0.0%	8.5%	28.2%
TRALI	24	56.5%	25.9%	2.3%	0.5%	13.9%	0.9%
bacterial infection	18	56.6%	35.8%	6.9%	0.0%	0.0%	0.6%
haemosiderosis	4	90.0%	0.0%	0.0%	0.0%	0.0%	10.0%
post-transfusion purpura	1	80.0%	20.0%	0.0%	0.0%	0.0%	0.0%
other infection	0	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%
graft versus host disease	0	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%
other (immediate or delayed reaction)	51	52.7%	42.7%	0.9%	0.9%	1.1%	1.7%
unknown	591	66.0%	29.0%	2.5%	0.5%	1.7%	0.3%
Mean number in % depending on LBP	**5 598**	**67.5%**	**26.6%**	**2.6%**	**0.6%**	**1.9%**	**0.7%**
Mean number per 10,000 LBP	***21.5***	***18.0***	***82.0***	***39.9***	***2.6***	***7.0***	

1) LBP 1st line, for further details on the distribution per product please refer to annex 8
(2) Others: ACG, reconstituted blood, total blood, non-LBP, NR

3.4.1. The most serious and most certain RAR

We record on average 139 grades 3-4 and imputability 3-4 RAR per year from 2000 to 2008 (63.4% with PRBC, 25.9% with APC, 3.1% PCM, 7.2% with plasmas). Table 19 shows the evolution of the distribution of these types of products (a more detailed table is provided in annex 8.1.2 that allows the identification since 2006 of the RAR concerning new products, in particular platelets and plasmas).

9 *2000-03: calculated transfusion year (GIFIT source), 2004-08: declared transfusion year (e-fit source)*

Table 19. RAR grade 3-4 and imputability 3-4 investigation completed – according to the type of products

	2000	2001	2002	2003	2004	2005	2006	2007	2008
PRBC	66	62	85	85	78	81	92	111	132
APC	25	31	35	36	38	42	32	49	36
PCM	6	2	0	3	1	3	2	12	10
VIP	1	2	0	0	0	2	1	4	10
FFPs	8	5	9	9	8	3	6	18	4
Others	0	1	0	0	1	0	0	2	0
Total	**106**	**103**	**129**	**133**	**126**	**131**	**133**	**196**	**192**
Number of RAR per 100,000 LBP	4.2	4.1	5.2	5.3	4.9	5.1	5.0	7.1	6.7

Table 20 presents the mean yearly number of diagnoses between the two periods 2001-04 and 2005-08. An increase in the overloads and unknown diagnoses has been observed, the comparison with the TRALI is not possible as this diagnosis only started to be recorded in the e-fit database since 2004.

Conversely, we observe a decrease in immunological incompatibilities, bacterial infections and NHFR and a stability in allergies.

Table 20. RAR grade 3-4 and imputability 3-4 investigation completed – Comparison of the periods 2001-04 and 2005-08

Diagnosis	Annual mean number RAR (%)		Number RAR per 100,000 LBP	
	2001-04	2005-08	2001-04	2005-08
		Increase in numbers		
volemic overloads	50 (0.11)	61(0.08)	2.01	2.25
TRALI	9 (0.43)	17 (0.32)	0.35	0.63
unknown	5 (0.01)	7 (0.00)	0.21	0.27
		Decrease in numbers		
immunological incompatibility	15 (3.24)	7 (2.45)	0.60	0.26
including ABO	5 (2.27)	1 (1.71)	0.21	0.05
bacterial infection	4 (0.33)	3 (0.25)	0.14	0.13
non-haemolytic febrile reaction	5 (2.27)	1 (1.71)	0.19	0.02
		Stable numbers		
allergy	32 (0.73)	32 (0.55)	1.29	1.17
viral infection	0	0		

Note: Values in parenthesis: contribution to chi-2; Chi-2=31.57(global all diagnosis), degrees of freedom df=7, p-value <0.0001

3.4.2. Grades 1 and 2 RAR

Table 21 distinguishes the evolutions of the diagnoses during the two periods 2001-04 and 2005-08. Thus, we observe an increase in the appearance of irregular antibodies, unknown diagnoses and volemic overloads and a decrease in NHFR, allergy and immunological incompatibilities.

Table 21. RAR grade 1-2 and imputability 2 to 4 investigation completed – Comparison of the periods 2001-04 and 2005-08

Diagnosis	Annual mean number RAR (%)		1 RAR per 10,000 LBP	
	2001-04	2005-08	2001-04	2005-08
		Increase in numbers		
appearance of irregular antibodies	1310 (17.87)	1604(18.24)	5.23	5.92
unknown	507 (14.47)	681(14.77)	2.02	2.51
volemic overload	122 (0.89)	141 (0.91)	0.49	0.52
TRALI	3 (0.83)	7 (0.85)	0.01	0.03
		Decrease in numbers		
non-haemolytic febrile reaction	1613 (16.58)	1272 (16.93)	6.43	4.69
allergy	1442 (2.12)	1305 (2.16)	5.75	4.81
immunological incompatibility	262 (0.003)	255 (0.003)	1.04	0.94
viral infection *	97 (34.11)	10 (34.83)	0.39	0.04
bacterial infection	17 (3.85)	4 (3.93)	0.07	0.01
haemosiderosis	5 (0.23)	3 (0.23)	0.02	0.01

Note: Values in parenthesis: contribution to chi-2; Chi-2=186.47(global all diagnosis), degrees of freedom df=10, p-value <0.0001

** viral infections cannot be analysed in this context as they must be considered as a function of the date of the transfusion.*

3.5. Other events

3.5.1. SAE with transfusion of LBP without RAR

Table 22 shows the number of grade 0 SAE declared on RARF according to the inter-regions, starting on 2002, as their notification started in November 2002 retroactively. While the annual increase of this number is of approximately 8.3% since 2003, the spread of inter-regions has changed, the increase of grade 0 SAE of the North East (+14.2) compensated the decrease of those of the North West (-14.1%).

Table 22. SAE declared in grade 0 RAR per inter-region

Inter-regions	2002	2003	2004	2005	2006	2007	2008
South West	7 (13.5%)	11 (8%)	23 (15.4%)	12 (8.1%)	15 (10.9%)	26 (14.5%)	23 (11.7%)
South East	16 (30.8%)	36 (26.1%)	36 (24.2%)	40 (27%)	28 (20.3%)	48 (26.8%)	52 (26.5%)
North West	12 (23.1%)	35 (25.4%)	27 (18.1%)	21 (14.2%)	26 (18.8%)	20 (11.2%)	22 (11.2%)
North East	8 (15.4%)	22 (15.9%)	28 (18.8%)	41 (27.7%)	36 (26.1%)	32 (17.9%)	59 (30.1%)
Ile-de-France	8 (15.4%)	33 (23.9%)	33 (22.1%)	31 (20.9%)	25 (18.1%)	45 (25.1%)	36 (18.4%)
DOM-TOM	1 (1.9%)	1 (0.7%)	2 (1.3%)	3 (2%)	8 (5.8%)	8 (4.5%)	4 (2%)
Total	52 (100%)	138 (100%)	149 (100%)	148 (100%)	138 (100%)	179 (100%)	196 (100%)

Figure 17 shows the evolution of the frequency of grades 0 per 100,000 LBP per inter-region and figure 18 on the site of dysfunctions, for which the main remains over the 7 years the health establishments.

Figure 17. Evolution of number of SAE declared in RAR grade 0 per 100,000 LBP

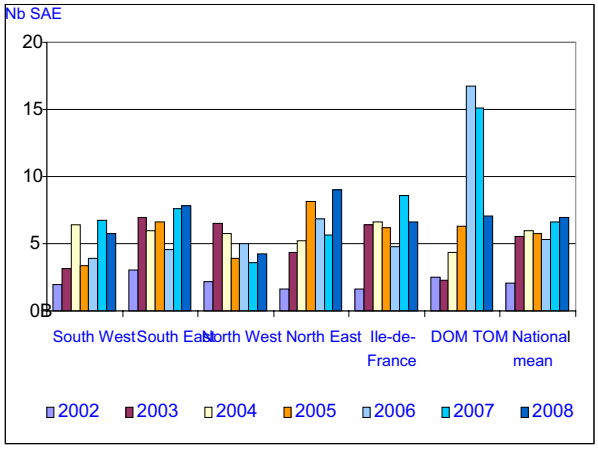
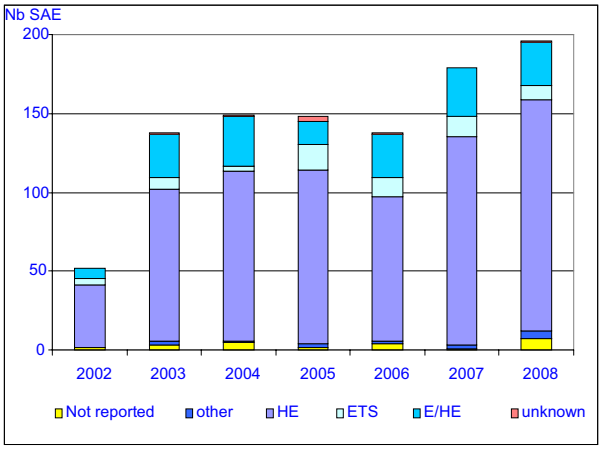


Figure 18. Evolution of SAE declared in RAR grade 0 according to site of dysfunction



3.5.2. SAE with transfusion of LBP that caused a RAR (grade higher than or equal to 1)

The number of SAE is on average of 53 between 2000 and 2008. During this period, 70.9% occurred in HE, 12.0% both at the BE and HE, 10.9% in BE and 6.1% in other sites (figure 19).

The tendency is downwards since 2000-2001. Table 23 illustrates this evolution per inter-region since 2000.

Figure 19. Evolution of SAE associated with RAR grade higher than or equal to 1 according to dysfunction site

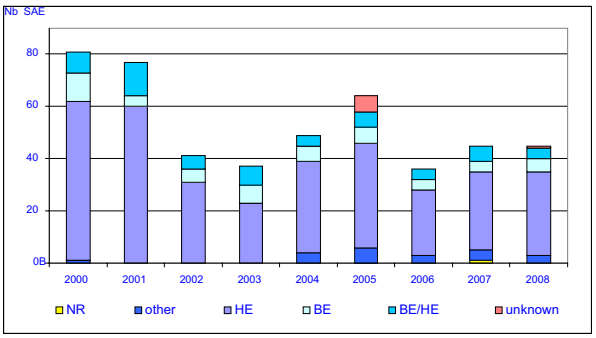


Table 23. SAE associated with RAR grade higher than or equal to 1 per inter-region

Inter-regions	2000	2001	2002	2003	2004	2005	2006	2007	2008
South West	7 (8.6%)	10 (13%)	3 (7.3%)	2 (5.4%)	7 (14.3%)	5 (7.8%)	1 (2.8%)	3 (6.7%)	5 (11.1%)
South East	22 (27.2%)	21 (27.3%)	6 (14.6%)	10 (27%)	7 (14.3%)	14 (21.9%)	4 (11.1%)	7 (15.6%)	4 (8.9%)
North West	12 (14.8%)	20 (26%)	15 (36.6%)	9 (24.3%)	13 (26.5%)	8 (12.5%)	5 (13.9%)	9 (20%)	10 (22.2%)
North East	18 (22.2%)	15 (19.5%)	5 (12.2%)	8 (21.6%)	9 (18.4%)	13 (20.3%)	11 (30.6%)	20 (44.4%)	20 (44.4%)
Ile-de-France	17 (21%)	10 (13%)	8 (19.5%)	6 (16.2%)	8 (16.3%)	18 (28.1%)	6 (16.7%)	5 (11.1%)	4 (8.9%)
DOM-TOM	5 (6.2%)	1 (1.3%)	4 (9.8%)	2 (5.4%)	5 (10.2%)	6 (9.4%)	9 (25%)	1 (2.2%)	2 (4.4%)
Total	**81 (100%)**	**77 (100%)**	**41 (100%)**	**37 (100%)**	**49 (100%)**	**64 (100%)**	**36 (100%)**	**45 (100%)**	**45 (100%)**

3.5.3. SAE without transfusion of LBP

This category of events only concerns those detected before transfusion. The number of notifications in 2008 was of 119, versus 47 in 2007 (for 8 months of notification as the declarative system for these events was set up in May 2007).

3.5.4. DSAR

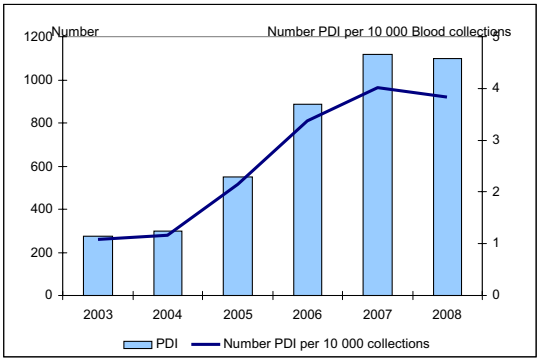
In 2006, the notification of DSAR was performed on an experimental basis. Since 322 forms have been notified to the Afssaps in 2007 and 321 in 2008, i.e. a rate of 1.2 per 10,000 collections in 2007 and 1.1 in 2008.

3.5.5. PDI

PDI are declared since October 2002.

Their number has multiplied four-fold between 2003 and 2007, to decrease slightly in 2008 (figure 20).

Figure 20. Evolution of the number and ratio of PDI (per 10,000 collections)



4. Work carried out in 2008

4.1. Participation in the elaboration of legislative and regulatory texts

See chapter 1.1.

4.2. National haemovigilance commission and work groups

The members of the NHC met twice in 2008 and the experts of each work group (WG) on average 6 times (due to the coexistence between new groups to be organised and existing groups that had not completed their tasks).

The objective of this chapter is to provide a summary profile of the work performed by these groups:

1. NHVN (National haemovigilance network) WG

Each objective of the group is declined in a small number of actions, the progress of the performance is assessed from the meeting reports. This simple method could be used as a base by the other groups, in order to homogenise the work groups, and then compile the assessments in a common document for the NHC.

The activity of the NHVN group covers the following domains:

- Evaluate the monitoring system (RAR, SAE, DSAR, PDI) on recognised methodological bases (CDC criteria).

- Accompany the electronic-notification system evolutions (e-fit2) taking into account the demands and contributions of all the levels of the networks and theme groups, and writing the data acquisition, validation and consolidation rules.

- Elaborate and validate the technical data sheets combining them in a coherent document.

- Write the guides for filling-in e-fit2 and integrating them into a complete documentation of the notification system.

- Monitor the coherence and harmonisation of proposals from theme groups, and integrate their production in the common documentation.

- Identify transfusion safety problems ensuing from the monitoring of RAR and SAE: overload APO, identity-vigilance.

- Elaborate a haemovigilance and transfusion safety indicators document in the form of a small number of robust indicators, calculated from the data available, to propose adjustment measures (haemovigilance network activity indicators, risk measurement indicator).

- Promote the distribution of haemovigilance products, in particular by translating the main documents into English.

2. TTBI (Transfusion transmitted bacterial infection)

The objectives of this WG were to analyse the TTBI suspicions declared on e-fit, elaborate recommendations on the methodology of analysis of suspected TTBI, provide its expertise, elaborate recommendations for the management of suspected TTBI, ensure an optimal reactivity and think about the implementation of prevention measures.

After selection by the haemovigilance unit, 109 RARF were evaluated during 6 meetings in 2008.

To date, 55 bacterial strains have been centralised at the Afssaps.

For a better understanding of the TTBI diagnosis RARF coding, a blood product imputability grid in the occurrence of bacterial infections has been prepared. This tool wishes to be educational and didactic. Its application was tested by members of the two work sub-groups in the analysis of the e-fit database

for the drafting of two publications. The communication of this document for the network participants will take place via the e-FIT network and the RHC.

The group also specified the modifications required in order to improve the filling-in of the TTIB suspicion entry forms in the next version of e-fit, in particular taking into account the LBP “soiling” concept.

The WG followed the organisation of certified laboratories in application of the circular dated 15 December 2003 concerning TTBI: 59 laboratories have been certified in 2008 (26 in the PU outside CHU, 25 in CHU, 4 at the EFS, 1 at the CTSA and 3 in private laboratories).

However, the considerations of the group target the major residual difficulties for a quality analysis of TTBI, including the absence of involvement of clinicians in the diagnosis and analysis of RAR, the lack of commitment of bacteriologists in the LBP cultures result report, the consultation deficit between the different actors of the transfusion chain to agree on a conclusion diagnosis and the imputability criteria. The improvement proposals concerning the three domains come up against the reality of the field in the current context. The TTBI group draws the attention of the NHC on the double finality of the e-fit database in the framework of the French regulation, which requires the exhaustive notification of any RAR irrespective of its severity. What inclusion criteria, what articulations between a declarative database that allows steering the network and an epidemiological database with quality criteria that cannot be ignored ?

3. TRALI/overload pulmonary oedema WG

The objectives of the WG were:

- to describe more accurately the epidemiological characteristics of TRALI and overload pulmonary oedema in France, first essential step;

- favour their knowledge by the actors of the national haemovigilance network;

- present to the commission the risk reduction priorities.

The group has elaborated a method of analysis and classification of pulmonary oedema notifications, in order to have case review method over the 2007-2008 period. It is based on a logical diagram and a definition grid of its items, the will replace the additional HE form. These tools aim at the application of a common, consensual and reproducible analysis scheme for the experts, coherent with the international definitions. Furthermore, educational virtues may be expected and an improvement in the quality of the data once it has been distributed to the network participants.

The additional information collection form intended for health establishment correspondents has been remade in order to improve the quality and objectivity of the information without complicating it while decreasing the tasks of the correspondents. The questionnaire for the TRALI or overload accident diagnosis has been simplified. It has been drafted in a manner that it also constitutes a diagnosis assistance tool by integrating the logical diagrams. The correspondents have been asked to attach a hospitalisation report, rendered anonymous, if possible.

A good number of TRALI and haemodynamic APO notifications and certain unknown nature incident notifications were examined using these schemes by all the experts with a concordance study and resolution of difficult cases by consensus. The examination of all the TRALI notifications from 2007 and 2008 are being completed. The extraction of the elements that allow describing the typology of TRALI cases in France on the consolidated database may then start at the end of June.

The information collection form has been submitted for examination to the network participants. We are expecting the opinion returns. It may then be distributed to the network, after any possible adjustment.

The initial observations are the following:

- The number of TRALI cases retained by the WG is lower that the number of cases declared. It should be noted that real risk is under-estimated for multiple reasons. The regional disparities demonstrate a variable degree of non-recognition and under-notification. Even though the proportion of TRALI related to an immunological conflict is lower than in the international literature, it seems that one of the means to reduce the risk of TRALI is to sensitise clinicians and network participants on the

importance of the recognition and notification, in order to eliminate donations that are immune conflict vectors.

- There is a large number of overload APO. The analysis of these cases is difficult due to their number and the reticence of the correspondents to document these cases. A detailed and reliable descriptive analysis of overload APO requires a different approach, concentrating the study on a short period and/or on certain regions. However, it would seem that the mechanism is fairly stereotypical, and in several of these cases, it follows an inappropriate prescription. The reduction of this frequent risk involves the education of prescribers. The existence of recurrent predisposing factors of an organisational nature cannot currently be excluded, but requires a more detailed analysis.

4. Allergy WG

• The Allergy WG, has set up a work method after obtaining a consensus on the definition of allergy*.

**The term allergy covers several diseases and is not limited to reactions involving IgE.*

• A descriptive data analysis was performed (analysis and classification of cases recorded in e-fit),

• Drew up an assessment of the work already carried out and the bibliography

• Drew up the allergy technical data sheet.

• And proposed an additional clinical and biological information compilation form specific to severe allergic reactions

The WG was also asked to give its opinion on the conduct to follow in case of serious allergic reactions in a transfusion including methylene-blue treated plasma context and to participate in the elaboration of a protocol to be proposed to the haemovigilance network, in the form of an exploration procedure of these reactions during transfusions including MB-VIP.

5. ARC (Analysis of root causes) WG

The WG evaluated the efficacy of the SAE notification system and made the following observations:

• Analysis of the SAE notification system:

  – Unfriendly system (paper notification)

  – Complex notification circuit (dichotomy: immediate notification (ID) by SAE and differed notification by annual report (AR))

  – SAEF poorly adapted to the SAE capture objectives and especially to the Analysis of Root Causes

  – Time consuming annual report for the declaring establishments, non-exhaustive, unusable at a national level

  – Heterogeneity of the declaring health regions (4 regions total 74% of notifications)

• Analysis of SAE declared (approximately 240 SAEF, RARF declared in grade 0 and RARF grade ≥ 1):

  – Heterogeneity of investigations on declared SAE (absence of thesaurus)

  – Impossibility to analyse all SAE in depth

  – 3 subjects identified for priority analysis: Identity-vigilance, final pre-transfusion controls (ex: ABO), information systems

• Inventory of ARC methods available:

  – Audition of users of several methods: choice of the ENEIS method by the WG

  – Elaboration of a standard ARC grid and a training kit

In view of these observations, the WG proposes an evolution of the SAE notification system in order for it to be integrated to e-FIT2, especially eliminating the dichotomy of notification between the SAEF

and the annual report, on the development of a thesaurus, and on the in-depth analysis of SAE targeted as priorities. It suggests that the collaboration with the haemovigilance network and the research organisations should be incited for the statistical and scientific analysis of data on SAE that have not undergone in-depth analysis (statistical analysis). Finally, it insists on the need for a broad communication campaign with respect to the haemovigilance network, health professionals, learned societies, target the information on risk perception and on the understanding the objectives of the new actions.

4.3. The haemovigilance portal project of the Afssaps site (www.afssaps.fr)

A lay-out of the haemovigilance portal was prepared in 2008. Its objective is to group all the information concerning haemovigilance, which up to now were dispersed in various spaces of the Afssaps site www.afssaps.fr. In compliance with the graphic charter of the "Vigilance" portals of this site, the haemovigilance portal includes 9 windows:

- Haemovigilance (news, work in progress, published or distributed work, etc.)
- Organisation of haemovigilance
- Help on reporting and notification
- Evaluation of the severity and imputability of events and adverse reactions
- Contacts in the haemovigilance unit
- Training of correspondents
- National haemovigilance commission
- Work groups or cells attached to the NHC
- Regulatory texts

Available in intranet in November 2008, the Haemovigilance portal will be accessible to the general public and health professions in January 2009.

4.4. Communications and publications

4.4.1. Communications in congresses

1. VIIth National haemovigilance and Transfusion safety Congress (SFVTT) 19-21 November 2008 – Perpignan (France)

- 2 posters were presented:

  * 2007, 1st year of notification of haemovigilance data to the European Commission - Recipient serious adverse reactions: VO Mai M-P, Caldani C

  * Role of a certified bacteriology laboratory in the use of a suspected transfusion transmitted bacterial infection (TTBI): Eb F, Weinbreck P, Ounnoughene N, Caldani C

2. XXXth international congress of the International Society of Blood Transfusion (ISBT) – 7 to 12 June 2008 – Macao (China)

  * Presentation of a poster: Adverse reactions associated with inappropriate transfusion of labile blood products without any biologic or clinical effect - Between 2003 and 2007 in France: VO Mai M-P, Caldani C, Legras JF, Willaertl B, Sandid I, Zorzi P

  * Participation in an oral communication: Reduction of septic transfusion reactions related to bacteria contamination without implementing bacteria detection. This communication has been published: ISBT Science Series 2008, 3, 124-132: Andreu G, Caldani C, Morel P.

4.4.2. Publications

Bulletin Haemovigilance n° 16 – 2008:

- Decision of 7 May 2007,
- Haemovigilance in the United Kingdom,
- Analysis of grades 0 on e-fit between 2003 and 2006

Bulletin Haemovigilance n° 17 – 2008:

- Regulatory approach of banks,
- Blood bank in a laboratory,
- Comparative analysis of recipient adverse reactions (RAR) observed after transfusion of labile blood products (LBP) distributed by blood banks or blood transfusion establishments and declared on the e-fit base.

4.5. Other communications or studies

4.5.1. INTS/UNCAM survey

At the request of the Director General of the Union nationale des caisses d'assurance maladie (UNCAM), a study was initiated, concerning the conditions of performance and use of immuno-haematology (IH) analysis to ensure the immuno-haematological safety of blood transfusions. The RHC and the haemovigilance unit were asked to establish the list of public hospital centres and PSPH that perform their IH laboratory activity themselves or have a contract with a BLM or EFS. This concerns routine IH (blood groups, RAI screening, etc.) and not expert IH (antibody identification, etc.).

4.5.2. Health information technology

The haemovigilance unit participated in AFNOR standardisation work in the field of health information technology and in other multi-disciplinary and inter-institutional groups (InVS for donor epidemiology, INTS for training of professionals, DGS, EFS, etc.).

4.5.3. International cooperation

The Afssaps has also participated:

- in EHN general assemblies, that meet during European or international congresses.

- several “Working party on haemovigilance” of the ISBT (International society of blood transfusion).
- meetings of the expert ad hoc group of the European commission in charge of proposing a common approach between Member States of haemovigilance annual reports.

5. Actions carried out and improvement proposals

5.1. Evolution of e-fit

The evolution of e-fit is part of one of the priority projects of the computerisation master plan of the Afssaps. A service provider has been charged with designing the new version of e-fit, “e-fit2”, concerning more specifically:

1. The management of RAR in order to integrate the modifications requested by the haemovigilance network since 2004 (since the implementation of e-fit) and the requests formulated from the results of the NHVN/e-fit work group as well as those of the unit.

Examples of modifications at the initiative of the groups:

- Allergy WG: Addition of LBP age and donor gender items, reorganisation of table 2-3 of clinical and biological manifestations by grouping the symptoms by organ class, allowing to choose a defined number of signs in a drop-down list for each class, classification of table 3.3 LBP in chronological transfusion order and designation of LBP during which the RAR occurred.

- TRALI WG: Plan on-line assistance (if a grade is ticked, reminder in another window the criteria of the grade), coherence controls: data concordance algorithms, integration of new diagnosis: TAD, ALI (SDRA) instead of TRALI.

2. The management of DSAR, SAE and PDI (major evolutions)

It has been planned to carry out a public survey (acceptability survey) of the new lay-out of the e-fit evolutions by “training” users such as the RHC, BE HVC, HVC of CHU and some private HE HVC (or HE highly involved in haemovigilance).

5.2. Organisation of a “Review of traceability directives” sub-group

It seemed necessary to organise a “Review of traceability directives” sub-group (sub-group of the CNIT group), in order to review certain technical directives, due to the following observations:

1. The technical circulars and directives concerning the traceability of LBP date from 1994 for the paper traceability and 1997 for the computerised traceability.
2. Computerised traceability is still based on experimental specifications.
3. The participants identified in the technical circulars and directives above are no longer the same.

5.3. Other actions to be carried out

The elaboration of the following technical data sheet has been planned for the 2009 programme:

1. Immunological incompatibility
2. Haemochromatosis
3. Viral serology

6. Evaluation of actions carried out previously and follow-up of measures

6.1. Training on the e-fit tool

A training on the current e-fit* tool was carried out in July and September 2008 (i.e. 4 sessions) and concerned approximately 50 HE and BE correspondents and 9 RHC.

**The Afssaps makes available for haemovigilance correspondents an internet site (https://e-fit.afssaps.fr/rnhv/rnhv/loginApplet.html) for the on-line notification of adverse reactions occurring in recipients of labile blood products since 2004.*

6.2. The exploration of cases of allergy with methylene blue treated plasma transfusions (MB-VIP)

In July 2008, the EFS provided prescribers with a new LBP, methylene blue virus-inactivated frozen fresh plasma (MB-VIP). This product has undergone a pathogen agent inactivation treatment using a technique that combines methylene blue and an illumination in visible light. It is intended to replace quarantine secured fresh frozen plasma (FFPs) whose distribution has been progressively stopped.

Starting in September 2008, the haemovigilance unit of the Afssaps observed a higher than expected frequency of serious allergic reaction notifications occurring during transfusions including MB-VIP: 1 per 5,900 MB-VIP versus 1 per 19,800 FFPs, i.e. a ratio higher than 3.

The Afssaps expert group from the National Haemovigilance Commission gave the following opinion:

- *to date there is no argument justifying a MB-VIP withdrawal proposal;*
- *in case of a suspected serious allergic reaction (Grade 3 according to the definition of the Decision of 5 January 2007 setting the form, content and transmission procedures of the notification form for an adverse reaction occurring in a recipient of labile blood product), the patients must be examined according to the protocol defined by the work group;*
- *following an initial allergic reaction associated with a transfusion including MB-VIP, the work group recommends not to transfuse this product again before the additional tests allow eliminating a sensitisation to the MB-VIP components in particular to methylene blue; it is important that the EFS makes sure that the timelines for the constitution of stocks of available products are as short as possible, including in the banks;*
- *the work group believes it necessary to propose to the RHC a common aetiological investigation procedure, that the RHC will adapt to the regional conditions and will distributed to the CSTH and the haemovigilance and transfusion safety sub-commission, so that they may be applied in each health establishment following the validation of the sampling, distribution and storage procedures of the receiver samples and the LBP involved, or even samples from the donors concerned.*

This work group has written a “Serious allergic reactions exploration procedure (grades 3 and 4) during a transfusion including MB-VIP" that was distributed to the HE and BE via the RHCs.

At the same time, the Afssaps, communicated its position in order to provide the transfusion participants information on the level of risk and the methodology to be employed to document it better. Since the first cases did not benefit from a specific exploration of the allergy, it was impossible to confirm the mechanisms of these reactions or to attribute in a certain manner these reactions to the MB-VIP, especially as there were numerous possible biases and confusion factors, as for example the simultaneous transfusion of several types of LBP in certain transfusion episodes involved. The Afssaps also asked a group of experts to draft a guideline on the use of methylene blue virus-inactivated Fresh Frozen Plasma.

Finally, the learned societies have distributed a document reminding that “the indications and contraindications of MB-VIP are no different from those of other therapeutic plasma apart from known history of methylene blue allergy that must be determined during the interrogation of the future transfused patient, and that any inconsiderate widening of the contraindications could lead to plasma supply difficulties, that may transform a potential risk in real accident".

6.3. The other recommendations in 2008

Following analyses of TTBI type RAR:

These analyses are still confronted with the absence of insufficiency of microbiological data, which do not always allow the TTBI WG experts to reach a conclusion. It has been proposed that the results be collated on the same form type document to be filled-out by the microbiologist and to add the soiling concept in the RARF, the simultaneous presence of two micro-organisms as responsible agents has been observed 2 times out of 60 cases.

7. Summary and conclusion

7.1. Highlights of the year 2008

- General comments:

1. Regulatory context

At a regulatory level, the year 2008 was marked by 4 Decisions of the Director General of the Afssaps concerning:

- the standard template for annual summary report of adverse events and incidents of the transfusion chain

- the new codes of therapeutic labile blood products

- the new codes of the blood transfusion establishments and to the complementary codes of the therapeutic labile blood products

- the questionnaire filled-in by the blood donation candidate

2. Transfusion activity

- 2,870,835 LBP were distributed for 512,300 patients (50.9% women and 49.1% men) in 2008, these LBP were traced up to 98.9%. 73% of patients were over 60 years old.

- Approximately 1,630,800 donors in 2008 (50.4% women and 49.6% men) gaved 2,869,647 collections (2,377,570 in total blood and 492,077 in aphaeresis). More than 1 out 3 donors was under 30 years old.

- Adverse reactions and transfusion chain events

1. Recipient adverse reactions (RAR)

- 7 298 RAR[10] were declared in 2008, including 12 deaths with imputability score of 2 to 4. Among these 12 cases, 5 were imputability 3 and 4. However, after the analysis of the cases by the experts groups of the NHC, 2 of them were reclassified as imputability 2 (2 volemic overloads). The remaining 3 deaths concerned 1 TRALI, 1 allergy and 1 bacterial infection.

Related to the number of LBP distributed, the RAR notification ratio per 1,000 LBP distributed is of 2.5 and the incidence rate of imputability 2 to 4 deaths of 0.4 per 100,000 LBP.

- 5,494 of 7,298 RAR declared are imputability 2 to 4, a decrease with respect to 2007. This decrease concerns almost all the diagnoses and we do not observe any increase that could have an epidemiological significance.

2. Donor serious adverse reactions (DSAR)

The number of DSAR declared in 2008 is of 322, i.e. the notification rate is of 11.2 per 100,000 donations. 77% grade 2 (effects requiring an external consultation) and 23% grade 3 (effects requiring hospitalisation).

3. Serious adverse event of the transfusion chain (SAE)

360 SAE were declared in 2008, i.e. 45 incidents associated with a RAR, 196 incidents with LBP transfusion without RAR (declared in RAR grade 0) and 119 isolated incidents, without transfusion of LBP.

10 *Number of RAR notifications of all grade and imputability levels*

These incidences were often the result of multiple dysfunctions. More than 70%, were declared by the health establishments irrespective of their categories.

The notification rate of SAE associated with LBP transfusion (i.e. SAE having caused a RAR of grade ≥ 1 and SAE without RAR/grade 0) is of 8.4 SAE per 100,000 LBP.

4. Post-donation information (PDI)

The haemovigilance unit of the Afssaps received in 2008 1,099 PDI, i.e. 3.8 PDI per 10,000 collections.

- National Haemovigilance Commission

The NHC adopted for the 1st time in 2008 the summary report 2007 established by the Afssaps concerning haemovigilance in compliance with article R. 1221-28 of the public health code,

It also created 3 new theme groups (allergy, TRALI/volemic overloads and cause-root of transfusion chain incidents), and accompanied 2 existing work groups in their work: TTBI and NHVN.

7.2. Major tendencies

- Transfusion activity

The consumption LBPs continues to increase since 2001, at a rate of + 2.2% per year, consecutive to a slight increase in the number of products transfused per patient.

- RAR

There is a downward tendency in the number of RAR notifications since 2001 as well as in their notification rate (7,298 in 2008 versus 7,936 RAR in 2001 and 2.5 versus 3.2 for the notification rate).

Nearly 78% of imputability grade 2 to 4 RAR recorded between 2000 and 2008 were declared in NHFR, allergies and appearance of irregular antibodies.

Among the most serious and most certain diagnoses (grades 3-4 and imputability 3-4), an increase in volemic overloads and unknown type diagnosis has been observed, and conversely a decrease in immunological incompatibilities, bacterial infections and NHFR. The ratio of these serious RAR fluctuates between 4.1 and 7.0 per 100,000 LBP distributed between 2000 and 2008.

- DSAR

The notification of DSAR started in 2006, on a voluntary basis, and 192 forms have been addressed to the Afssaps. In 2007, the number was of 322 and in 2008 of 321.

- SAE declared in RARF grade 0

The notification of these SAE started in November 2002, and their number progressively increased 138 in 2003 and 196 in 2008. Their rate of occurrence per 100,000 LBP distributed is of 5.9 on average between 2003 and 2008.

- PDI

The PDI notification system is still voluntary (organised since October 2002). Their number has been multiplied by 4 since 2003, to go up to 1099 in 2008. The ratio during the last 3 years was of 3.7 per 10,000 collections.

7.3. Conclusion

In order to be able to provide useful transfusion safety recommendations, it is important to be able to base them on reliable, suitably analysed data.

Some examples illustrate this approach.

- In the past, the expert groups in charge of analysis the bacterial incidents from haemovigilance notifications was able to separate cases of bacterial infections from those of “shivers - post-transfusion hyperthermia", and on the other hand isolate in the first group, better defined, the infections attributable to labile blood products. This allowed the Afssaps, when the DGS asked about the interest of bacterial detection for platelet concentrates, to provide an answer based on more accurate data than in other countries.

- More recently, the haemovigilance unit of the Afssaps detected a ratio of apparently allergic reactions to plasma treated with methylene blue, higher than the ratios previously observed for frozen fresh plasma secured by quarantine or treated with other inactivation methods. The resulting warning led to a statistical verification, confirming the interest of a rapid expertise that allowed the identification of practical risk reduction measures. It was then possible to communicate them to the haemovigilance network and to prescribers, in relationship with the learned societies concerned. A communication without preliminary analysis or prevention measure includes a risk, for example of disruption of supply of an alternative product or the under-use of the product, which may lead to a higher real risk than the theoretical risk that motivated the warning.

Furthermore, the recommendations should be ordered as a function of their impact and possibilities of action.

Therefore, the recommendations concern the following points:

- Improvement of the quality of data transmitted. In order to do this, clinical elements (for example: chronology of reactions, different blood products and medicinal products administered in case of allergy, clinical details and chest X-ray for overload accidents or TRALI) must be provided in accordance with the guidelines distributed by the Afssaps, which requires the awareness of clinicians and haemovigilance correspondents.

- This involves on the one hand the continuation of work on the definition of reactions: drafting and distribution of guidelines; on the other hand a haemovigilance correspondents training action aimed at the appropriation of these guidelines. The large number of haemovigilance correspondents requires starting the action with the regional haemovigilance coordinators, regional transfusion establishment haemovigilance correspondents and those of the larger health establishments.

- Given that the compilation of this information requires lots of time, it would be suitable to focus on improving certain reactions as a function of their frequency, potential severity and avoidability: acute pulmonary oedema, allergic appearance shocks, bacterial infections, patient error (with or without transfusion and, in case of transfusion, with or without adverse reaction). Among these reactions, we should privilege the quality of compilation and analysis effort on the most severe cases (grades 3 and 4). The objective is to attain a better classification of these reactions and a better estimate of their imputability to the transfusion. It is also important to be able to evaluate the portion of the transfusion reaction in the clinical condition of the patient. An effort must be made on all cases for the exceptional reactions. For those which are less rare, it is important to have in-depth complicated analyses that can only be based on the voluntary contribution of certain teams.

- Furthermore, the reporting of all adverse reactions, irrespective of what they are and their severity, which was desired from the start of the haemovigilance, constitutes a major indicator, but also a “background noise” from which the pertinent signals must be extracted. The use of this large mass of data can only be based on statistical analyses that allow distinguishing the tendencies from the background noise. Contracts with external teams should be encouraged with this objective.

- Finally, the mobilisation of the haemovigilance network involves communication actions that aim to demonstrate the usefulness of the data provided by the declaring persons and

haemovigilance correspondents, in terms of furthering the knowledge and improvement of practices. The matter is understanding to be able to act.

This report has used data that were not previously collected from regional haemovigilance coordinators, in particular in order to advance the determination of relationships between adverse reactions with data concerning the recipient population, as entered in the regional coordinators database. The form of this report has also changed in comparison to that of the previous years in order to make reading easier. However, the compilation and analysis must be stabilised to facilitate automation and allow comparisons between different years. Therefore, we propose to keep the same requests and the same analysis for future haemovigilance annual reports during the duration of the mandate of the members of the present Commission.

8. Annexes

8.1. Key values

8.1.1. General comments:

Table 24. Key values for 2008

General comments: Number	Ratio
Number of patients transfused: 512 300	Number of patients transfused per 1,000 inhabitants: 8,1
Number of donors: 1 630 800	Number of donors per 100 inhabitants: 4.1 (18-65 years)
Number of collections: 2 869 647	Number of collections per donor: 1,8
Number of LBP distributed: 2,870,835 Number of LBPs not traced: 31074 Computerisation via pivot formats (number of HE concerned and number of LBP): 117 HE in 12 regions for 642 317 LBPs distributed	Number of LBP distributed per patient: 5.5 Destruction rate: 1.7% Traceability rate: 98.9%%
Number of transfusion HE: 1,520 out of 2014 HE Number of blood banks: 728 including 207 dispensing (estimate)	
Transfusion effects and incidents: Number	**Ratio**
Number of RAR (apart grade 0 RARF): 7,298 including: • 2,137 imputability 2, • 2,349 imputability 3 • 1,267 imputability 4 Number of deaths, investigation completed: 13 including: • 8 imputability 2, • 2 imputability 3 • 3 imputability 4	Ratio of RAR per 1000 LBP transfused: 2.5
Number of SAE: 360 including: • 196 declared in RARF grade 0, • 45 grade ≥ 1 RAR with dysfunction, • 119 SI without transfusion	Ratio of SAE with LBP transfused per 100,000 LBP: • 8.4 for SI of all grades • 6.8 for SI declared in grade 0 RARF
Number DSAR: 321	Ratio of DSAR per 10,000 donations: 1.1
Number of PDI: 1 099	Ratio of PDI per 10,000 donations: 3.8

8.1.2. Distribution of RAR per products and product family

Table 25. RAR imputability 2-4, all grades, investigation completed – as a function of the types of products and diagnoses in 2008

		Diagnoses[11]														
Family of products	1st LBP	DIA	NHFR	allergy	unknown	Over.	II	TRALI	oth	TTBI	haem	viral	purpura	GVH	Total	including ABO
erythrocyte	PRBC	1461	1237	344	379	247	104	32	32	3	1	2	1	1	3844	7
	PRBC-AUTO		1												1	
	RB	1		2											3	
	TB										1				1	
platelet	APC	59	92	620	78	6	65	4	2	2					928	3
	APC-IA	2	2	7	2										13	
	APC-SS	24	60	144	40	2	36	1	6	3					316	1
	SPC			1											1	
	PCM	16	13	8	2		4	1							44	
	PCM-GEN			1											1	
	PCM-IA	7	14	4	2										27	
	PCM-SS	59	24	32	12	2	20	2		1					152	
plasma	FFPs	3	3	57	11	1		4							79	
	SD-VIP	1	2	32	3	3		1							42	
	MB-VIP*			30	2										32	
	IA-VIP	1	1	2											4	
CGA				2	1	1									4	
NR		1			1										2	
Total		**1635**	**1449**	**1286**	**533**	**262**	**229**	**45**	**40**	**9**	**2**	**2**	**1**	**1**	**5494**	**11**

**Note: During the second semester of 2008, a higher than expected number of allergic reactions related to MB-VIP (new plasma distributed by the EFS) was observed. An allergic mechanism was detected in certain serious reactions (positive histamine and/or tryptase assay) and a methylene blue allergy was confirmed in two BM-VIP recipients. However, it was impossible to state that all the serious allergic reactions observed were related to the BM-VIP transfused, as not all the cases were subjected to a specific examination.*

Table 26. Grade 3-4 and imputability 3-4, investigation completed, RAR as a function of the type of products and diagnoses in 2008

		Diagnosis[11]								
Family of products	1st LBP	over.	allergy	TRALI	II	unknown	Oth.	NHFR	TTBI	Total
erythrocyte	PRBC	**90 (21)**	**8 (1)**	**17 (5)**	**6 (4)**	**6 (0)**	**3 (2)**	**2 (0)**		**132 (33)**
platelet	APC	**4 (1)**	**11 (2)**	**3 (2)**	**2 (1)**	**2 (0)**			**1 (0)**	**23 (6)**
	APC-SS	**1 (0)**	**5 (1)**			**3 (0)**	**1 (0)**		**3 (3)**	**13 (4)**
	PCM-SS		**6 (1)**	**1 (1)**	**2 (1)**				**1 (1)**	**10 (4)**
plasma	FFPs	**1 (1)**	**1 (1)**	**2 (2)**						**4 (4)**
	SD-VIP	**1 (0)**	**5 (1)**							**6 (1)**
	BM-VIP		**4 (2)**							**4 (2)**
Total		**97 (23)**	**40 (9)**	**23 (10)**	**10 (6)**	**11 (0)**	**4 (2)**	**2 (0)**	**5 (4)**	**192 (54)**

Reading: values in parenthesis = grade 3-4 and imputability 4 RAR

11 *Legend: AIA: appearance of irregular antibodies, NHFR: non-haemolytic febrile reaction, over.: volemic overload, II: immunological incompatibility, oth: Other Immediate or delayed, TTBI: bacterial infection, haem: haemosiderosis, viral: viral infection, gvh: graft versus host*

Table 27. RAR grade 3-4 and imputability 3-4 investigation completed – according to the type of products – 2000-08

Family of products	1st LBP	2000	2001	2002	2003	2004	2005	2006	2007	2008
erythrocyte	PRBC	65	62	85	85	79	81	92	110	132
	PRBC-AUTO	1							1	
	GEN-R[12]								1	
platelet	APC	25	31	35	36	38	42	23	32	23
	APC-IA								1	
	APC-SS							9	16	13
	SPC	1								
	PCM	5	2	0	3	1	1	1	9	
	PCM-IA								2	
	PCM-SS						2	1	2	10
plasma	FFPs	8	5	9	9	8	3	6	18	4
	SD-VIP	1	2				2	1	3	6
	VIP-BM									4
	IA-VIP								1	
NR[13]			1							
Total		**106**	**103**	**129**	**133**	**126**	**131**	**133**	**196**	**192**

8.1.3. Organisational data per inter-region

Table 27. Number of transfusion sites and transfusing HE per inter-region in 2008

Inter-regions	Transfusion sites	Transfusing HE*
South West	21 (12.9%)	210 (14.9%)
South East	39 (23.9%)	336 (23.9%)
North West	36 (22.1%)	263 (18.7%)
North East	25 (15.3%)	292 (20.8%)
Ile-de-France	37 (22.7%)	264 (18.8%)
DOM-TOM	5 (3.1%)	40 (2.8%)
Total	163 (100%)	1405 (100%)

** Data to be used with caution due to the likely existence of double entries and missing data (reminder number of transfusing HE in 2007: 1573)*

Table 28. Number of HE, BE and RHC haemovigilance correspondents per inter-region in 2008

Inter-regions	Number of transfusing HE HVC*	Number of BE HVC	Number of RHC
South West	213 (14%)	24 (17.1%)	5 (17.2%)
South East	420 (27.6%)	34 (24.3%)	6 (20.7%)
North West	266 (17.5%)	20 (14.3%)	4 (13.8%)
North East	310 (20.4%)	27 (19.3%)	8 (27.6%)
Ile-de-France	272 (17.9%)	30 (21.4%)	3 (10.3%)
DOM-TOM	40 (2.6%)	5 (3.6%)	3 (10.3%)
Total	1521 (100%)	140 (100%)	29 (100%)

** Data to be used with caution due to the likely existence of double entries and missing data (reminder number of transfusing HE HVC in 2007: 1583)*

[12] *GEN-R: POBR*
[13] *NR: not reported (taken from 2001 GIFIT)*

8.2. List of centralised strains since 2003

The microorganisms isolated in 22 TTBI are:

5 Staphylococcus aureus
4 Staphylococcus epidermidis
2 Klebsiella pneumoniae
2 Bacillus cereus
2 Serratia marcescens
2 Escherichia coli
1 Yersinia enterocolitica
1 Streptococcus dysgalactiae
1 Proteus mirabilis
1 Enterococcus faecalis
1 Enterobacter cloacae

For each TTBI, 2 to 5 strains of microorganisms isolated from LBPs cultures, haemocultures, or any other specimen cultured during the investigation were centralised at the Afssaps (i.e. 55 bacterial strains stored).

8.3. Definitions

8.3.1. Adverse reaction, serious adverse reaction, incident and serious adverse event

The following definitions apply for the application of article R1221-23 of the PBC:

1º Adverse reaction: a harmful reaction occurring in donors and related or likely to be related to the blood collection or occurring in recipients, related or likely to be related to the administration of a labile blood product;

2º Serious adverse reaction: an adverse reaction resulting in death or life-threatening, resulting in an invalidity or incapacity, or provoking or prolonging hospitalisation or any other morbid condition;

3º Event/incident: an event related to the collection of blood, biological qualification of donation, preparation, storage, distribution, dispensing or use of the labile blood products, due to an accident or error, likely to affect the safety or quality of the product and result in adverse events;

4º Serious adverse event: an event likely to result in serious adverse events.

8.3.2. Severity levels

8.3.2.1. Severity of RAR

Grade 4: death of recipient.

Grade 3: immediate threat to life. (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 threat to life or long-term morbidity. (Adverse reaction with minor symptomatology. Therefore, it concerns all transfusion RAE which are not grades 2, 3 or 4.

8.3.2.2. Severity of DSAR

Grade 2: prescription of external consultation by the BE physician.

Grade 3: hospitalisation of the donor.

8.3.2.3. Severity of SAE

There are no levels of severity defined for transfusion chain SAE.

As a reminder, the SAE currently declared in RARF grade 0 corresponded to the existence of one or several dysfunctions of the transfusion chain having resulted in the inappropriate transfusion of a LBP without any clinical and/or biological consequence observed in the recipient at the time of the report. However, while waiting the implementation of the tele-notification of all SAE, notification of these SAE in "grade 0" RARF continue to be declared on e-fit to allow their analysis.

8.3.3. Imputability levels

The imputability is defined as the probability that an adverse reaction that occurred in a LBP recipient is attributed to the products transfused, or that an adverse reaction that occurred in a blood donor is attributed to the collection of blood or blood components; by definition, imputability does not apply to chain incidents.

8.3.3.1. Imputability of RAR

For each adverse reaction notification, a case-by-case analysis should allow establishing a causality link between the transfusion of the LBP and the occurrence of the adverse reaction. The imputability levels are classified according to the following criteria:

Imputability 4: Certain: The assessments prove the transfusion origin of the adverse reaction.

Imputability 3: Probable: the adverse reaction does not seem to be explained by an intercurrent cause, and orientation elements in favour of the transfusion origin of the effect are retained.

Imputability 2: Likely/Possible: the adverse effect could be explained either by a transfusion origin or by an intercurrent cause without being able to decide at the stage of the investigation.

Imputability 1: Doubtful: the adverse reaction does not seem to be fully explained by the administration of the labile blood product, without totally excluding it.

Imputability 0: Excluded: it was proven that the labile blood product is not involved in the occurrence of the adverse reaction.

8.3.3.2. Imputability of DSAR

For each adverse reaction notification, a case-by-case analysis should allow establishing a causality link between the blood or blood component collection and the occurrence of the DSAR.

The imputability levels are classified according to the following criteria:

Imputability 3: Certain: when proving elements cannot be doubted and allow attributing the adverse reaction to the donation of blood or of blood component;

Imputability 2: Probable: when the assessment elements available clearly lead to attributing the adverse reaction to the donation of blood or of a blood component;

Imputability 1: Possible: when the assessment elements available do not clearly allow attributing the adverse reaction to the donation of blood or of a blood component nor to other causes.

Imputability 0: Excluded or improbable: when proving elements cannot be doubted and allow attributing the adverse reaction to causes other than the donation of blood or of blood components, or when the assessment elements available clearly lead to attributing the adverse reaction to causes other than the donation of blood or of a blood components.

NA imputability: Non-assessable: when the data is insufficient to assess the imputability.

NB: these levels are those defined in directive 2005/61/CE of the European commission.

8.3.4. RARF investigation levels

Level 0: Cannot be performed

Level 1: In progress

Level 2: Completed

Level 3: Not performed

8.3.5. Distribution and issue definitions

Decree no. 2006-99 dated 1 February 2006 art. 2 defines the following:

1º Distribution of labile blood products: the supply of labile blood products by a blood transfusion establishment to other blood transfusion establishments, to health establishments that manage blood banks and to manufacturers of health products derived from human blood or from its components;

2º Issue of labile blood products: the dispensing of labile blood products on medical prescription for their administration to a given patient. It is performed verifying the immunological compatibility, in compliance with the medical prescription and the implementation of haemovigilance rules.

8.3.6. Definition of inter-regions

Table 29. List of departments and corresponding inter-regions

Depar-tment	5-Inter region	Depar-tment	4-Inter region	Depar-tment	3-Inter region	Depar-tment	2-Inter region	Depar-tment	1-Inter region	Depar-tment	Inter region
09	South West	01	South East	02	North East	14	North West	75	Ile-de-France	97	DOM-TOM
12	South West	03	South East	08	North East	18	North West	77	Ile-de-France	98	DOM-TOM
16	South West	04	South East	10	North East	22	North West	78	Ile-de-France	9A	DOM-TOM
17	South West	05	South East	21	North East	27	North West	91	Ile-de-France	9B	DOM-TOM
19	South West	06	South East	25	North East	28	North West	92	Ile-de-France	9C	DOM-TOM
23	South West	07	South East	39	North East	29	North West	93	Ile-de-France		
24	South West	11	South East	51	North East	35	North West	94	Ile-de-France		
31	South West	13	South East	52	North East	36	North West	95	Ile-de-France		
32	South West	15	South East	54	North East	37	North West				
33	South West	26	South East	55	North East	41	North West				
40	South West	30	South East	57	North East	44	North West				
46	South West	34	South East	58	North East	45	North West				
47	South West	38	South East	59	North East	49	North West				
64	South West	42	South East	60	North East	50	North West				
65	South West	43	South East	62	North East	53	North West				
79	South West	48	South East	67	North East	56	North West				
81	South West	63	South East	68	North East	61	North West				
82	South West	66	South East	70	North East	72	North West				
86	South West	69	South East	71	North East	76	North West				
87	South West	73	South East	80	North East	85	North West				
		74	South East	88	North East						
		83	South East	89	North East						
		84	South East	90	North East						
		2A	South East								
		2B	South East								

This department grouping was inspired by that of the telephone area codes in France.

8.4. List of PBL abbreviations

Table 30. List of abbreviations used

Type of LBP	Abbreviation	LBP definition
Homologous	TB	Total blood
	RB	Reconstituted blood
	PRBC	Packed red blood cells
	SPC	Standard platelet concentrate
	PCM	Platelet concentrate mix
	PCM-SS	Platelet concentrate mix in storage solution
	PCM-IA	Platelet concentrate mix in Amotosalem inactivated storage solution
	APC	Aphaeresis platelet concentrate
	APC-SS	Aphaeresis platelet concentrate in storage solution
	APC-IA	Aphaeresis platelet concentrate in Amotosalem inactivated storage solution
	FFPsd	Solidarised fresh frozen plasma
	FFPs	Secured fresh frozen plasma
	IA-VIP	Plasma Virus-inactivated with Amotosalem
	BM-VIP	Plasma Virus-inactivated with Methylene blue
	VIP-GEN	Virus-inactivated plasma
	SD-VIP	Plasma Virus-inactivated with Solvent detergent
	AGC	Aphaeresis granulocyte concentrate
	CTSA	CTSA plasma
Autologous	TB-AUTO	Total blood
	PRBC-AUTO	Packed red blood cells
	APC-AUTO	Aphaeresis platelet concentrate
	FFP-AUTO	Fresh frozen plasma
Others	GEN-R	Erythrocyte family
Non LBP	Non LBP	

8.5. Lexicon

AABB: American association of blood banks

AE: Adverse Event

AFNOR: Association française de normalisation (French standardisation association)

AFS: Agence française du sang (French blood agency)

Afssaps: Agence française de sécurité sanitaire des produits de santé (French healthcare products safety agency)

AIA: Appearance of irregular antibodies

ALI: Acute Lung Injury

APO: acute pulmonary oedema

ARDS: Acute Respiratory Distress Syndrome

ATNC: Non-conventional transmissible agents

BE: Blood Establishment

BML: Biological Medical Laboratory

CDC: Centers for Disease Control and Prevention

CHU: Centre hospitalier universitaire (University hospital centre)

CMV: cytomegalovirus

EC: European commission

ES: Health Establishment

CSTH: Comité de sécurité transfusionnelle et d'Hémovigilance (Transfusion Safety and Haemovigilance Committee)

CTSA: Centre de Transfusion Sanguine des Armées (Armed Forces Blood Transfusion Centre)

DGS: Direction Générale de la Santé (General direction of Health - Ministry of Health)

DH/DHOS: Direction des hôpitaux/Direction de l'Hospitalisation et de l'Organisation des Soins (Hospitals Department/Healthcare Organisation and Hospitalisation Department)

DOM-TOM: Département d'outre-mer-Territoire d'outre-mer (overseas department or territory)

DRASS: Direction Régionale des Affaires Sanitaires et Sociales (Regional Health and Social Affairs Department)

DSAR/DSARF: Donor serious adverse reaction/donor serious adverse reaction form

e-fit: internet application of the NHVN, set up since the 24 may 2004, and whose access is reserved to all NHVN participants: CHV ES, CHV BE et CHV des sites transfusionnels, RHC, Afssaps, CTSA and EFS.

EFS: Etablissement français du Sang (French Blood Establishment)

EHN: European haemovigilance network

ENEIS : Etude Nationale sur les Evénements Indésirables liés aux Soins (National study on the adverse Events connected to the Health Care)

HVC: Haemovigilance correspondents

HE: Health establishment

HBB: hospital blood banks

FY: Duffy

GIFIT: Old computer management of transfusion RAR form application

HBV: Hepatitis B Virus

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

HLA: Human leukocyte antigen

INTS : Institut National de la Transfusion Sanguine (National institute of the Blood transfusion)

InVS: Institut de Veille Sanitaire (Health Monitoring Institute)

ISBT: International society of blood transfusion

JK: Kidd

LBP: Labile blood products

LBP billed: LBP from the cession records of the EFS or CTSA

MB-VIP: methylene blue virus-inactivated plasma

NHC: National haemovigilance commission

NHFR: Non-haemolytic febrile reaction

NHVN: Réseau national d'hémovigilance (National Haemovigilance network)

NR: Not Recorded

PHC: Public Health Code

PDI: Post-donation information

POBR: Per-operative blood recovery

PSPH: Etablissements de santé privés participant au service public hospitalier (Private establishments of health participating in the public utility)

RAR/RARF: Recipient adverse reation/Recipient adverse reation form

RH: Rhésus

RHC: Regional haemovigilance coordinator

SAE/SAEF: Serious adverse event of the transfusion chain / Serious adverse event form

sCSTH: sub-commission in charge of transfusion safety and haemovigilance

SDRA: Syndrome de Détresse Respiratoire Aiguë (Acute pulmonary distress syndrome)

SFAR: Société française d'anesthésie-réanimation (French anaesthesia-intensive care society)

SFTS: Société française de transfusion sanguine (French blood transfusion society)

SFVTT: Société française de vigilance et de thérapeutique transfusionnelle (French transfusion vigilance and therapeutics society)

TAD: Transfusion Associated Dyspnea

TRALI: Transfused related acute lung injury

TTBI: Transfusion transmitted bacterial infection

UNCAM: Union Nationale des Caisses d'Assurance Maladie (National Health Insurance Network)

WG: Work group