afssaps

Agence française
de sécurité sanitaire
des produits de santé

France Annual Haemovigilance report 2009

CONTENTS

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FOREWORD

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

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

The principal objectives of this report are as follows:
- to supply national data on the 2009 declarations:
• of adverse reactions associated with transfusion,
• of serious adverse reactions associated with blood donation,
• of serious adverse events,
• of post-donation information,
- to analyse the evolution over time of the frequency of events over the period from 2000 to 2009 (overall and per diagnosis),
- to pinpoint the issues requiring further analysis.

It is important to underline that the data compiled in this report reflects:

- declarations submitted by the haemovigilance correspondents (HVCs) at the healthcare facilities (HFs) and blood establishments (BE) to Afssaps.
- the data from the activity reports issued by the regional haemovigilance coordinators
- and the transfusion monitoring and activity databases introduced by Afssaps in 1999.

The information provided is as complete as possible and is relatively detailed. This very large database, which is based on multiple sources, cannot be entirely faultless due to the difficulty in obtaining and the time required to obtain certain information as well as the existence of possible – though rare – errors in the declarations[1], irreducible variability between declarants or between regions, etc. The year-on-year variability in the overall adverse event (AE) figure in relation to their severity or imputability reflects the work in analysing and, if necessary, recovering these notions carried out by the task forces. These differences, which only have a strictly minimal affect on the data presented in this report, must nonetheless be taken into account in order to interpret certain of the results presented.

[1] Examples: declaration of a dysfunction without transfusion as an RAR of grade 0, in the event of transfusion and incompatible LBPs (chapter 2.2)...

SPEECH BY MR. JEAN MARIMBERT, DIRECTOR GENERAL OF AFSSAPS
(Summary of the meeting of the French National Haemovigilance Commission held on 4 December 2009)

The Director General wishes to address the French National Haemovigilance Commission (NHC) for two reasons: firstly, this is the last meeting of the 2007/2010 term of office and, secondly, the Commission must be informed of the discussions held by the Agency following the tragic event which occurred in Lyon, where a female blood donor died following plasmaphaeresis.

The work carried out by the Commission must be put into perspective with the development of haemovigilance. A number of salient points arose between 2007 and 2009, including the following, non-exhaustive list:

● The progress made regarding the regulatory framework for haemovigilance, resulting in the publication of the Decisions by the Director General of Afssaps on the declaration of adverse reactions affecting recipients and donors and serious adverse events;
● The works by the NHVC, which have been structured and extended. In spite of 6 plenary meetings, the need to work in smaller, specialised groups led to the wide-scale growth of work in numerous groups (TF), which resulted in the drawing up of methodologies (as is clearly necessary in newly-introduced systems), case analyses, case groups (clusters) and systemic effects;
● The organisation of the network, which increased, in particular through meetings with the regional haemovigilance coordinators (RHC), as haemovigilance can only exist as a network featuring multiple participants and levels;
● Feedback on the e-FIT adverse effect or event declaration system, allowing its upgrading and the introduction of e-FIT V2, a tool to help improve case descriptions and therefore data processing;
● The regional traceability computerisation projects, under the aegis of the French National Labile Blood Product Traceability Computerisation Committee (CNIT), which aim to improve both electronic connections between healthcare facilities (HFs) and blood establishments (BE) and exchanges of traceability data;
● The international promotion of the activities of the French haemovigilance network, which particularly resulted in the drawing up of annual reports for the European Commission, and particularly contributed to better highlighting the important distinction between operational responsibilities for transfusions and the regulation of the public transfusion service by assessment, inspection and monitoring bodies;
● The processing of the underlying cases required collaboration between Afssaps, the NHC and the RHCs.

The issue of methylene blue virus-inactivated plasma (VIP-MB) has concerned us for more than a year; the Director General monitors week-on-week the development of declarations of cases of serious allergic reactions, which he reports to the RSS (Reunion de Sécurité Sanitaire = Health & Safety Committee); supplies of solvent-detergent virus-inactivated plasma (VIP-SD) shall be restricted for longer than hoped following the work carried out on the EFS production site in Bordeaux and the difficulties pinpointed following this work lead us to suspect that there will be a few more months of imbalance in the production of the different plasmas, whereas the incidence of serious allergic reactions appeared 3 to 4 times higher with VIP-MB than with the other plasmas, upon initial assessment, prior to the in-depth imputability assessments that were introduced by the agency from spring 2009 in accordance with the NHC. VIP-SD production therefore needs to return to its previous level as quickly as possible. The increase in the production of plasma treated with Amotosalen only involves a few BE and cannot offer a comprehensive substitution solution in the short-term. The Director General therefore agrees that the NHC shall continue its work on the imputability of the declared cases of serious allergic reactions to VIP-MB, even if the existence of the joint administration of other LBPs can complicate the analysis. In this same context, in case of supply chain difficulties, the Director General informed the Chair of the EFS of the opinion of the competent TFs (LBP evaluation and TRALI/TACO) on the EFS's decision to accept donations from non-nulligravida female donors, having been pregnant no more than 2 times, in order to prepare virus-

inactivated plasma in case of plasma supply chain issues.

The second issue relates to the discussions held and measures taken by the Agency following the event that occurred in Lyon. The Director General, like the entire blood transfusion community, was deeply shocked by this event; all those involved feel that it is unacceptable for a perfectly healthy, young female donor to die following plasmaphaeresis. The different enquiries that were launched (haemovigilance enquiry, judicial enquiry, IGAS (Inspection Générale des Affaires Sociales = General Inspectorate for Social Affairs) administrative enquiry) were intended to minimise insofar as possible the risk of similar events occurring in the future. Accordingly, the internal measures taken by EFS should be applauded. Afssaps also took internal measures with this objective in mind. As no plenary meeting was scheduled in the very short term, the Director General requested that an ad hoc meeting with the chairs of the NHC and the relevant TFs be held to debrief this event; he attentively read these experts' analysis, which was one of the two raw materials used to draw up Afssaps' action plan, with interdepartmental cooperation and the key issues already pinpointed during discussions with the IGAS team. 5 areas for action were therefore defined:

● Reinforcing and homogenising EFS's capacity to manage serious events affecting blood donors. The medical management was different in Rennes and in Lyon (i.e. approach). Internal procedures must be homogenised: emergency kit, drugs available, donor informed in advance; the decision to inject calcium must be taken quickly in case of doubt.
● Promoting the implementation of measures to increase the safety of the medical devices used during plasmaphaeresis. On 19 November, Afssaps organised a meeting with both equipment and solution manufacturers. Certain possibilities were ruled out and others retained, such as increasing the safety of the different types of connections and taking additional measures regarding tube colouring. Finally, the classification of these instruments shall be reviewed, as, according to the MEDDEV guide, if a medical instrument is designed to be used at the same time as the administration of a drug, as is the case for plasma separators, the medical instrument must be listed in class III.
● Revising the procedure for declaring serious adverse reactions affecting blood donors (DSAR). The initial calibration, taking into account the fact that the instrument did not exist beforehand and that the culture of donor risk was not widespread, produced both results and a substantial flow of declarations.

However, with hindsight, this calibration undoubtedly placed the bar too high and it should be lowered to a reasonable extent. For DSARs and serious adverse events (SAE), a declaration must be submitted even if the event was dealt with correctly and successfully by the BE team, in order to learn lessons from the event outside the site where it occurred; events that are correctly managed must be entered into the declaration system. The notion of death must also explicitly feature on the declaration form; EFS's reticence in 2007 and the lack of recollection of a donor death had convinced the Director General to accept the absence of this item, but the same choice cannot be made in the current context. The decisions regarding the declaration of DSARs and SAEs shall therefore be reviewed accordingly.

● Updating and adding to Afssaps' internal procedures for the exchange of information on DSARs and SAEs. This procedure already existed and was adapted to determine the level of response according to the type of report received. Once a certain level of severity (e.g. donor suffers a life-threatening heart attack) is reached, the internal sharing of information within the Agency is compulsory (ad hoc meeting); however, the information must also be shared with all the RHCs in order to enable them to detect systemic effects more quickly. In the case of the precursory event in Rennes, the declaration was submitted to Afssaps immediately, the local participants and EFS head-office cooperated correctly, the local decision-making process was effective, but, regarding the pinpointing of the systemic issues liable to have an impact on a national scale, the analysis shows that there is room for improving how we work. Clearly, it is the duty of the NHC Root Cause Analysis TF (RCA TF) to analyse the reports and pinpoint the root causes.
However, upstream, Afssaps is responsible for immediate health & safety decision-making in the

case of urgent reports. How the roles are shared out is clearly defined: urgent management by Afssaps, less short-term assessment of the systemic issues by the Commission's task forces, with a view to submitting proposals for risk management measures to the Director General of Afssaps.
● Increasing the flow of information between the central body (Afssaps) and the regional bodies (RHCs) in order to better pinpoint the systemic issues based on the individual cases that are correctly declared and managed on a local basis.

In conclusion, it is important for each participant to learn lessons from these events, based on joint analysis with the other participants, and for them all to reach agreement on the necessary follow-up measures and their order of importance.

Reciprocal interaction between haemovigilance, materiovigilance, inspection and monitoring of LBPs must be improved, but must not lead to them being mixed up, as each activity has its own characteristics: haemovigilance is different from both inspection and materiovigilance. The central bodies (Afssaps, EFS) must interact with the regional bodies, whose organisation is currently being modified (introduction of the ARS – Agences Régionales de Santé = Regional Health Agencies). This consolidation work must begin without delay, with deadlines that are realistic but as short as possible. In order to avoid any risk of impact on donations, this type of accident must not be repeated, all the more so as the consumption of LBPs is increasing and will undoubtedly increase further in the future. It is therefore essential to maintain a high level of confidence in the donation process.

1. Introduction

1.1. News in 2009

2009 was principally marked by:

● The occurrence of a donor serious adverse effect (DSAR) during plasmaphaeresis that resulted in the death of a female donor. The measures immediately put in place and those envisaged in the short- and medium-term have been analysed; the enquiry is still in progress.
In any case, Afssaps decided to urgently put in place an electronic declaration system, including the declaration of SAEs and DSARs, which were previously only declared on paper: e-FIT V2 beta[2] (March 2010). This system shall offer the haemovigilance network the possibility of immediate responsiveness, via the simultaneous communication of information to all the participants. The introduction of a system similar to the configuration of the current declaration for recipient adverse reactions (RAR) was also scheduled for 2011 with e-FIT V3.

● The publication of 9 decisions by the director general, including 6 relating to the task forces and their missions: these task forces have been operational since 2008 and report to the National Haemovigilance Committee (NHC).

● The drawing up by the "Allergy" task force of a procedure for the examination of serious allergic reactions (grades 3 and 4) during transfusions involving VIP-MB (05/06/09) and warning on the issues regarding:
- The examination of patients according to a protocol drawn up by the task force
- Recommendations for transfusion-related care
- A proposal submitted to the RHCs for a common aetiological enquiry procedure
These documents are available on the Afssaps website: http://www.afssaps.fr

● The introduction in the 4th quarter of 2009 of the "test" platform for the new e-FIT V2 application. e-FIT V2 is intended to include the modifications requested:
- By the haemovigilance network since 2004 (since the introduction of e-FIT V1)
- By the NHVN / e-FIT task forces
- By the Afssaps haemovigilance unit
Its roll-out to the entire network is scheduled for the 1st quarter of 2010.

● As a result of the influenza A pandemic[3], EFS, with approval from DGS, decided, as a precautionary measure, to move forward to 30 April 2009 the date of the measures for the exclusion of the donation of blood by donors having returned from North America less than 28 days previously (as for the prevention of the transmission of the West Nile virus). This measure was repealed on 28/1/2010.

[2] e-FIT is the name of the computer application used for the electronic declaration and inputting into the national haemovigilance database of recipient adverse reactions.
[3] See chapter 3.2.3, type A (H1N1) RAR declaration

1.2. The new texts published in 2009

1.2.1. The principal European texts

● European Commission Directive 2009/135/EC dated 3 November 2009 allowing temporary derogations to certain admissibility criteria for whole blood and blood components donors laid down in Annex III to Directive 2004/33/EC in the context of a risk of shortage caused by the Influenza A (H1N1) pandemic.

1.2.2. The principal national texts

ORDERS
● Order dated 12 January 2009 setting the selection criteria for blood donors

● Order dated 15 July 2009 modifying the order dated 3 December 2007 relating to the qualifications of certain hospital blood bank staff (articles R1221-20-1 and R1222-23)

● Order dated 24 December 2009 setting the form and content of the annual activity report by blood establishments provided for in article R1223-8 of the French Public Health Code

● Order dated 31 December 2009 allowing temporary derogations to the selection criteria for blood donors in the context of a risk of shortage caused by the Influenza A (H1N1) pandemic

DECREES
Decree n° 2009-802 dated 24 June 2009 relating to blood establishments and modifying articles D1221-D and D1223-23 of the French Public Health Code
In particular: "f) The detection of anti-malarial antibodies in donors having stayed in an endemic zone under the conditions set in the order provided for in article R1221-5. "

DECISIONS by the Director General of Afssaps, listed in chronological order

1. Decision dated 16 February 2009 modifying the decision dated 28 February 2006 setting the form and content of the questionnaire filled in by blood donation candidates in accordance with article R1221-5 of the French Public Health Code (including corrections)

2. Decision dated 5 June 2009 modifying the order dated 29 April 2003, modified, setting the list and characteristics of labile blood products

3. Decision n° 2009-122 dated 17 July 2009 creating the French Health Products Safety Agency's Allergy task force

4. Decision n° 2009-123 dated 17 July 2009 creating the French Health Products Safety Agency's root cause analysis task force

5. Decision n° 2009-124 dated 17 July 2009 creating the French Health Products Safety Agency's National Haemovigilance Network task force

6. Decision n° 2009-125 dated 17 July 2009 creating the French Health Products Safety Agency's TRALI and TACO task force

7. Decision n° 2009-126 dated 20 July 2009 creating the French Health Products Safety Agency's Transfusion-Transmitted Bacterial Infection validation task force

8. Decision dated 24 July 2009 relating to good manufacturing practice

9. Decision n° 2009-180 dated 29 July 2009 appointing the French Health Products Safety Agency to the National Haemovigilance Network task force

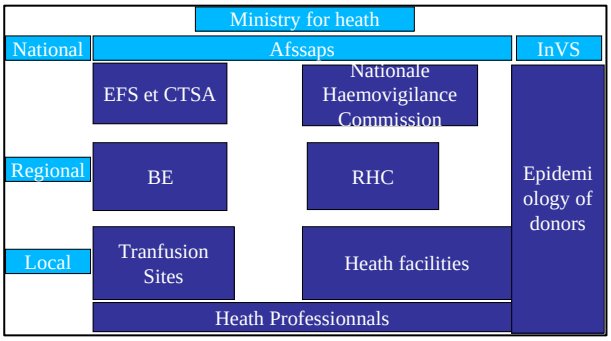
The principal national and European texts on haemovigilance published before 2009 are available on the Afssaps' website at the following address: http://www.afssaps.fr

1.3. Organisation of haemovigilance

The organisation of haemovigilance in 2009 did not change from the way it was organised in 2008, meaning that this chapter includes the same main descriptions as the report from last year, updated with recent figures.

According to Decree n° 2006-99 dated 1 February 2006 relating to the Etablissement Français du Sang and haemovigilance and modifying the French Public Health Code (Art. R1221-24.), the national haemovigilance system consists of[4]:
- the French Health Products Safety Agency (Afssaps);
- the National Haemovigilance Commission (NHC);
- the regional haemovigilance coordinators (RHC) mentioned in article R1221-32;
- the EFS (Etablissement Français du Sang = French Blood Transfusion Organisation) and the CTSA Centre de Transfusion Sanguine des Armées = Armed Forces Blood Transfusion Centre);
- the InVS (Institut de Veille Sanitaire = Health Monitoring Institute);
- the healthcare facilities (HF) and armed forces hospitals (haemovigilance correspondents (HVC), transfusion safety and haemovigilance committees (CSTH) or facility medical commission sub-commissions);
- all health professionals.

Diagram 1. The 3 oragnisational levels of haemovigilance



In 2009, the haemovigilance network consisted of:
- 1,501 haemovigilance correspondents (HVCs)[5] and 1,525 transfusing healthcare facilities[6],
- 18 referring haemovigilance correspondents from the BEs and 140 BE-certified staff on the distribution sites (site correspondents), 3 members of the Vigilance section of the EFS and 1 member of the haemovigilance unit of the CTSA,
- 29 Regional Haemovigilance Coordinators (RHCs),
- the InVS for blood donor epidemiology,
- the Afssaps haemovigilance unit (5 members).

[4] See "The regulatory roles of each participant" on the Afssaps website at the following address: www.afssaps.fr.
[5] More than 300 haemovigilance correspondents were also listed for healthcare facilities that performed no transfusions in 2009.
[6] Transfusing healthcare facility = facility having performed at least one LBP transfusion in 2009, incomplete data

1.4. The process

1.4.1. Reporting

Any healthcare professional who observes or becomes aware of an adverse effect or a serious incident must report it, without delay and no more than 8 hours later, to the HF and/or BE haemovigilance correspondent.

1.4.2. Declaration

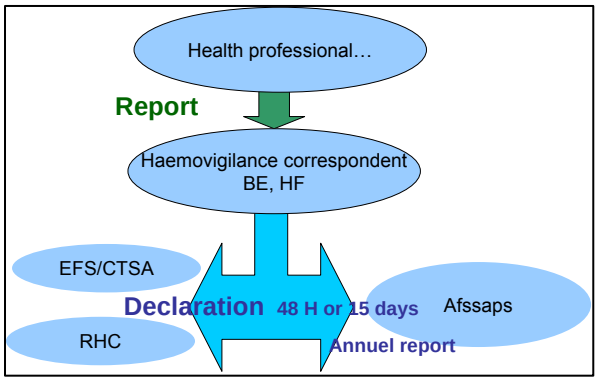
Haemovigilance initially focused on adverse reactions affecting LBP recipients[7]. Its scope has been extended over the years, particularly following the transposition of the European directives, to adverse reactions affecting donors (DSAR)[8], post-donation information (PDI) and finally to the highly important upstream field of pre-transfusion safety (SAE)[9].
While all adverse reactions affecting LBP recipients must be declared, irrespective of their severity, only serious adverse events affecting blood donors and serious adverse events need to be reported. The definitions and degrees of severity are provided in the annexes.
The donor and recipient adverse reaction declaration forms, as well as the serious adverse events forms, must be sent simultaneously to Afssaps and the RHC. EFS and CTSA are each sent the declaration forms for the events relevant to them.

1.4.3. Declaration deadlines

1.) Serious adverse events

1.a) Serious adverse events (SAE):
Reporting procedures: immediately and no more than eight hours later
Declaration procedures:
- The relevant HVC(s) can declare the SAE either via an immediate declaration using the serious incident form (SAEF) or via a differed declaration in the annual report of SAEs that occurred in their facilities. The choice of the method of declaration for each SAE is made by the HVC who carried out the necessary investigations and examinations, according to the criteria concerning the fate of the LBP, the stage of the process, any repetition and the existence, or not, of a warning system:
- Declaration deadline: maximum of fifteen days in which to transmit the declaration form. However, if the incident is liable to have an impact on transfusion safety or the LBP supply chain, in every case where a SAE should be made public, or whenever the HVC deems it necessary, the declaration is submitted as soon as possible and no more than 48 working hours after the occurrence of the incident.

Diagram 2. Reporting and declaration of serious adverse events



[7] Decision by the Director General of Afssaps dated 5 January 2007 setting the form, content and procedure for the transmission of forms for the declaration of serious adverse reactions affecting labile blood product recipients.
[8] Decision by the Director General of Afssaps dated 7 May 2007 setting the form, content and procedure for the transmission of forms for the declaration of serious adverse reactions affecting donors.
[9] Decision by the Director General of Afssaps dated 7 May 2007 setting the form, content and procedure for the transmission of forms declaring serious adverse events

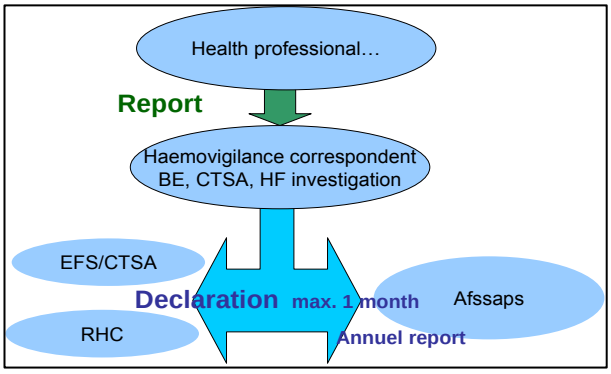
1.b) Post-donation information (PDI):

The declaration of certain donor-related information obtained after donation (PDI) is not regulated and is covered by an agreement between Afssaps, EFS and CTSA. The recommended deadline varies from 48 hrs to 15 days after obtaining the information. The declaration to Afssaps is only submitted if the LBPs from the donations in question have left the BE.

2.) Donor serious adverse event (DSAR)

Reporting procedures: immediately and no more than eight hours afterwards
Declaration procedures: maximum of one month to round off the investigations and submit the declaration form. The declaration is submitted immediately when the HVC from the BE deems it necessary or in certain cases provided for in the regulations.
A report on all the serious adverse reactions affecting blood donors is drawn up on an annual basis and appended to the BE's annual activity report

Diagram 3. Reporting and declaration of donor serious adverse events

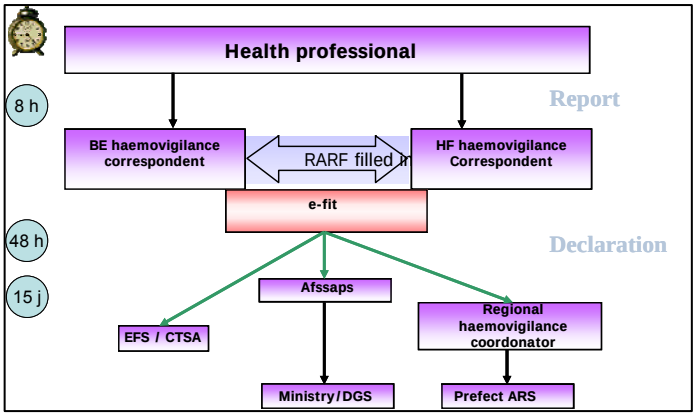


3.) Recipient adverse reaction (RAR)
Recipient adverse event (RAE)

Diagram 4. Declaration of recipient adverse effects

Reporting procedures: immediately and no more than eight hours afterwards

Declaration procedures: 15 days in which to enter the declaration into the e-FIT application.



The 15-day deadline is reduced to 48 hours when the form is said to be “reported”, i.e. in the following cases: adverse effects likely to endanger the safety of at least one other recipient, irrespective of the grade
grade 2, 3 or 4 adverse effects excluding grade 2 adverse events with the appearance of irregular anti-erythrocyte antibodies,
suspected bacterial incidents, irrespective of the grade;
ABO incompatibility, irrespective of the grade

1.4.4. Traceability

In accordance with the French Public Health Code, BE and HFs are required to compile, file and exchange information concerning the issue of LBPs, enabling their traceability from donor to recipient.

The respect of donor anonymity, under the responsibility of the BE, as well as medical secrecy concerning the recipient, are guaranteed.
The traceability data is reported for each transfusing HF in the annual RHC activity report. Afssaps compiles this data in a national database.

1.4.5. Annual report

Every year, Afssaps draws up a summary report regarding all the declarations for the events that occurred over the year in question. This document also contains an analysis of the trends regarding the evolution (since 2000) of the principal indicators featured in the report. This makes it possible, if required, to review the data from previous reports in order to take into account information obtained after they were written. This report is for the year 2009.

2. 2009 data

2.1. Methodological reminder

2.1.1. Data sources

Afssaps is responsible for the compilation of the haemovigilance data. To do so, it starts by using the HVC declarations on electronic media (e-FIT for RARs) or not (for SAEs, DSARs and PDIs), and then uses the RHC activity reports. It also uses the CSTH reports.
In total, the data taken into account in this report is taken from several sources:
- RARs: declarations submitted by HVCs, HFs and BE via the "e-FIT" database[10]
- DSARs: HVC BE declarations
- SAEs: HVC, HF and BE declarations
- PDIs: HVC BE declarations
- National transfusion activity data: EFS and CTSA (number of LBPs distributed (i.e. billed), donations and donors)
- Regional transfusion activity data: RHC (number of LBPs distributed, issued, transfused, destroyed, traced, number of sites and their activities in terms of collection, preparation and distribution). The RHC report is prepared using the data provided by the HF and BE haemovigilance correspondents. The data certified by the HF may differ from the BE data, especially due to the absence of any link in the HFs between the LBPs billed and the type of LBPs transfused. Furthermore, certain data concerning the HFs are sometimes obtained from the BE.

Warning:
•As was the case last year, the regional data was grouped by inter-region in order to obtain sufficiently large sample sizes for the statistical comparisons (see annex 8.3).
• For data that may be obtained from several sources, differences, which are most often minimal, may appear, depending on the source used.
• Regarding the exhaustive nature of the data, two types of difficulties were principally pinpointed:
1) missing data, when the requested items were never filled in,
2) incomplete data, when information or figures is/are partially provided.
• All the databases were frozen on 28 February 2010.

Furthermore, concerning the "transfused patients" data, this should be considered with caution due to the existence of multiple entries and missing data. The 2009 annual report by the RHC Conference, covering 26 regions, calculated the margin of error to be approximately 5% for the declared data.

Finally, as for the 2008 report, the 2009 report includes data that makes it possible to establish the distribution of recipients and donors per sex and per age group. For certain regions, the information provided remains incomplete and non-homogeneous. An estimate of the missing or incomplete figures was calculated under these conditions, taking into account the characteristics of the regions for which the information existed (standardisation method). This estimate applied to approximately 7% of all patients and 3% of donors.

[10] See indicator regarding the use of the e-FIT tool by the HF and BE HVCs: annex 8.1

2.1.2. Validation of the data

The RAR form data validation system in 2009 remained the same as the system from 2007-2008, meaning that this chapter is almost identical to that described in the previous report.

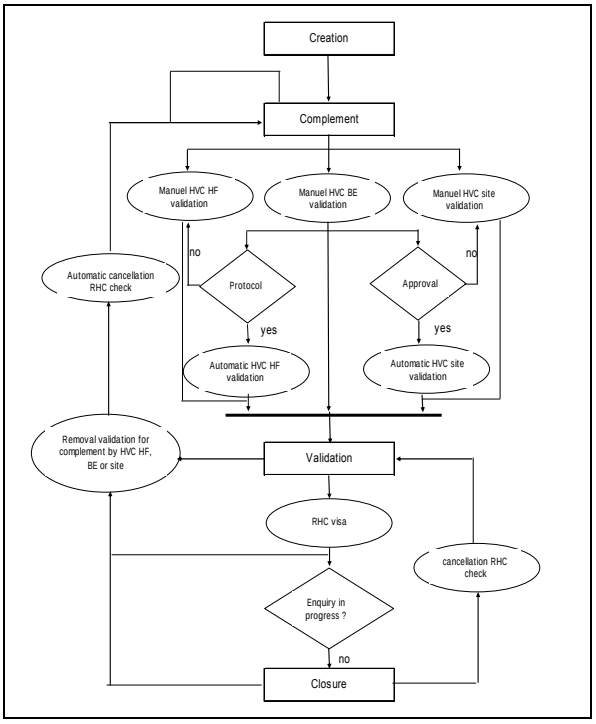
1. RAR declaration via e-FIT
The HVCs have access, on the e-FIT on-line declaration site, to automatic processing of a certain number of incoherencies (in particular, the existence of multiple entries, date and choice of diagnosis incoherencies, etc.) and a guide for filling in the RAR form.
Each form must be checked by both the relevant haemovigilance correspondents (HF and BE HVCs), irrespective of who created it. The form is referred to as "validated" if both HVCs consider that it is coherent and its data is reliable. If applicable, a completed standard questionnaire (e.g.: ABO, TTBI, TRALI questionnaire) or any useful documents (copies of operative records, diagrams, in-house investigation results, etc.) may be appended 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 signing the form and certifying the quality of the data it contains.
It is important to highlight that the fact that a declaration form has been validated by the HVCs, or even approved by the RHC, does not mean that the enquiry on the declared event has been closed. In theory, any form may be modified if new information subsequently becomes available.

Table 1. The different RARF statuses according to their progress in the "e-FIT" process

Form status	Description of the status
Initial entry	When the RARF form has been entered and saved
Modification in progress	When one of the correspondents has saved a modification to one of the RARF items
Individual validation	When the RARF has been validated by one or both correspondents
Validated	When the RARF has been validated by all three correspondents: HF, blood site and BE
Checked	When the RARF has been checked by the RHC
Approved	When the RARF has been approved by the RHC
Invalidated, modification in progress	When one of the correspondents has invalidated the RARF in order to make modifications.
Closed	Closure is an automatic process, which occurs on a differed basis (per batch) once the RARF has been validated and checked and the enquiry is no longer ongoing. At this stage of the process, the information on the RARF may be considered as stable.

The follow-up of the forms, performed on a daily basis by the Afssaps haemovigilance unit also contributes to improving data quality. Certain forms, especially the so-called "reported" forms, receive special follow-up.
The monitoring of certain diagnoses (TTBI, TRALI, TACO, allergies, etc.) is performed by ad-hoc task forces.

Diagram 5. Logical diagram of the saving of RARs in e-FIT from creation to closure



2. Paper declaration (SAEF, PDI, DSARF)
These declarations, as well as any related documents, are sent to the Afssaps Haemovigilance unit (fax, post, e-mail, etc.), whose contact details are available on the Agency's web site (www.afssaps.sante.fr).

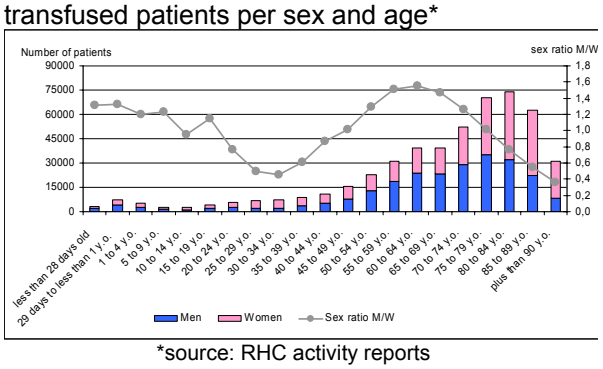
2.2. Transfusion activity: general data

2.2.1. Number of patients transfused

In 2009, the number of transfused patients was estimated[11] to be 538,506: 52% were women, 48% men.
82% of the transfused patients were more than 55 years old and 66% were more than 65 years old (figure 1).

11 *see chapter 2.1.

Figure 1. Distribution of the number of transfused patients per sex and age*



*source: RHC activity reports

Table 2. Ratio of transfused patients per age group and sex *

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

* Number of patients per 1,000 inhabitants

The ratio of transfused patients was 8.3 per 1,000 inhabitants; this ratio varied greatly according to age, as shown in table 2. Except for the DOM-TOMs, the ratio of transfused patients differed little from region to region (table 4). Every patient received an average of 5.5 LBPs but this figure varied from inter-region to inter-region (7 for the Ile-de-France, 4 for the North West: table 4).

Table 3. Ratio of transfused patients and number of transfused inhabitants in the 6 inter-regions

	Inhabitants in thousands and % (1)	Transfused patients and % (2)
South West	8,532 (13,3%)	77,894 (14,5%)
South East	15,341 (23,9%)	130,535 (24,2%)
North West	12,538 (19,5%)	104,394 (19,4%)
North East	14,305 (22,2%)	121,731 (22,6%)
Ile-de-France	11,764 (18,3%)	92,454 (17,2%)
DOM-TOM	1,841 (2,9%)	11,515 (2,1%)
Total	64,321 (100%)	538,526 (100%)

Source (1) INSEE – provisional results up to the end of 2009, (2) RHC activity report

Table 4. Ratio of patients transfused per 1,000 inhabitants and average number of LBPs per transfused patient

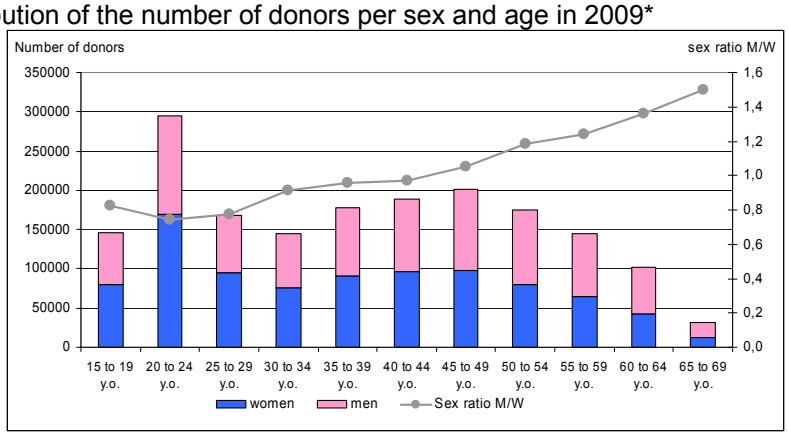
	Number of transfused patients per 1,000 inhabitants	Number of LBPs per transfused patient
South West	8.5	6.4
South East	7.9	5.9
North West	7.8	4.3
North East	7.9	6.0
Ile-de-France	7.3	6.9
DOM-TOM	5.8	5.7
Standard deviation excl. DOM-TOM	0.43	0.99

2.2.2. Number of donors and donations

The number of donors[12] rose to 1,773,374 in 2009. They constituted 4.1% of the population between 18 and 69 years old. The donors were equally spread over both sexes. The sex ratio was 1 but varied greatly according to age, as shown in figure 2. 34% of donors were less than 30 years old. These donors provided 3,071,238 samples, i.e. 1.7 donations per donor. Samples of whole blood constituted 81% of donations, the remaining 19% being aphaeresis.

[12] see chapter 2.1, total number of donors – declared in the RHC Activity Reports was 1,773,374 and 1,741,633 in the EFS and CTSA Activity Report (provisional data – start of June 2010)

Figure 2. – Distribution of the number of donors per sex and age in 2009*



*source: RHC activity reports

2.2.3. Release/issue[13] of labile blood products (LBPs)

● Distribution/issue: all products

In 2009, 2,979,117 LBPs were distributed, 79% red blood cells (RBC), 9% platelets and 12% plasmas (table 7). Homologous products constituted the vast majority of this number (table 5). The figure given for autologous LBPs was the number of samples taken in the event of a scheduled autologous transfusion package (including autologous red blood cells and fresh frozen plasma)

The number of LBPs distributed per 1,000 inhabitants was 46 and was homogenous over the entire territory, excluding the DOM-TOMs (table 6). It should be noted that this figure was 56 in the European Community (23 countries declaring to the SARE), i.e. a figure 10 units higher than in France (see chapter 8.1)

Table 5. Homologous and autologous LBPs

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

* Source: EFS and CTSA ** package

Table 6. Issue of LBPs in 2009 per inter-region

Type of LBP*	Total number of LBPs (%)	Number of LBP per 1,000 inhabitants
South West	415,476 (14%)	49
South East	694,688 (23,4%)	45
North West	544,568 (18,3%)	43
North East	676,756 (22,8%)	47
Ile-de-France	577,331 (19,4%)	49
DOM-TOM	60,386 (2%)	33
Total	2,969,205 (100%)	46
Standard deviation excl. DOM-TOM		2.38

* Source RHC activity report

Table 7. Issue of LBPs in 2009 per type of product

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

* Source: EFS and CTSA ** package

[13] see chapter 2.1: there was still a difference in the total number of LBPs declared nationally and regionally (tables 5 and 6), the national data comes from the distribution/billing files for the EFS, while the RHC data comes from the BE distribution files (LBPs distributed – LBPs returned).

● Product destruction

- The number of homologous LBPs destroyed was 44,940, i.e. a rate of destruction of 1.5%.

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

2.2.4. LBPs transiting through Hospital Blood Bank (HBB)

Twenty-two of the 26 regions were able to provide data on the activity of the HBBs in 2009 (the data for Brittany, Centre, Corsica and the Ile-de-France was missing). For these regions, 636,151 LBPs transited through the banks, i.e. 31% of all the distributed LBPs. Of these LBPs, 251,843 were dispensed[14] by banks (table 8).

Table 8. Distribution of the number of LBPs dispensed by HBBs according to their type* in 2009

	Nbr of LBPs dispensed by HHBs	%	Nbr of HHBs	%
Issue HHBs	223,720	88.8%	180	26.9%
Relay HHBs	378	0.2%	30	4.5%
Vital emergency HHBs	7,096	2.8%	177	26.5%
Vital emergency + relay HHBs	20,649	8.2%	281	42.1%
Total	251,843	100.0%	668	100.0%

* definition of the different types of banks in annex 8.3

2.2.5. LBPs traceability

The average national traceability rate in 2009 was 99.2% and exceeded 94% in every region (figure 3).
Computerised procedures were used for the traceability process for only 29% of LBPs[15], essentially from three inter-regions. The electronic exchanges of traceability data between the HFs and the BE complied with the AFNOR NF S97-530, NF S97-531, NF S97-532 and XP S97-536 norms (figure 4).

Figure 3. Product traceability in 2009

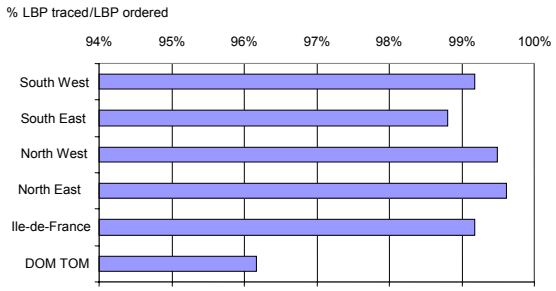
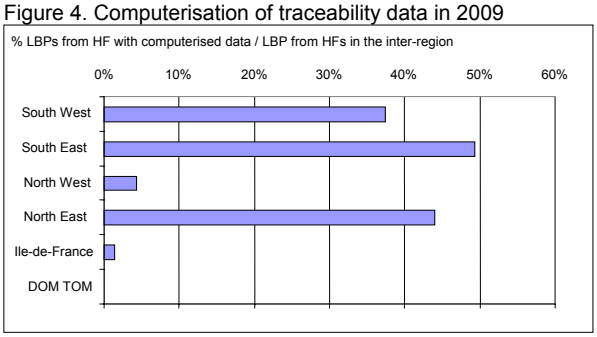


Figure 4. Computerisation of traceability data in 2009



[14] Number of LBP allocated and issued by the banks. By definition, LBPs transiting through banks = LBPs allocated and issued + LBPs returned + LBPs re-issued + LBPs destroyed
[15] i.e. 818,211 LBPs for 147 HF in 13 regions

2.3. Recipient adverse reaction (RAR)

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

2.3.1. The number of declarations and their frequency

In 2009, the number of RAR declarations, including all grades, levels of imputability and enquiries, stood at 7,808, i.e. a frequency of 2.6 per 1,000 distributed LBPs (table 9).

Nearly 48.3% were of high imputability (imputability 3 = likely, imputability 4 = certain), 30.3% of possible imputability (imputability 2) and 21.4% of excluded or doubtful imputability (0 and 1).
As regards severity, 70% were of grade 1, 24.2% grade 2, 5.1% grade 3 and 0.4% grade 4 (death). For the 32 deaths, the responsibility of the transfusion was excluded (imputability 0) or deemed doubtful (imputability 1) after enquiry in 20 of the cases (63%); for 4 deaths, the imputability to the transfusion was likely or certain.

- RAR declarations – all LBPs

Table 9. Distribution of 7,808 RARs declared in 2009 per grade and imputability, irrespective of the level of enquiry

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

* definition of the levels of imputability according to e-FIT V1: with e-FIT V2 the definition shall be different but match the international scale (see chapter 8.3)

- RAR declarations with autologous LBPs

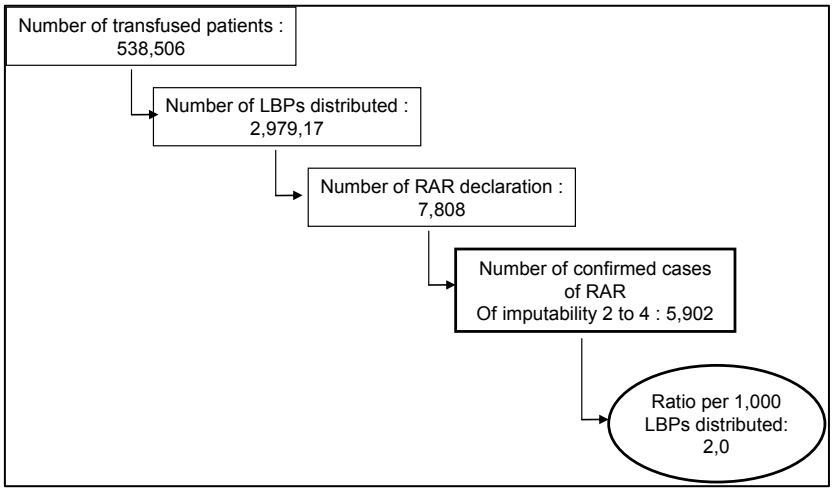
Two RARs relating to the transfusion of autologous RBC were reported in 2009, with the following diagnoses: one bacterial infection of grade 1 and imputability 0 (and enquiry closed), one FNHTR of grade 1 and imputability 3 (and enquiry closed). This case is presumably an error as the RBC involved was autologous but the transfusion was declared to be homologous[16].

2.3.2. Confirmed[17] cases of imputability 2 to 4

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

[16] See number of autologous LBP transfused in chapter 2.2.3
[17] An RAR is considered as a confirmed case when the form includes the words "enquiry closed"

Diagram 6 – Confirmed RARs: imputability 2 to 4



2.3.2.1. Analysis per diagnostic category

● Per diagnosis and level of imputability

As for the previous years, 2009 (table 10) saw variable levels of imputability per diagnosis: 87% of cases of imputability 4 involved appearances of irregular antibodies, 34% of cases of imputability 3 allergies and 45% of cases of imputability FNHTR.

Table 10. Distribution per diagnosis of adverse events of imputability 2 to 4 in 2009

Diagnoses	Imputability score, N (%)			Total
	Imputability 2	Imputability 3	Imputability 4	
appearance of irregular antibodies	114 (5.1%)	632 (25.5%)	1,054 (87.1%)	1,800 (30.5%)
FNHTR	1,000 (45.1%)	506 (20.4%)	2 (0.2%)	1,508 (25.6%)
allergy	464 (20,9%)	847 (34.2%)	51 (4.2%)	1,362 (23.1%)
immunological incompatibility	82 (3.7%)	182 (7.4%)	52 (4.3%)	316 (5.4%)
including ABO with RBC	3 (0.1%)	2 (0.1%)	6 (0.5%)	11 (0.2%)
TACO	83 (3.7%)	161 (6.5%)	23 (1.9%)	267 (4.5%)
TRALI	13 (0.6%)	15 (0.6%)	14 (1.2%)	42 (0.7%)
bacterial infection [18]	4 (0.2%)	2 (0.1%)	4 (0.3%)	10 (0.2%)
viral infection		2 (0.1%)	1 (0.1%)	3 (0.1%)
other (immediate or delayed effects)	32 (1.4%)	27 (1.1%)	7 (0.6%)	66 (1.1%)
unknown [19]	424 (19.1%)	102 (4.1%)	2 (0.2%)	528 (8.9%)
Total	2 216 (100%)	2 476 (100%)	1,210 (100%)	5,902 (100%)

● Distribution per immediate and delayed diagnosis:

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

* 1,508 febrile non-haemolytic transfusion reactions (FNHTR), i.e. 25.6% of all RARs

[18] RARF item refers to clinical and/or biological symptoms suggesting – or arousing suspicion – that the recipient had a bacterial infection liable to be linked to the transfusion procedure and therefore to the transfused LBP(s).

[19] Definition of an RAR of unknown diagnosis according to the user guide: RAR for which all the tests performed gave negative results; RAR with insufficient detail, tests performed not enabling conclusion or RAR for which it is not possible to decide between several possible diagnoses.

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

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

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

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

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

● Per diagnosis and per inter-region

For the principal diagnoses, there was relative heterogeneity in the declarations per inter-region for TRALI, immunological incompatibilities and febrile non-haemolytic transfusion reactions (table 11).

Table 11. Number of diagnoses per 10,000 LBPs distributed per inter-region of imputability 2 to 4 that occurred in 2009

	Total	Inter-region						Total	
Diagnoses	Nbr of RARs	Ile-de-France	North East	North West	South East	South West	DOM-TOM	Average	Standard deviation
appearance of irregular antibodies	1,800	5.11	7.55	5.03	7.36	4.65	2.65	6.06	1.40
febrile non-haemolytic transfusion reaction	1,508	2.41	3.77	5.56	7.60	6.28	3.64	5.08	2.05
allergy	1,362	5.35	5.25	4.26	3.53	5.10	1.49	4.59	0.78
Immunological incompatibility*	316	0.50	0.87	1.82	1.22	1.03	0.17	1.06	0.49
* including ABO	11	0.00	0.01	0.09	0.06	0.02	0.00	0.04	0.04
TACO	267	0.81	0.92	0.99	1.02	0.70	0.66	0.90	0.13
TRALI	42	0.16	0.10	0.31	0.12	0.02	0.00	0.14	0.11
bacterial infection	10	0.03	0.01	0.02	0.01	0.12	0.00	0.03	0.05
viral infection	3	0.02	0.00	0.00	0.03	0.00	0.00	0.01	0.01
purpura	2	0.00	0.00	0.02	0.01	0.00	0.00	0.01	0.01
haemosiderosis	1	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.01
other (immediate and delayed effects)	63	0.31	0.16	0.09	0.09	0.51	0.33	0.21	0.18
unknown	528	1.07	1.89	2.24	2.00	1.76	0.66	1.78	0.44
Total	5,902	15.80	20.52	20.35	22.99	20.17	9.60	19.88	2.60

(1) Standard deviation excl. DOM-TOM

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

Table 12. Average number of diagnoses per 10,000 units of LBP distributed of imputability 2 to 4 that occurred in 2009[20]

Diagnoses	RBC	APC	PCM	VIP	FFPs	All LBPs
appearance of irregular antibodies	7.05	3.80	8.87	0,08	7,26[21]	6,04
FNHTR	5.48	8.51	6.26	0.41	0.00	5.06
allergy	1.60	39.73	9.65	4.56[22]	0.00	4.57
immunological incompatibility	0.70	6.05	4.83	0.03	0.00	1.06
including ABO	0.03	0.21	0.13	0.00	0.00	0.04
TACO	1.06	0.48	0.39	0.14	0.00	0.90
TRALI	0.11	0.64	0.13	0.05	0.00	0.14
bacterial infection	0.01	0.32	0.26	0.00	0.00	0.03
viral infection	0.01	0.00	0.00	0.00	0.00	0.01
other (immediate or delayed effects)	0.19	0.86	0.39	0.08	0.00	0.22
unknown	1.46	7.12	4.57	0.19	0.00	1.77
Total	17.68	67.52	35.36	5.54	7.26	19.81

Note 1: The recorded deviations relating to the total incidence in tables 11 and 12 were due to the denominators, i.e. the differences in the total number of distributed/dispensed LBPs declared nationally and regionally (see tables 6 and 7).
Note 2: see the breakdown of the number of RARs according to the type of products in chapter 8.1

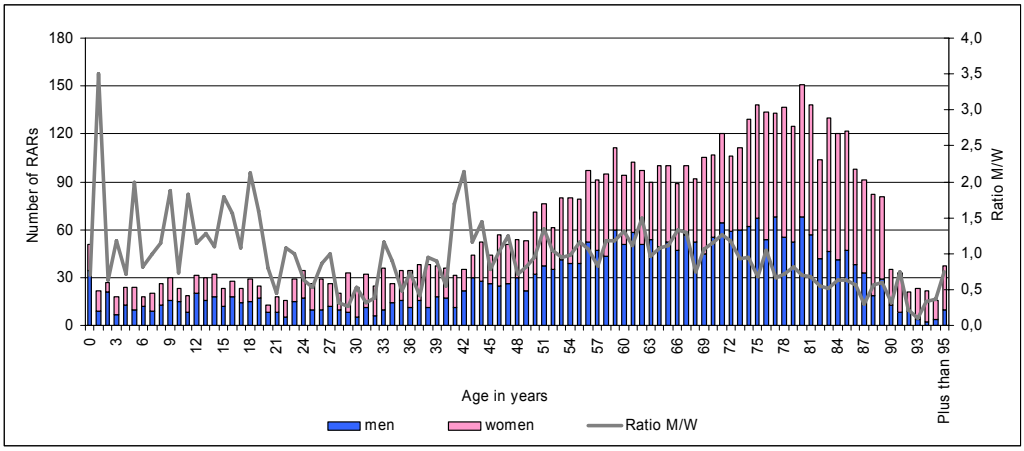
2.3.2.2. Frequency according to the age of the transfused patients

● Number of RARs per sex and age

Figure 5 demonstrates an increase in the frequency of declarations according to age, as well as a reduction in the sex ratio of RARs after the age of 74.

Figure 5. Distribution of confirmed RARs of imputability 2 to 4 per sex and age

[20] Product declared to be the most likely to have caused the RAR during the transfusion process
[21] One appearance of irregular antibodies declared in 2009 of imputability 4 (RH3) for 1,378 FFPs distributed, verification in progress.
[22] 114 cases of allergic reactions of imputability 2 to 4 were declared in the event of transfusion of VIP-BM, i.e. a frequency of 5.6 RARs per 10,000 VIP-BMs distributed (or 1 per 1,797). However, for the most serious and certain cases of grade 3 or 4 and imputability 3 to 4 (i.e. 8), the frequency fell to 0.4 per 10,000 VIP-BMs distributed (or 1 per 25,602).



● Frequency of RARs per sex and age group

The frequency of RARs per age was very heterogeneous, irrespective of the sex: overall average of 11.0 and standard deviation of 10.2 (table 13).

It particularly appeared that the ratio of RARs in adolescents was clearly higher than in the patients in the other age groups, i.e. a ratio of 31 as opposed to 10[23]. However, as we do not have the number of transfused LBPs according to the sex and age of the patients, it is difficult to go further than this statement.

Table 13. Number of RARs per 1,000 transfused patients – imputability 2 to 4 that occurred in 2009

Sex	Age group				Average	Standard deviation
	Less than 1 y.o.	1-19 y.o.	20-54 y.o.	55 y.o. and over		
Men	5,3	32,3	16,6	8,8	10,6	10,7
Women	3,5	29,4	16,8	9,8	11,3	9,8
Total	4,5	31,0	16,7	9,3	11,0	10,2

● Frequency of RARs per sex and age group for certain aetiologies (appearance of irregular antibodies, allergy, TACOs, bacterial infections)

Table 14 shows that allergies appeared more frequently in children and adolescents[24] and TACOs in new-born babies and infants. Allo-immunisations appeared to increase with age. The frequency of TRALI and bacterial infections remained low, irrespective of the age of the transfused patients.

[23] A study by G. Daurat, M. Feissel, H. Rech, D. Mathieu-Daude, F. Destruel presented to the 2008 SFVTT Conference in Perpignan "Demography of LBP recipients in Languedoc-Roussillon from 2000 to 2007" demonstrated that "Per age group, the average number of LBPs transfused per year and patient peaks between the ages of 5 and 25 before falling in almost linear fashion". If the transfusion pattern in this region were to be confirmed in other regions, there could be an element of confusion regarding the number of RARs per 1,000 patients transfused in the age group from 1 to 19 years old.

[24] The same comment applies to children and adolescents as for table 13 (possible confusion effect).

Table 14. Average number of diagnoses per 1,000 transfused patients (imputability 2 to 4)

Diagnoses	Age group					
	Less than 1 y.o.	1-19 y.o.	20-54 y.o.	55 y.o. and over	Average	Standard deviation
appearance of irregular antibodies	0.27	1.64	3.50	3.45	3.34	1.56
allergy	1.50	19.42	5.77	1.32	2.53	8.53
TACO	23.59	0.39	0.22	0.56	0.98	10.60
TRALI	0	0.07	0.23	0.05	0.08	0.10
bacterial infection	0	0	0.02	0.02	0.02	0.01

- Frequency of RARs per inter-region for four aetiologies

The most striking fact in table 15 is that children and adolescents in the North East and South West appeared more exposed to allergy, i.e. a frequency of 30 RARs per 1,000 transfused patients compared to a national average of 19 for this age group.

Table 15. Number of diagnoses per 1,000 transfused patients per inter-region of imputability 2 to 4 that occurred in 2009

Diagnoses	Ile-de-France	North East	North West	South East	South West	DOM-TOM	Average*	Standard deviation*
appearance of irregular antibodies								
Less than 1 y.o.	0.58	0	0	0.36	0.96	0	0.27	0.41
1-19 y.o.	2.15	1.33	1.16	1.79	0.00	3.05	1.64	0.82
20-54 y.o.	3.24	4.18	2.96	4.25	2.32	2.63	3.50	0.82
55 y.o. and over	3.32	4.41	2.67	4.00	2.58	0.50	3.45	0.81
Total	3.19	4.20	2.62	3.91	2.48	1.39	3.34	0.76
allergy								
Less than 1 y.o.	1.74	1.21	1.72	1.80	1.92	0	1.50	0.27
1-19 y.o.	19.31	30.08	12.41	17.88	30.07	2.03	19.42	7.85
20-54 y.o.	5.76	7.13	5.78	4.72	6.96	1.32	5.77	0.99
55 y.o. and over	1.54	1.54	1.34	0.94	1.47	0.33	1.32	0.25
Total	3.34	2.92	2.22	1.88	2.72	0.78	2.53	0.58
TACO								
Less than 1 y.o.	0.58	0.30	0.57	0	0	2.80	0.44	0.29
1-19 y.o.	0.78	0.88	0	0	0	0	0.39	0.46
20-54 y.o.	0.28	0.32	0.14	0.16	0.20	0.00	0.22	0.08
55 y.o. and over	0.55	0.54	0.59	0.64	0.41	0.33	0.56	0.09
Total	0.51	0.51	0.52	0.54	0.37	0.35	0.50	0.07
TRALI								
Less than 1 y.o.	0	0	0	0	0	0	0	0.00
1-19 y.o.	0	0	0	0.36	0	0	0.07	0.16
20-54 y.o.	0.28	0.16	0.35	0.26	0.10	0	0.23	0.10
55 y.o. and over	0.06	0.04	0.14	0.02	0	0	0.05	0.05
Total	0.10	0.06	0.16	0.06	0.01	0	0.08	0.06
bacterial infection								
Less than 1 y.o.	0	0	0	0	0	0	0	0.00
1-19 y.o.	0	0	0	0	0	0	0	0.00
20-54 y.o.	0.06	0	0	0	0.10	0	0.02	0.05
55 y.o. and over	0.01	0.01	0.01	0.01	0.06	0	0.02	0.02
Total	0.02	0.01	0.01	0.01	0.06	0	0.02	0.02

* excl. DOM-TOM

2.3.2.3. The most serious RARs

2.3.2.3.1. According to sex, age group and clinical signs

Sixty percent of the grade 3 or 4 adverse reactions declared in 2009 affected patients more than 60 years old and 24% patients more than 80 years old (figure 6), which respectively constituted 73% and 33% of the transfused patients.

However, the level of declared effets per 1,000 transfused patients reached a peak for the 10-29 y.o. age group, irrespective of sex, then fell in regular fashion (figure 7).

The shapes of figures 6 and 7 tend to suggest an "age" effect and undoubtedly an "age dependent" under-declaration effect for figure 7.

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

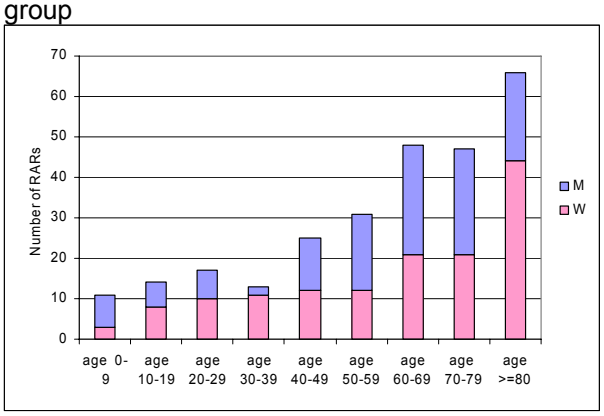


Figure 7. Number of grade 3 and 4 RARs per 1,000 patients per sex

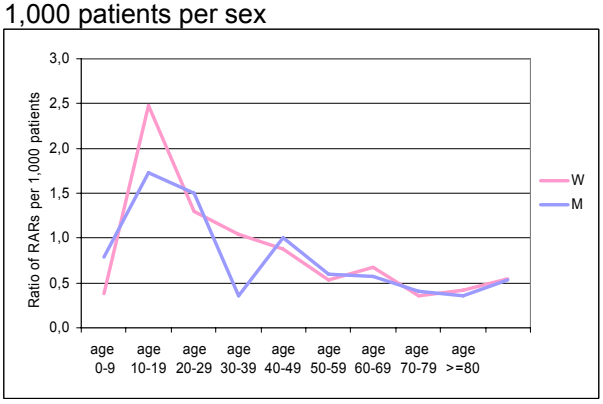
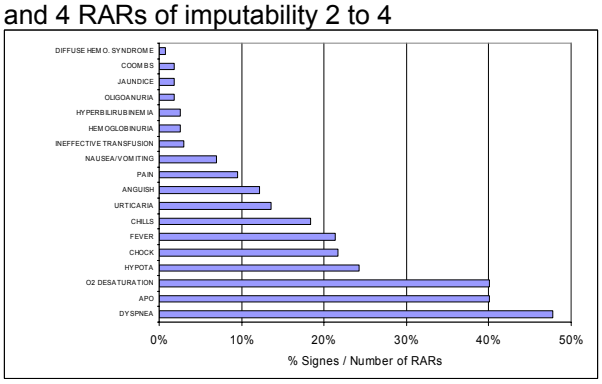


Figure 8 shows the relative levels of frequency of the clinical signs observed during grade 3 and 4 RARs; in descending order, these were dyspnoea, APO, oxygen desaturation, hypotension, shock, fever, etc.

Figure 8. Clinical or biological signs of grade 3 and 4 RARs of imputability 2 to 4



2.3.2.3.2. Death

Eight deaths (8 cases of imputability 2 to 4) were identified in 2009 in France, corresponding to enquiries conducted and closed (table 16). They involved 3 women and 5 men, aged from 41 to 89 years old. 4 of these 8 cases were of certain or probable imputability.

Table 16. Distribution of the 8 deaths according to the type of LBPs distributed

Per type of LBP	Imputability 2 to 4		Inc. imputability 2		imputability 3 and 4[25]	
	Number	per 100,000 LBPs	Number	per 100,000 LBPs	Number	per 100,000 LBPs
RBC	7	0,3	4	0,2	3	0,2
APC-SS	1	1,8			1	1,8
Total	8	0,3	4	0,1	4	0,1

The 4 cases of imputability 3 and 4 involved:

[25] Comparison of the incidences of deaths of imputability 3-4 in EC countries in annex 8.1

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

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

● One diagnosis of "immunological incompatibility" (JK1): a 50-year-old man, hospitalised for treatment of post-traumatic haemorrhagic shock with a haematoma on the left thigh and immediate generalised jaundice. Profound anaemia and haemostasis problems on non-weaned chronic alcoholic ground justified the prescription of LBP. Faced with the relative inefficacy of the transfusion and in the absence of an external haemorrhage, the hypothesis of acute haemolysis was raised and this was confirmed by the detection of the anti-JK1 antibody the day before the patient's death. In spite of the subsequent use of pheno-compatible transfusions, the patient died on the 7th day of hospitalisation. The enquiry conducted found the notion of transfusion of RBC 8 months before the patient's death, in another facility in the same region. The imputability was graded 3.

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

Erratum "Death" chapter (p19/55) of the Haemovigilance Report 2008
In the haemovigilance report 2008, a death linked to a TRALI of certain imputability was described in a 64-year-old, HIV-positive man treated for a RAEB, transfused with a PCM in additive solution and a RBC. The biological assessment conducted in 2008 led to conclusion of the involvement of the PCM in this TRALI with an immunological mechanism "faced with the presence of class II anti-HLA antibodies in 2 female PCM donors with a positive cross match".
However, after further examination of the records by the TRALI TF, it appeared that the class II anti-HLA antibodies were present in one female PCM donor but also in the female RBC donor. The TRALI should in fact be imputed to the latter product (conflict between class II HLA, anti-DR1 present in the female donor, patient group DR1, with positive cross match).

2.3.2.3.3. Grade 3 RARs

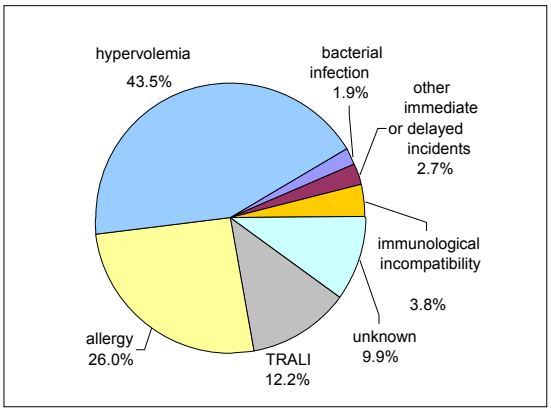
In 2009, 264 grade 3 adverse reactions were recorded: 181 (69%) of imputability 3 or 4 and 83 (31%) of imputability 2 (table 17).
The frequency was higher for platelets (PCM and APC), i.e. 28 RARs per 100,000 platelets distributed compared to 7 RARs per 100,000 RBCs.

Table 17. Distribution of the 264 confirmed RARs of imputability 2 to 4 and grade 3 according to the type of LBP[26] (number and per 100,000 distributed LBPs)

Type of LBP	Imputability 2 to 4		Incl. imputability 2		Imputability 3+4	
	N & %	per 100,000 LBPs	N & %	per 100,000 LBP	N & %	per 100,000 LBPs
RBC	167 (63.3%)	7.14	63 (75.9%)	2.69	104 (57.5%)	4.44
APC	44 (16.7%)	36.71	4 (4.8%)	3.34	40 (22.1%)	33.37
APC-IA	3 (11%)	29.47	1 (1.2%)	9.82	2 (1.1%)	19.64
APC-SS	11 (4.2%)	19.40	3 (3.6%)	5.29	8 (4.4%)	14.11
PCM	1 (0.4%)	7.58	(0%)	0.00	1 (0.6%)	7.58
PCM-IA	4 (1.5%)	34.52	2 (2.4%)	17.26	2 (1.1%)	17.26
PCM-SS	10 (3.8%)	19.28	4 (4.8%)	7.71	6 (3.3%)	11.57
VIP-SD	5 (1.9%)	3.51	1 (1.2%)	0.70	4 (2.2%)	2.81
VIP-MB	17 (6.4%)	8.30	5 (6%)	2.44	12 (6.6%)	5.86
AGC	1 (0.4%)				1 (0.6%)	393.70
other	1 (0.4%)				1 (0.6%)	
Total	264 (100%)	8.86	83 (100%)	2.79	181 (100%)	6.08

The 3 principal diagnoses involved in grade 3 RARs were, in descending order: TACOs (43%), allergies (26%) and TRALI (12%).

Figure 9. Distribution per diagnosis of grade 3 RARs



2.3.2.4. Grades 1 to 2 RARs

The vast majority (95%) of the RARs of imputability 2 to 4 were of grade 1-2 (5,630 RARs). The calculated frequency was 2 per 1,000 distributed LBPs. The distribution per diagnosis (figure 10) was different from the distribution for the grade 3 adverse effects, with only 3% TACOs, and nearly 0.2% for TRALI. However, allo-immunisations accounted for 32% of the declarations, and febrile non-haemolytic transfusions reactions for 27%.

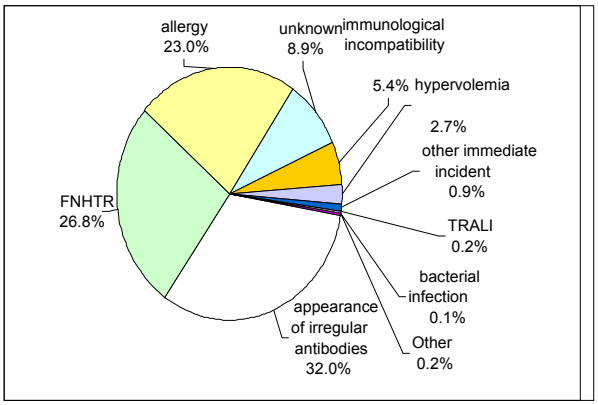
[26] Product declared to be the most likely to have caused the RAR during the transfusion process

Table 18. Distribution of grade 1-2 RARs in 2009 (imputability 2 to 4) according to the type of LBP

Type of LBP	Number of RARs (%)	RAR per 100,000 distributed LBP
RBC	3,969 (70.5%)	169.34
APC	1,202 (21.3%)	643.63
PCM	256 (4.5%)	333.99
VIP	183 (3.3%)	49.42
FFPs	1 (0%)	72.57
AGC	2 (0%)	787.40
Other products or NS **	17 (0.3%)	
Total	5,630 (100%)	189.00

* 3 RB, 1 WB, 1 BP-GEN, 6 Non-LBP, 6 NS

Figure 10. Distribution per diagnosis of grades 1-2 in 2009 (imputability 2 to 4)



2.4. Serious adverse events (SAE)

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

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

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

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

Figure 11. Sites of dysfunction of the 176 SAEs declared on the RARF as grade 0 in 2009

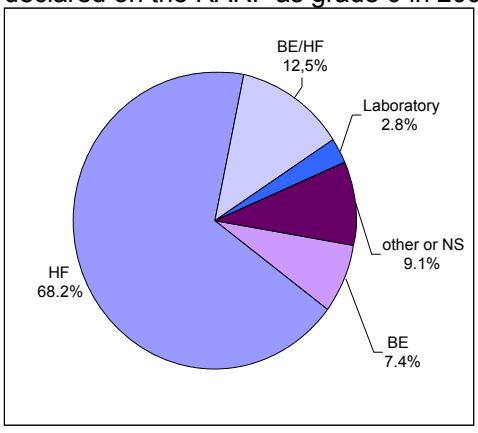


Table 19. Distribution of the 176 SAEs declared in the RARFs as grade 0 in 2009 per type of LBP

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

2- Data per inter-region

The frequency of SAEs declared on the RARFs as grade 0 varied between 4.9 and 7.2 according to the inter-regions. This heterogeneity must undoubtedly – at least partially – be linked to the fact that the declarations were not exhaustive (table 20)

Table 20. Distribution per inter-region of SARs declared in the RARFs as grade 0 – 2009

Inter-regions	Number of grade 0 and %	Per 100,000 distributed LBPs
South West	24 (13.6%)	5.1
South East	37 (21%)	5.1
North West	29 (16.5%)	7.0
North East	49 (27.8%)	7.2
Ile-de-France	34 (19.3%)	5.7
DOM-TOM	3 (1.7%)	4.9
Standard deviation excl. DOM-TOM		1.0

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

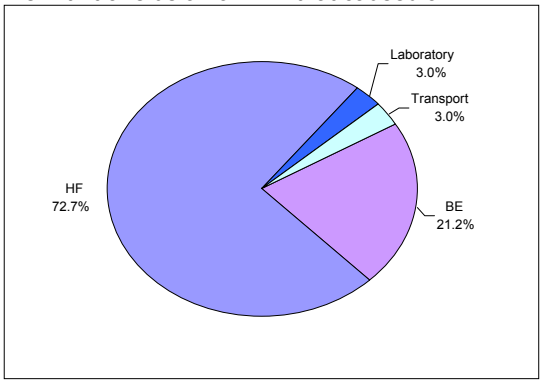
In 2009, 33 incidents were associated with an RAE of grade ≥ 1, of which 73% occurred in HFs. 21 were of grade 1, 5 grade 2, 5 others grade 3 and 2 grade 4.

73% of the anomalies or errors principally occurred in HFs, figure 12.

Table 21. Distribution per grade of the SAEs associated with RARs

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

Figure 12. Distribution per site of dysfunction of the SAEs with transfusion of LBP that caused an RAR



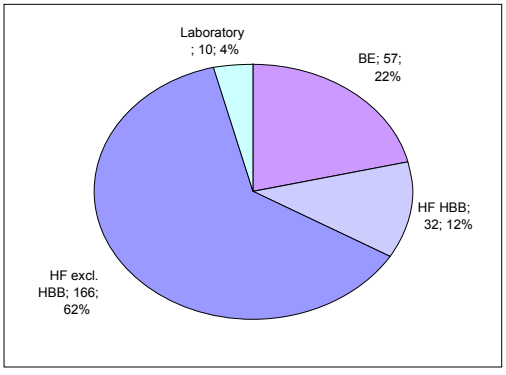
2.4.3. SAEs without transfusion of LBP

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

Figure 13 details the distribution per site of occurrence: 74% of the declarations of SAEs without transfusion involved HFs (including banks).

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

Figure 13. Sites of dysfunction of the SAEs without transfusion of LBP



2.5. Serious adverse reactions in donors (DSAR)

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

2.5.1. The number of declarations and their frequency

In 2009, 475 DSARs were declared (irrespective of the level of imputability) per 3,071,238 donations made (table 22), i.e. 15.5 DSARs per 100,000 donations.

Table 22. Distribution of DSARs per grade and per imputability*

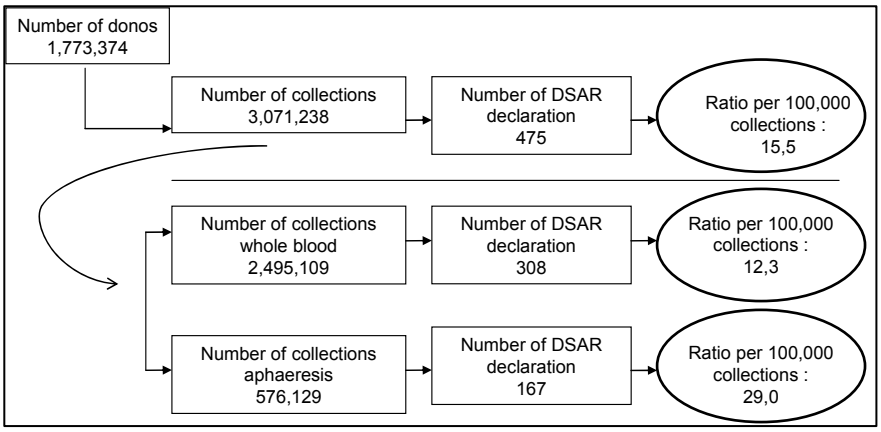
Imputability	Grade 2	Grade 3	Grade 4	NS	Total
NE – Non-assessable	5 (1.4%)	2 (1.8%)	0	0	7 (1.5%)
0 – excluded	7 (1.9%)	4 (3.6%)	0	1 (50%)	12 (2.5%)
1 – possible	56 (15.5%)	27 (24.5%)	0	0	83 (17.5%)
2 -probable	120 (33.1%)	50 (45.5%)	0	0	170 (35.8%)
3 – certain	174 (48.1%)	27 (24.5%)	1 (100%)	1 (50%)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

* refer to the grade and imputability definitions given in chapter 8.3

79% of the 475 recorded declarations had a level of imputability of probable or certain.

In 65% of the declarations (diagram 7), the event occurred during a donation of whole blood and in 35% during a donation of aphaere SARs.
The ratio of declared DSARs appeared 2 times higher for aphaere SARs procedures than for donations of whole blood (29.0 per 100,000 aphaere SARs donations versus 12.3 per 100,000 donations of whole blood).

Diagram 7. DSARs according to collection method[27] (all grades and per imputability)



2.5.2. The principal characteristics of the DSARs of imputability NE and 1 to 3[28]

Warning: As imputability to the transfusion was excluded for 12 declared DSARs (7 grade 2; 4 grade 3 and 1 grade not specified), the following analysis shall not take them into account.

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

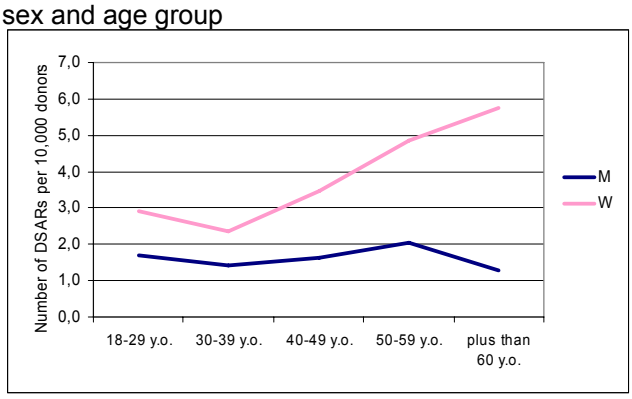
● According to donor age and sex
The ratio of DSARs per 10,000 female donors[29] appeared to increase with age, rising from 2.9 in donors between the ages of 18 and 29 to 5.8 in those over the age of 60 (figure 14).
The ratio for male donors appeared more stable, varying between 1.5 and 2.1 per 10,000 donors.

[27] Definition: chapter 8.3
[28] This analysis is available per region, see RHC activity report
[29] The "number of donations according to donor age and sex" data is not available

Table 23. Distribution of the number of DSARs according to sex and age

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

Figure 14. Ratio of DSARs per 10,000 donors per sex and age group



- According to the level of severity and collection method

According to table 24, 77% of DSARs were declared as grade 2 (external consultation required), 23% as grade 3 (AR requiring hospitalisation) and 0.2% as grade 4 (death[20]).
The severity was not specified on 0.2% of the forms.
* In September 2009, a plasmaphaeresis procedure caused a cardiac arrest and the subsequent death of the female donor, in spite of the measures taken to resuscitate her. The enquiry is in progress[30]. However, a set of measures aiming to increase the safety of donors faced with this type of risk has been drawn up and has begun to be implemented.

Table 24. Distribution of DSARs per grade and type of donation

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

[30] see Speech by Jean Marimbert, Director General of Afssaps (4th December 2009) pages 6-8 and see Bulletin de l'Afssaps (Afssaps newsletter) – Vigilances • N°50 • June 2010 / page 9
http://www.afssaps.fr/var/afssaps_site/storage/original/application/5f3307eab05ea50e734a4e012f68074f.pdf

● According to donor seniority and sex

71% of the DSARs involved known donors, i.e. 2.5 DSARs per 10,000 known donors (compared to 2.9 per 10,000 new donors).

67% of the DSARs involved women, whereas they constituted 51% of donors in 2009.

As for the declaration ratio, it was 3.4 DSARs per 10,000 female donors as opposed to 1.7 per 10,000 male donors).

Table 25. Distribution of the DSARs according to donor seniority and sex*

Sex	Known donor	First donation	First donation for this type of donation	NS	Total	Ratio per 10,000 donors
M	102 (68%)	35 (23.3%)	13 (8.7%)	(0%)	150 (100%)	1,7
W	224 (72%)	58 (18.6%)	27 (8.7%)	2 (0.6%)	311 (100%)	3,4
NS	1 (50%)	(0%)	(0%)	1 (50%)	2 (100%)	
Total	327 (70.6%)	93 (20.1%)	40 (8.6%)	3 (0.6%)	463 (100%)	2,7
Ratio per 10,000 donors	2.5	2.9			2.7	

* see number of donors: see chapter 2.2

● According to the time of appearance of the clinical signs and the existence of subsequent complications

The clinical signs occurred after donation in 74% of cases (table 26).
However, 75% of the forms reported no secondary complications (table 27).

Table 26. Time of appearance of the clinical signs

	Number	% DSAR
During donation	110	23.8%
After donation	343	74.1%
NS	10	2.1%
Total	463	100.0%

Table 27. Distribution of DSARs per grade with or without subsequent complications

Subsequent complications	grade 2	grade 3	grade 4	NS	Total
With complication	83 (76.1%)	25 (22.9%)	1 (0.9%)	0	109 (100%)
Without complication	265 (76.4%)	81 (23.3%)	0	1 (0.3%	347 (100%)
NS	7 (100%)	0	0	0	7 (100%)
Total	355 (76.7%)	106 (22.9%)	1 (0.2%)	1 (0.2%	463 (100%)

● According to the clinical signs
Among the 463 DSARs, the most-frequently reported topical manifestations were: haematomas (51%), inflammatory reactions (9%) and nerve injuries (5%), table 28.

Table 28. Topical clinical manifestations of the DSARs according to the type of donation

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

Generalised manifestations were more frequent than topical manifestations; the most common were vasovagal attacks, loss of consciousness and extremely low blood pressure (table 29).

Table 29. Generalised clinical manifestations according to the type of donation

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

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

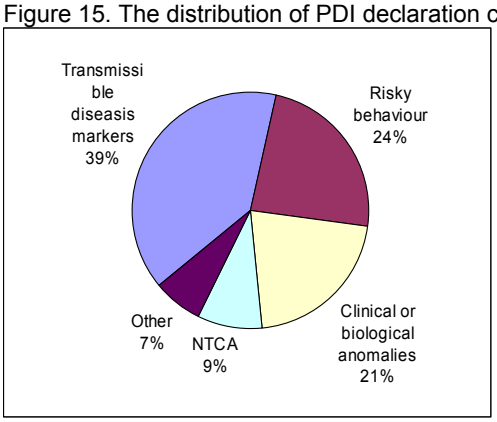
2.6. Post-donation information (PDI)

PDI is defined as any information provided after a donation likely to cast doubt on the quality and safety of the products from the donation. Their declaration to Afssaps was introduced in October 2002 and only applies to donations used to create LBPs having left the BE.

Given the "LBPs having left BE" criterion and the logistics of the storage of products at the BE, the number of PDIs declared to Afssaps was lower than the number of declarations/reports listed by the EFS (source – EFS: PDI received from Afssaps represented around 10% of the PDI recorded by the BE).

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

Figure 15. The distribution of PDI declaration causes.



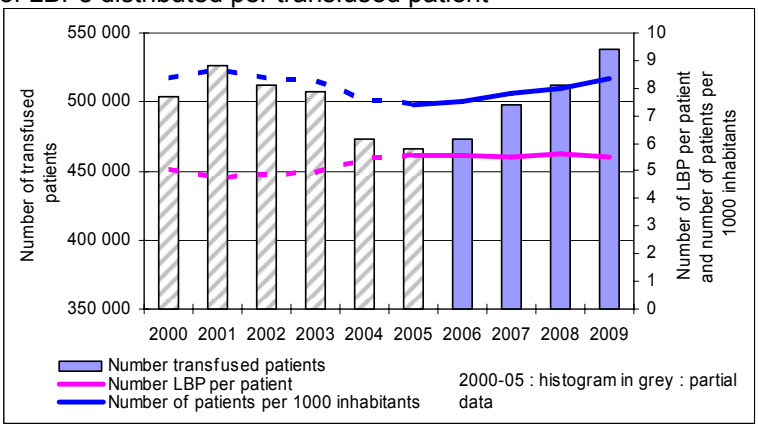
3. Changes from 2000-2009

3.1. Transfusion activity

3.1.1. Number of patients transfused

The historical data in figure 16 should be taken with precaution as, before 2006, certain regional data relating to patients was partial or missing (depending on the year: Aquitaine, Auvergne, Bourgogne, Brittany, Ile-de-France...).
Nonetheless, since 2006, there has been an increase in the number of transfused patients. The blue curve in the same figure representing the number of transfused patients per 1,000 inhabitants has also increased in the same way since 2006.
However, the number of LBPs per transfused patient (pink curve in figure 18) has been stable since 2006, i.e. 5.5.

Figure 16. Evolution of the number of transfused patients, the ratio of patients per 1,000 inhabitants and of the number of LBPs distributed per transfused patient

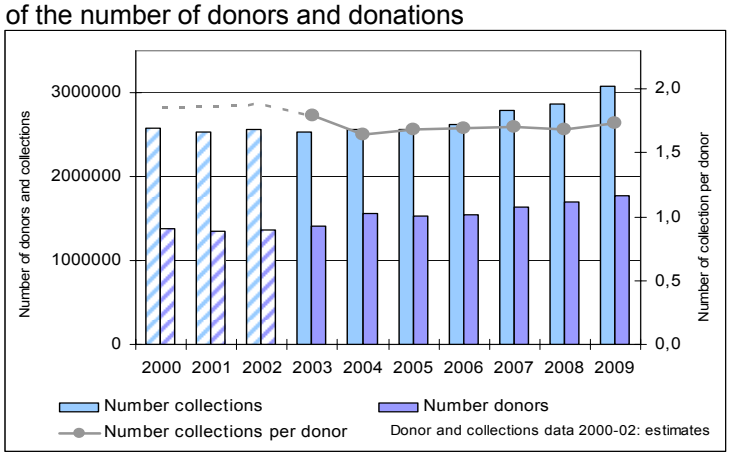


Sources: EFS, CTSA and RHC Activity Report

3.1.2. Number of donors and donations

Since 2003, the number of donors and donations has increased, respectively by 3.7% and 3.3% per year (figure 17). The number of donations per donor has remained around 1.7.

Figure 17. Evolution of the number of donors and donations



Sources: EFS and CTSA

3.1.3. LBP distribution/issue

The consumption of LBPs has grown at a rate of 1.2% per year since 2000. The progression has been higher for VIPs (+14%) and PCMs (+8%) than for the other products (figure 18).
The curve showing the change to quarantine-secured FFPs fell sharply in 2008, as they ceased to be dispensed at the end of September. This product has now been replaced by all types of virus-attenuated plasmas, particularly VIP-MB, which accounts for the increase in the VIP curve seen in 2008 (since mid-June 2008).
The rate of use of LBPs per 1,000 inhabitants has also grown by 1.0% per year since 2000 (figure 19).

Figure 18. Evolution of the consumption of different types of LBPs

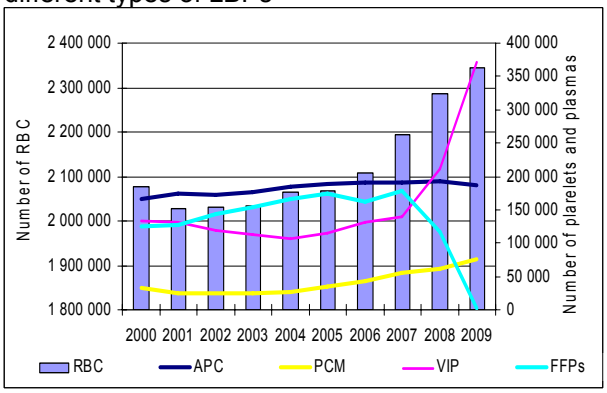
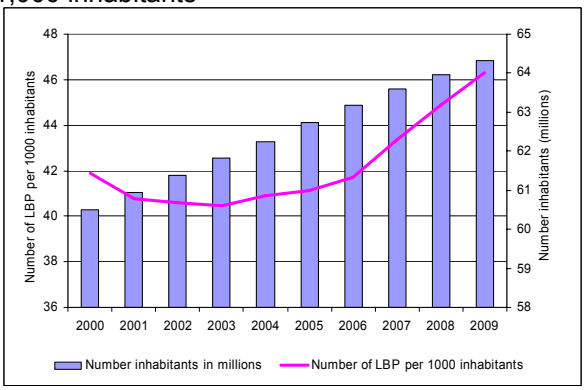


Figure 19. Evolution of the rate of use of LBPs per 1,000 inhabitants



3.2. Recipient adverse reactions (RAR)

3.2.1. Reminder of the principal modifications made to the RAR declaration form since 2001

- Year 2001: Declaration of TRALI (introduced in September 2001)
- Year 2002: Grade 0: Grade 0 forms started to reach Afssaps from November 2002
- Year 2003: Introduction of the adhitional “Bacterial incidents” table
- Year 2004: Introduction of e-fit and a new electronic declaration form whose principal new features included the grade 0 item (isolated dysfunction without clinical or biological manifestation) and diagnoses included: FNHTR, pre-transfusion serologies, post-transfusion purpura, intercurrent pathologies and the blank text section,

New sections were also added, such as additional bacteriological or immuno-haematological tests, identification of antibodies, ABO/RH1 LBP and ABO/RH1 patient groups.
- Year 2005: New version of RARF user guide, whose principal modifications were clarifications regarding pre-existing antibodies or newly-appeared antibodies, grade 0, viral infection and the RAR form numbering procedure.
- Year 2007: Updating of the RARF guide, publication of the SIF guide and FNHTR data sheet
- Year 2008: Procedure for investigating serious allergic reactions (grades 3 and 4) during transfusion involving VIP-MB

Warning: This analysis involves the data from the 2000-2009 period (years of occurrence). In the case of analysis of viral infections, which may be diagnosed several years after transfusion, the reference year will be the year of transfusion.

3.2.2. The number of reportings and their frequency

Having fallen from 2000 to 2006, the number of RAR declaration has increased since 2006 by nearly 2% per year (histogram in figure 20). However, this number in relation to 1,000 distributed LBPs has, conversely, followed a downward trend since 2001 (3.1 in 2000, 3.2 in 2001 and 2.6 in 2009).

Figure 20. Evolution of the number of RAR declarations, ratio of declared RARs per 1,000 transfused patients and per 1,000 LBPs – All products

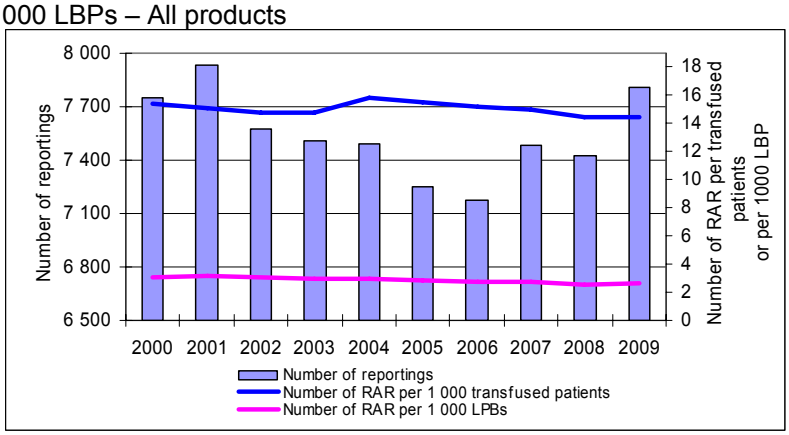
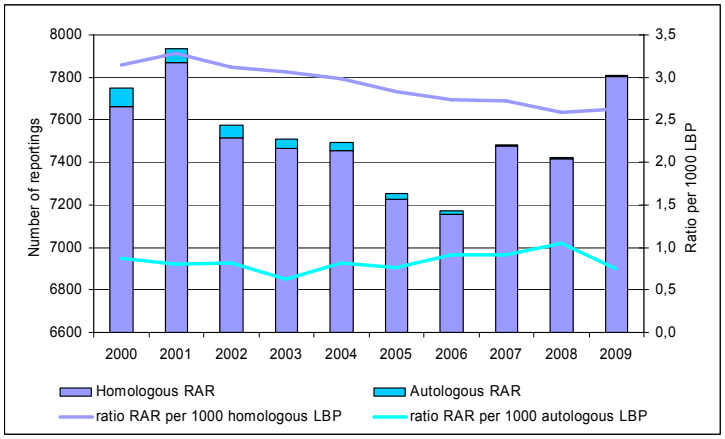


Figure 21 illustrates the slight decrease in RAR declaration rates with homologous LBPs. The rate of declaration of autologous RARs was on average nearly 1 RAE per 1,000 autologous transfusions packages[31].

Figure 21. Evolution of the number of declarations of homologous and autologous RARs and ratios of RARs declared per 1,000 homologous LBPs distributed / autologous transfusions packages provided.

[31] Scheduled autologous transfusion package (including autologous red blood cells and fresh frozen plasma)

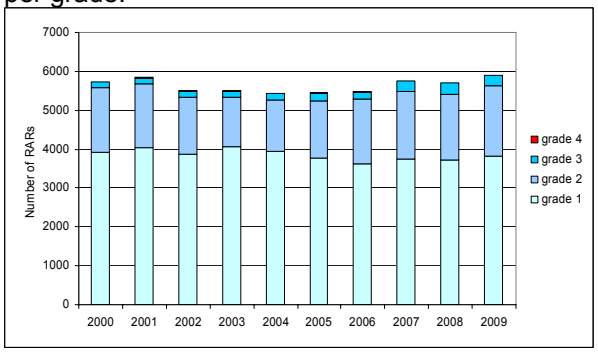


3.2.3. Confirmed cases of imputability 2 to 4[32]

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

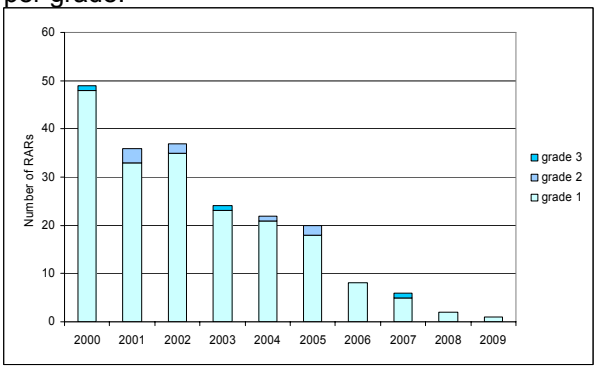
The distribution per grade of the homologous RARs of imputability 2 to 4 varied only a little over the past 10 years (figure 22).

Figure 22. Distribution of the homologous RARs per grade.



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

Figure 23. Distribution of the autologous RARs per grade.



3.2.3.2. According to diagnosis

Table 30 specifies the principal diagnoses of the RARs and their evolution over the last 10 years:

- increase in the frequency of declarations of:

. TACOs (4% of diagnoses): growth of 5% per year

. allo-immunisations (26% of diagnoses over the period): average growth of 3% per year

. "unknown" aetiologies (10% of diagnoses): average growth of 10% per year

. TRALI (data available since 2003: i.e. 1% of diagnoses between 2003 and 2009 and average growth of 29% per year over this period)

[32] See definition in annexe 8.3

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

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

The most rare diagnoses are described in chapter 3.3.3.7

Table 30. Evolution of the number of grade 1 to 4 and imputability 2 to 4 RARs, enquiry closed, over the 2000-09 period

Diagnosis	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2000-09 *
appearance of irregular antibodies	1,426	1,427	1,349	1,201	1,266	1,430	1,627	1,732	1,686	1,800	5.69
FNHTR	1,768	1,854	1,817	1,762	1,068	1,003	1,202	1,439	1,501	1,508	5.68
allergy	1,364	1,400	1,379	1,545	1,598	1,443	1,319	1,375	1,337	1,362	5.37
immunological incompatibility	353	305	259	257	292	288	258	284	238	316	1.08
including ABO	28	20	21	12	17	14	12	11	13	11	0.06
TACO	174	180	168	209	191	208	219	253	277	267	0.82
viral infection	219	189	100	54	44	24	15	8	3	3	0.25
TRALI	1	1	9	18	24	34	37	47	54	42	0.10
bacterial infection	40	21	16	35	13	6	8	11	9	10	0.06
other (immediate or delayed)	72	80	54	58	59	38	53	50	52	66	0.22
Unknown**	363	424	387	394	901	1005	745	565	552	528	2.23
Total	5,780	5,881	5,538	5,533	5,456	5,479	5,483	5,764	5,709	5,902	21.51

* average number of RARs between 2000 and 2009 per 10,000 LBPs distributed

** Unknown diagnoses constituted a significant portion of all RARs, i.e. 6 to 18% depending on the year in question. The strong growth from 2004 to 2006 should be put into perspective with the change in tool for the declaration of RARs (e-FIT) and its opening to a higher number of declarants. Furthermore, when the data from the old GIFIT database (2000 to 2004) was recovered, a large portion of the diagnoses were reclassified as FNHTRs when signs of shivering and/or fever were observed (ISBT consensus criteria, Vancouver, August 2002).

3.2.3.3. According to type of product

Table 31 shows that though the RARs related to RBC transfusion were usually the most common in terms of number (68%), RARs related to platelets had a much higher incidence, i.e. a ratio of 81 RARs per 10,000 APC transfused and 39 RARs per 10,000 PCM transfused.

Table 31. Distribution of diagnoses of adverse reactions of imputability 2 to 4 that occurred between 2000 and 2009, and % according to the type of LBP[33]

	Number	Percentage according to type of LBP(1)					
Diagnosis	Average 2000-09	RBC	APC	PCM/SPC	VIP	FFPs	Others (2)
appearance of irregular antibodies	1,494	92.5%	4.1%	2.6%	0.1%	0.3%	0.4%
FNHTR	1,492	81.6%	15.0%	2.0%	0.4%	0.6%	0.4%
allergy	1,412	27.9%	61.2%	3.6%	2.8%	4.3%	0.1%
unknown	586	65.9%	28.6%	2.9%	0.6%	1.5%	0.4%
immunological incompatibility	285	54.2%	38.7%	6.1%	0.3%	0.5%	0.2%
including ABO	16	66.7%	23.5%	2.5%	3.7%	3.1%	0.6%
TACO	215	92.5%	4.9%	0.6%	0.6%	1.1%	0.4%
viral infection	66	61.8%	0.5%	1.1%	0.0%	8.3%	28.4%
TRALI	27	57.3%	27.0%	2.2%	0.7%	11.6%	1.1%
bacterial infection	17	54.4%	37.3%	7.7%	0.0%	0.0%	0.6%
other (immediate or delayed effects)	58	57.9%	36.9%	1.2%	1.2%	0.7%	2.1%
Total	5,653	67.8%	26.1%	2.8%	0.9%	1.7%	0.7%
Nbr per 10,000 distributed LBPs	21.4	18.1	80.8	39.1	3.4	7.0	

(1) For further details on the distribution per product, please refer to annex 8.1
(2) Others: AGC, reconstituted blood, whole blood, non-LBP, NS

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

● Distribution per product

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

Table 32. Confirmed RARs of grade 3-4 and imputability 3-4 – according to the type of products[34]

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

A more detailed table is provided in annex 8.1.2, enabling identification of the 2009 RARs relating to new products, particularly platelets and plasmas.

[33] Product declared to be the most likely to have caused the RAR during the transfusion process
[34] ditto note[28]

● Comparison of the two periods: 2004-04 and 2005-09
Table 33 shows the average annual number of diagnoses of grade 3-4 and imputability 3-4 for the two periods: 2000-04 and 2005-09. The statistically-significant changes included:
- the increase in declarations of TACO;
- the stable number of bacterial infections;
- the fall in immunological incompatibilities;
Comparison with TRALI was not possible as this diagnosis only began to be recorded in the e-FIT database from 2004.

Table 33. Number of RARs of grade 3-4 and imputability 3-4, enquiry closed

diagnosis	Average annual number of RARs Confidence interval of 95.0% for the average		difference between the averages for the 2 periods (average 1 – average 2)
	Average 1 2000-04	Average 2 2005-09	
Number increased			
TACO	49.4 [41.2 _ 57.5]	77.6 [61.1 _ 94.1]	-28.2 [-43.5 _ -12.9] (1)
allergy	31.4 [28.7 _ 34.1]	44.2 [28.6 _ 59.7]	-12.8 [-25.9 _ 0.3] (2)
TRALI	7.2 [-0.6 _ 15.0]	21.8 [15.8 _ 27.8]	-14.6 [-22.8 _ -6.5]
unknown	5.4 [4.0 _ 6.8]	9.2 [5.8 _ 12.6]	-3.8 [-6.9 _ -0.7]
Number stable			
bacterial infection	4.0 [2.0 _ 6.0]	4.2 [2.4 _ 6.0]	-0.2 [-2.4 _ 2.0]
Number decreased			
immunological incompatibility	14.8 [12.7 _ 16.8]	8.8 [3.7 _ 14.0]	6.0 [1.4 _ 10.6]
FNHTR	4.4 [0.2 _ 8.6]	0.4 [-0.3 _ 1.1]	4.0 [0.5 _ 7.5]
ABO	5.4 [1.7 _ 9.1]	2.6 [1.2 _ 4.02]	2.8 [-0.5 _ 6.1]

Reading of the average comparison test (number of RARs and incidence), supposing equal variances
(1) 95.0% confidence interval for the difference between the averages of the TACOs varied from -43.5 to -12.9. As the interval does not contain the value 0, there is a statistically-significant difference between the averages for the 2 periods with a level of confidence of 95.0%.
(2) 95.0% confidence interval for the difference between the averages of the allergies varied from -25.9 to 0.3. As the interval contains the value 0, there is no statistically-significant difference between the averages for the 2 periods with a level of confidence of 95.0%.

● Comparison of the two periods: 2000-04 and 2005-09: incidences
In terms of incidence, it appears that there was no statistically-significant difference between the 2 periods, irrespective of the diagnosis (table 34).

Table 34. Incidences of RARs of grade 3-4 and imputability 3-4, enquiry closed, per 100,000 LBPs – Comparison of the two periods: 2000-04 and 2005-09

diagnosis	Incidence per 100,000 distributed LBPs Confidence interval of 95.0% for the average		difference between the average incidences (average 1 – average 2)
	Average 1 2000-04	Average 2 2005-09	
Increased incidence			
TACO	1.97 [1.63 _ 2.30]	2.82 [2.36 _ 3.28]	-0.85 [-1.32 _ -0.38] (1)
allergy	1.25 [1.13 _ 1.37]	1.60 [1.09 _ 2.10]	-0.35 [-0.78 _ 0.08] (2)
TRALI	0.29 [-0.02 _ 0.59]	0.79 [0.60_ 0.98]	-0.51 [-0.81 _ -0.21]
unknown	0.21 [0.16 _ 0.27]	0.33 [0.22 _ 0.44]	-0.12 [-0.22 _ -0.01]
Incidence stable			
bacterial infection	0.16 [0.08 _ 0.24]	0.15 [0.089 _ 0.21]	0.01 [-0.07 _ 0.09]
Decreased incidence			
immunological incompatibility	0.59 [0.51 _ 0.67]	0.32 [0.14 _0.49]	0.27 [0.11 _ 0.43]
FNHTR	0.18 [0.01 _ 0.34]	0.01 [-0.014 _ 0.038]	0.16 [0.02 _ 0.30]
ABO	0.22 [0.07 _ 0.36]	0.09 [0.047_ 0.14]	0.12 [-0.01 _ 0.25]

Reading of the incidence comparison test (number of RARs per 100,000 LBPs), supposing equal variances

(1) 95.0% confidence interval for the difference between the incidences of the TACOs varied from -1.32 to -0.38. As the interval does not contain the value 0 (higher value below 0), there is a statistically-significant difference between the incidences for the 2 periods with a level of confidence of 95.0%.
(2) 95.0% confidence interval for the difference between the incidences of the allergies varied from -0.78 to 0.08. As the interval contains the value 0, there is no statistically-significant difference between the incidences for the 2 periods with a level of confidence of 95.0%.

3.2.3.5. Grade 1 to 2 RARs

● Distribution per product

5,450 RARs of grade 1 and 2 and imputability 2 to 4 were declared per year between 2000 and 2009. The distribution per product was the same as in the previous chapter: 68% with RBCs, 26% with APCs, 3% with PCMs and 3% with plasmas (table 35).

Table 35. The number of RARs of grade 1-2 and imputability 2 to 4, enquiry closed – according to the type of products transfused

Type of LBP	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
RBC	3,828	3,856	3,576	3,511	3,460	3,475	3,641	3,881	3,800	3,969
APC	1,428	1,490	1,535	1,580	1,579	1,532	1,361	1,300	1,255	1,202
PCM/SPC	155	141	102	99	84	129	162	179	214	256
VIP	27	38	26	18	18	22	38	29	66	183
FFPs	94	99	90	107	113	92	79	97	74	1
Other	107	91	46	33	28	16	12	10	10	19
Total	5,639	5,715	5,375	5,348	5,282	5,266	5,293	5,496	5,419	5,630
Per 1,000 LBPs	2.2	2.3	2.2	2.1	2.1	2.0	2.0	2.0	1.9	1.9

● Distribution per diagnosis

Table 36 presents the average annual number of diagnoses of grade 1 and 2 and imputability 2 to 4 for the two periods: 2000-04 and 2005-09. There was a statistically-significant increase in declarations of allo-immunisation, of "unknown" diagnosis and TACOs; conversely, there was a statistically-significant decrease in declarations of FNHTR, allergies, immunological incompatibility, viral infection and bacterial infection.

Table 36. The number of RARs of grade 1-2 and imputability 2 to 4, enquiry closed – Comparison of the two periods: 2000-04 and 2005-09

diagnosis	Average annual number of RARs Confidence interval of 95.0% for the average		difference between the averages for the 2 periods (average 1 – average 2)
	Average 1 2000-04	Average 2 2005-09	
Number increased			
allo-immunisation	1333.6 [1209.8 _ 1457.4]	1654.8 [1480.3 _ 1829.3]	-321.2 [-498.9 _ -143.5]
unknown	476.2 [199.6 _ 752.8]	648.0 [399.6 _ 896.3]	-171.8 [-480.5 _ 136.9]
TACO	121.2 [108.9 _ 133.5]	144.8 [127.5 _ 162.1]	-23.6 [-41.2 _ -5.9]
TRALI	2.0 [-1.8 _ 5.8]	8.0 [5.5 _ 10.5]	-6.0 [-9.8 _ -2.2]
Number decreased			
FNHTR	1641.0 [1237.5 _ 2044.5]	1329.4 [1054.0 _ 1604.8]	311.6 [-94.2 _ 717.4]
allergy	1419.2 [1288.9 _ 1549.5]	1310.4 [1249.9 _ 1370.9]	108.8 [-10.5 _ 228.1]
immunological incompatibility	276.6 [227.5 _ 325.6]	266.4 [230.2 _ 302.6]	10.2 [-40.4 _ 60.8]
viral infection *	12.4 [2.4 _ 22.4]	2.4 [1.7 _ 3.1]	10.0 [1.7 _ 18.4]
bacterial infection	19.8 [7.4 _ 32.2]	3.8 [2.4 _ 5.2]	16.0 [5.7 _ 26.3]
ABO	13.8 [9.1 _ 18.5]	10.0 [7.9 _ 12.2]	3.8 [-0.5 _ 8.1]

* diagnoses per transfusion date

As for the most serious and most certain RARs, the change (increase or decrease) in incidences between 2000-04 and 2005-09 was not statistically significant, irrespective of the diagnosis (table 37).

Table 37. Incidences of RARs of grade 1-2 and imputability 2 to 4, enquiry closed – Comparison of the two periods: 2000-04 and 2005-09

diagnosis	incidence per 100,000 LBPs Confidence interval of 95.0% for the average		difference between the average incidences (average 1 – average 2)
	Average 1 2000-04	Average 2 2005-09	
Increased incidence			
allo-immunisation	5.23 [4.55 _ 5.91]	6.15 [5.84 _ 6.45]	-0.92 [-1.49 _ -0.34]
unknown	1.89 [0.81 _ 2.97]	2.39 [1.33 _ 3.46]	-0.50 [-1.76 _ 0.76]
TACO	0.48 [0.44 _ 0.53]	0.53 [0.49 _ 0.60]	-0.05 [-0.100 _ 0.004]
TRALI	0.01 [-0.01 _ 0.02]	0.03 [0.02 _ 0.03]	-0.02 [-0.03 _ -0.01]
Decreased incidence			
FNHTR	6.54 [4.88 _ 8.20]	4.82 [4.08 _ 5.57]	1.72 [0.20 _ 3.23]
allergy	5.65 [5.17 _ 6.13]	4.79 [4.31 _ 5.27]	0.86 [0.29 _ 1.43]
immunological incompatibility	1.10 [0.92 _ 1.29]	0.97 [0.83 _ 1.12]	0.13 [-0.07 _ 0.33]
Viral infection (1)	0.05 [0.01 _ 0.09]	0.01 [0.01; 0.01]	0.04 [0.01 _ 0.07]
bacterial infection	0.08 [0.03 _ 0.13]	0.014 [0.01 _ 0.02]	0.06 [0.03 _ 0.11]
ABO	0.056 [0.04 _ 0.08]	0.034 [0.02 _ 0.05]	0.02 [0.01 _ 0.04]

(1) by transfusion date

3.2.3.6. Rarest RARs [35]

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

● The diagnoses in question were as follows:

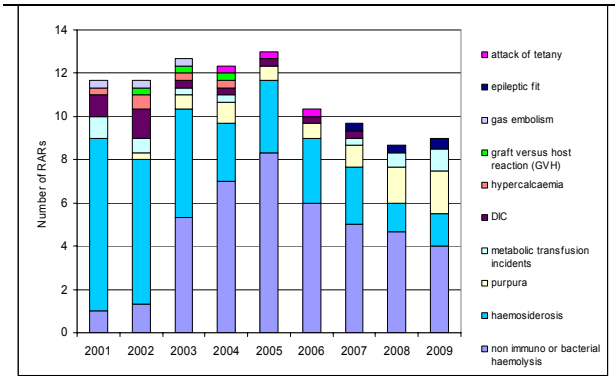
(N=cumulated number between 2000 and 2009, inc=incidence per million transfused LBPs over the same period)

- non-immune or post-septicaemic haemolysis N=47 inc=1.7
- haemosiderosis N=41 inc=1.6
- purpura N=8 inc=0.3
- transfusion-related metabolic accidents N=6 inc=0.3
- DIC N=5 inc=0.2
- hypercalcaemia N=2 inc=0.1
- graft versus host reaction (GVH) N=1, inc=0.04; ditto for the following 3 types of RAE:
- gas embolism
- epileptic fit
- tetany attack
- confirmed viral, parasitic or other infections[36]

[35] Excluding the "other immediate incidents" and "other delayed incidents" categories (non-specified or non-listed), reclassification in progress for the roll-out of e-FIT V2

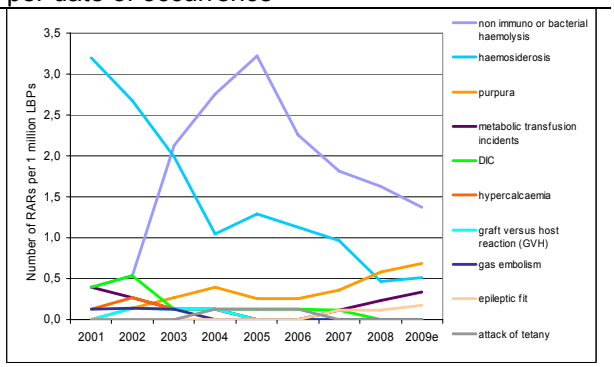
[36] It should be noted that in 2009, 3 H1N1 (influenza A) type RARs were declared in the e-FIT database: two of grade 1 and imputability 0, a second of grade 1 and imputability 1.

Figure 24. Evolution of confirmed rare effects of grade 1 to 4 and imputability 2 to 4 per date of occurrence*



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

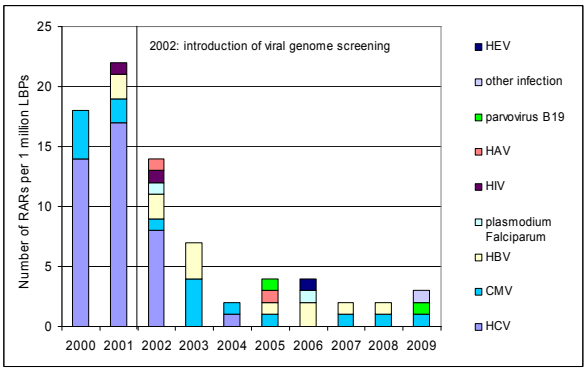
Figure 25. Evolution of incidence of confirmed rare effects of grade 1 to 4 and imputability 2 to 4 per date of occurrence



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

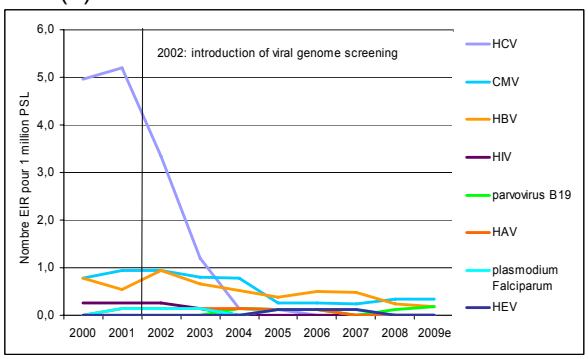
. 40 declarations of HVC infection (none since 2004)
. 16 declarations of CMV (average of 1 to 2 per year)
. 2 declarations of HIV infection (none since 2002)
. 2 declarations of Parvovirus B19 virus (in 2005 and in 2009)
. 2 declarations of HVA infection (in 2002 and 2005)
. 2 declarations of malaria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

Figure 26. Evolution of the number of viral, parasitic or other infections of grade 1 to 4 and imputability 2 to 4, enquiry closed, per transfusion date



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

Figure 27. Evolution of the incidence of viral, parasitic or other infections of grade 1 to 4 and imputability 2 to 4, enquiry closed, per transfusion date (1)



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

3.3. Serious adverse events (SAE)

3.3.1. SAEs with transfusion of LBP without RAR

Table 38 shows the number of SAEs declared on the RARF as grade 0 per inter-region, since 2002 (start of declaration in November 2002 on a retroactive basis). Excluding the 1st year of declaration, the number of declarations doubled in the North East and South West between 2003 and 2009, whereas it remained stable for the other inter-regions (excl. DOM-TOM).

Table 38. SAEs declared on the RARF as grade 0 per inter-region

Inter-region	2002	2003	2004	2005	2006	2007	2008	2009
South West	7 (13.5%)	11 (8%)	23 (15.4%)	12 (8.1%)	15 (10.9%)	26 (14.5%)	23 (11.7%)	24 (13.6%)
South East	16 (30.8%)	36 (26.1%)	36 (24.2%)	40 (27%)	28 (20.3%)	48 (26.8%)	54 (27.4%)	37 (21%)
North West	12 (23.1%)	35 (25.4%)	27 (18.1%)	21 (14.2%)	26 (18.8%)	20 (11.2%)	22 (11.2%)	29 (16.5%)
North East	8 (15.4%)	22 (15.9%)	28 (18.8%)	41 (27.7%)	36 (26.1%)	32 (17.9%)	58 (29.4%)	49 (27.8%)
Ile-de-France	8 (15.4%)	33 (23.9%)	33 (22.1%)	31 (20.9%)	25 (18.1%)	45 (25.1%)	36 (18.3%)	34 (19.3%)
DOM-TOM	1 (1.9%)	1 (0.7%)	2 (1.3%)	3 (2%)	8 (5.8%)	8 (4.5%)	4 (2%)	3 (1.7%)
Total	52 (100%)	138 (100%)	149 (100%)	148 (100%)	138 (100%)	179 (100%)	197 (100%)	176 (100%)

Figure 28 shows the evolution of the frequency of grades 0 per 100,000 LBPs per inter-region and figure 29 the site of the dysfunctions: healthcare facilities remained the principal site of dysfunction over the 8 years.

Figure 28. Evolution of the number of SAEs declared on the RARF as group 0 per 100,000 distributed LBPs

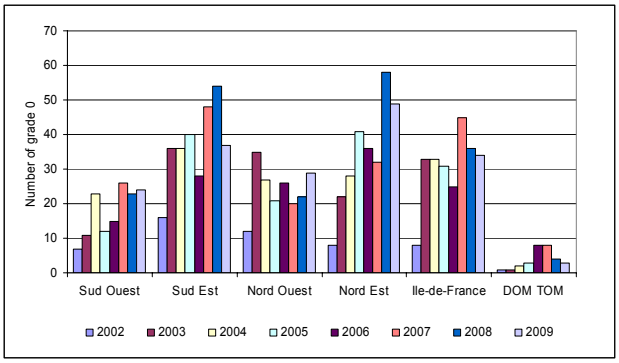
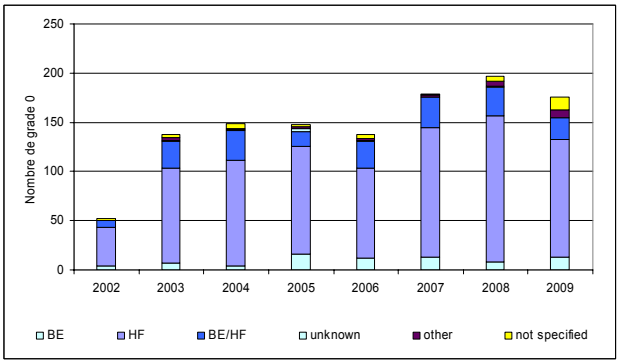


Figure 29. Evolution of SAEs declared on the RARF as grade 0 according to site of dysfunction



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

On average, 51 SAEs were declared between 2000 and 2009. During this period, 70.9% occurred in HFs, 11.4% both at the BE and HF, 11.6% in BE and 6.1% on other sites (figure 30).
Though the general trend has been downwards since 2000-2001, it has not been homogeneous per inter-region: table 39 illustrates this evolution.

Figure 30. Evolution of SAEs associated with RARs of a grade higher than or equal to 1 according to dysfunction site

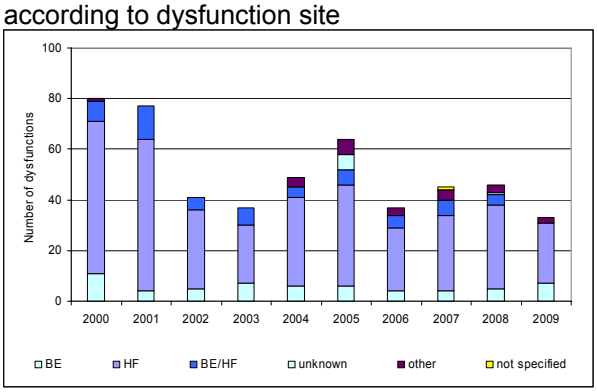


Table 39. SAEs associated with RARs of a grade higher than or equal to 1 per inter-region

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
South West	6 (7.5%)	10 (13%)	3 (7.3%)	2 (5.4%)	7 (14.3%)	5 (7.8%)	1 (2.7%)	3 (6.7%)	5 (10.9%)	3 (9.1%)
South East	22 (27.5%)	21 (27.3%)	6 (14.6%)	10 (27%)	7 (14.3%)	14 (21.9%)	4 (10.8%)	7 (15.6%)	4 (8.7%)	2 (6.1%)
North West	12 (15%)	20 (26%)	15 (36.6%)	9 (24.3%)	13 (26.5%)	8 (12.5%)	5 (13.5%)	9 (20%)	10 (21.7%)	8 (24.2%)
North East	18 (22.5%)	15 (19.5%)	5 (12.2%)	8 (21.6%)	9 (18.4%)	13 (20.3%)	12 (32.4%)	20 (44.4%)	21 (45.7%)	15 (45.5%)
Ile-de-France	17 (21.3%)	10 (13%)	8 (19.5%)	6 (16.2%)	8 (16.3%)	18 (28.1%)	6 (16.2%)	5 (11.1%)	4 (8.7%)	4 (12.1%)
DOM-TOM	5 (6.3%)	1 (1.3%)	4 (9.8%)	2 (5.4%)	5 (10.2%)	6 (9.4%)	9 (24.3%)	1 (2.2%)	2 (4.3%)	1 (3%)
Total	80 (100%)	77 (100%)	41 (100%)	37 (100%)	49 (100%)	64 (100%)	37 (100%)	45 (100%)	46 (100%)	33 (100%)

3.3.3. SAEs without transfusion of LBP

● Evolution of declarations between 2008 and 2009
This chapter covers the declarations from 2008 and 2009: the SI declaration system was introduced in May 2007 (47 SAEs over 8 months of declaration). Accordingly, 124 SAEs were declared in 2008 and 231 in 2009, i.e. an increase of 86%. Of these, those identified in HFs increased from 101 to 198, i.e. an increase of 75% (figure 31).
83% of the 355 SAEs declared between 2008 and 2009 were estimated to be potentially serious, 15% of a repetitive nature, 54% resulted in preventive measures and 86% corrective measures (table 40).

Figure 31. Sites of dysfunction of the SAEs without transfusion of LBP

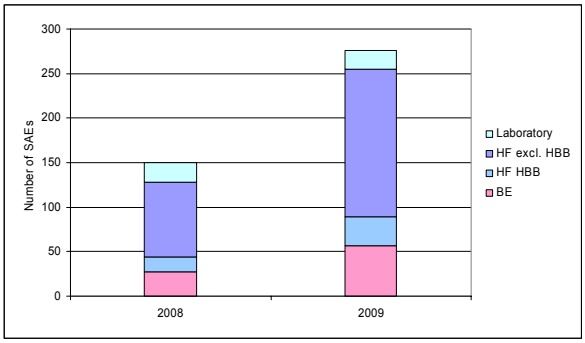


Table 4. Severity of SI and accompanying measures

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

● Evolution of declarations per inter-region

Tables 41 and 42 demonstrate that the North East, South East and South West were the inter-regions that submitted the most declarations: the frequency per 100,000 distributed LBPs was around 8.2 to 8.7.

Table 41. SAEs without transfusion of LBPs per inter-region

Inter-regions	2008	2009	2008-09
South West	2 (1.6%)	69 (29.9%)	71 (20%)
South East	55 (44.4%)	59 (25.5%)	114 (32.1%)
North West	9 (7.3%)	19 (8.2%)	28 (7.9%)
North East	46 (37.1%)	63 (27.3%)	109 (30.7%)
Ile-de-France	11 (8.9%)	11 (4.8%)	22 (6.2%)
DOM-TOM	1 (0.8%)	10 (4.3%)	11 (3.1%)
Total	124 (100%)	231 (100%)	355 (100%)

Figure 42. Number of SAEs without transfusion of LBPs per 100,000 distributed LBPs per inter-region[37]

Inter-regions	2 008	2009	2008-09
South West	0.5	16.6	8.7
South East	8.3	8.5	8.4
North West	2.4	3.5	3.0
North East	7.1	9.3	8.2
Ile-de-France	2.0	1.9	1.9
DOM-TOM	1.8	16.6	9.4
Total	4.6	7.8	6.2
Standard deviation*	3.4	5.8	3.3

* Standard deviation excl. DOM-TOM

3.4. Donor serious adverse reactions (DSAR)

3.4.1. Evolution of the number of DSAR declarations – all levels of imputability

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

However, the rate would appear to have been 2 times higher for DSARS occurring during Aphaeresis samples than for DSARs observed during sampling of whole blood (figure 32).

[37] Comparison of the frequencies of SAEs in EC countries in annex 8.1

Figure 33 demonstrates that over the 4 years in question, grade 2 DSARs (prescription of external consultation by the BE doctor) constituted 75% of declarations and grade 3 DSARs (hospitalisation of the donor) 26%. 2 DSARs of grade 4 were reported: 1 in 2008 of imputability 0 and 1 in 2009 of imputability 3.

Figure 32. Evolution of the number and ratio of DSARs per 100,000 donations

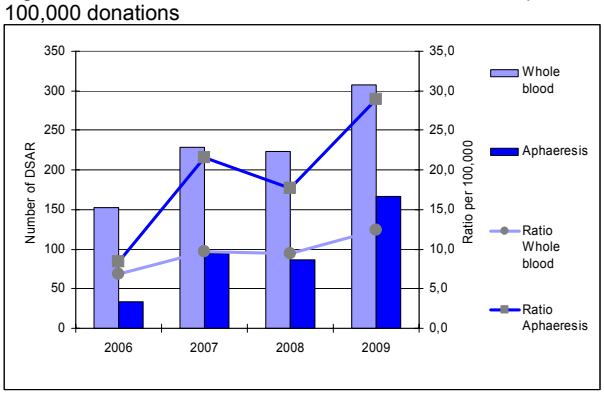
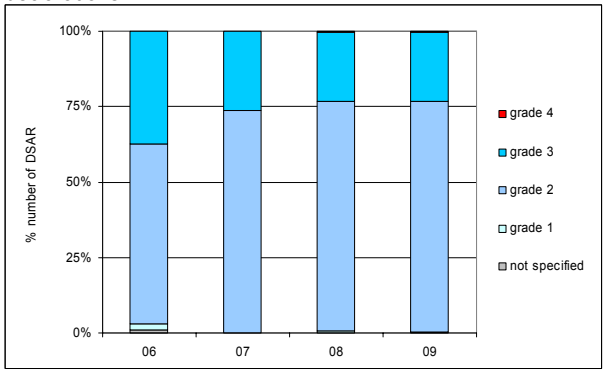


Figure 33. Evolution of the distribution per grade of DSAR declarations



3.4.2. Principal characteristics of the DSARs declared with imputability NE and 1 to 3 (2007-09)

Warning: As in chapter 2.5, the following analysis shall not take into account the DSARs of imputability 0, i.e. imputability excluded, as well as the declarations from 2006, as the data was non-exhaustive and, in general, incomplete.

Between 2007 and 2009, 1,084 DSARs were declared with imputability of NE and 1 to 3. We observed that:
- 84% of DSARs were of probable or certain imputability (figures 34 and 35)
- 76% grade 2 and 24% grade 3 (table 43). However, there was a grade 4 of certain imputability in 2009 (see chapter 2.5);
- 69% involved donations of whole blood, 31% Aphaeresis donations (table 43);
- 75% involved no subsequent complications and 25% caused genuine subsequent complications (table 44);
- 76% occurred after donation and 23% during donation: in 1% of the declarations this information was not specified.

Figure 34. Evolution of the distribution per year and per imputability of DSAR declarations

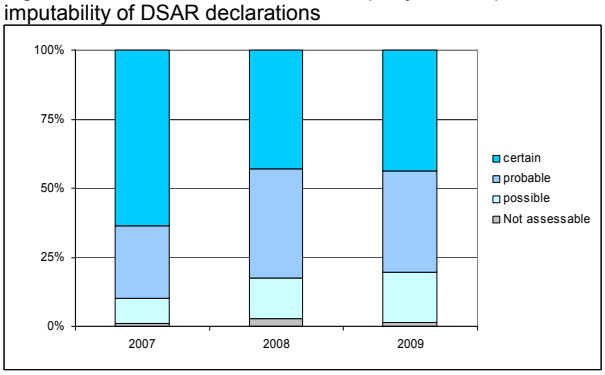


Figure 36. Proportions of DSARs with or without subsequent complication between 2007 and 2009

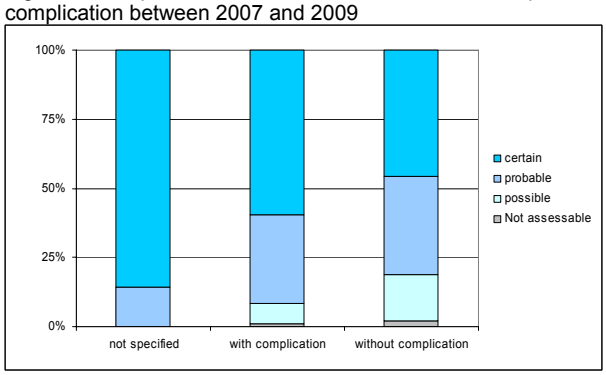


Table 43. Distribution of DSARs per grade and type of donation – Combined total 2007-09

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

* 2009 case: see chapter 3.3

Table 44. Number of DSARs presenting, or not, a subsequent complication during or after donation – Combined total 2007-09

	During donation	After donation	NS	Total
With complication	54 (22%)	214 (25.8%)	5 (50%)	273 (25.2%)
Without complication	190 (77.6%)	610 (73.6%)	4 (40%)	804 (74.2%)
NS	1 (0.4%)	5 (0.6%)	1 (10%)	7 (0.6%)
Total	245 (100%)	829 (100%)	10 (100%)	1084 (100%)

The frequency of these DSARs was 1.9 per 10,000 donors, varying between 1.5 and 2.8 excl. DOM-TOM (table 45).

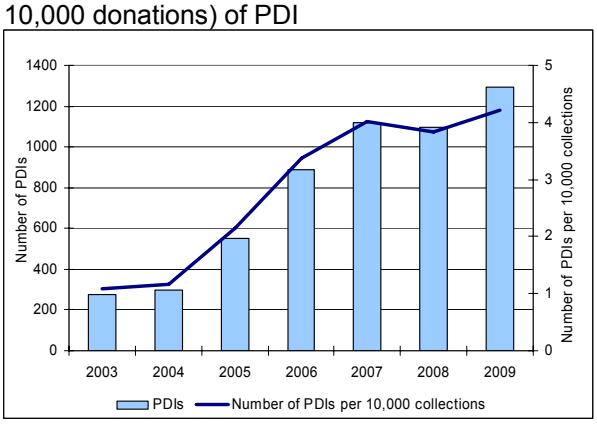
Table 45. Number and frequency of DSARs per inter-region

Inter-regions	Number				Frequency per 100,000 donors			
	2007	2008	2009	2007-09	2007	2008	2009	2007-09
South West	57	38	53	148	2.2	1.4	2.0	2,2
South East	69	82	112	263	1.5	1.8	2.3	1,5
North West	81	62	120	263	2.8	2.5	3.4	2,8
North East	73	75	126	274	1.9	1.8	3.2	1,9
Ile-de-France	36	47	52	135	1.7	2.0	2.5	1,7
DOM-TOM		1		1	0.0	0.3	0.0	0,0
Total	316	305	463	1,084	1.9	1.8	2.7	1,9
Standard deviation excl. DOM-TOM					0,5	0.4	0.6	0.5

3.5. Post-donation information (PDI)

PDI has been declared to Afssaps since October 2002, but only for products having left the EFS after donation.
Their number multiplied by 5 between 2002 and 2009, with a slight decrease in declarations in 2008 (figure 36).

Figure 36. Evolution of the number and ratio (per 10,000 donations) of PDI



4. Work carried out in 2009

4.1. Participation in the drawing up of legislative and regulatory texts

See chapter 1.2.

4.2. 2007-2009 end-of-mandate report by the National Haemovigilance Commission Task Forces

This chapter summarises the different works performed by the 5 TFs during their mandate:

4.2.1. NHVN task force

NB: the NHVN has jurisdiction over the full range of haemovigilance activities.
- During its mandate, it worked to improve the monitoring system, particularly by contributing to improving the quality of the RAR declaration data in e-FIT. It therefore oversaw the changes to the electronic data collection system and the design of e-FIT V2. It also assessed the other monitoring systems (DSAR and SI) and issued proposals for their integration into e-FIT version V3.
- Another of its aims has been to pinpoint the key transfusion safety issues, e.g.:
. Hypervolemic pulmonary oedema, the 5th biggest reaction in terms of the number of declarations, but whose consequences are often serious. We should therefore look for means to prevent this.
. Identito-vigilance,
. Serious adverse reactions affecting blood donors
. The introduction of computerisation in blood banks
- Entrusted by the NHC with monitoring the coherency and harmonisation of the works launched by the themed task forces, the NHVN TF also coordinated the proposals from the other TFs during the design of e-FIT2, particularly the design of the different thesauruses and data sheets.
- Finally, the group recently became involved in drawing up a set of haemovigilance and transfusion safety indicators: network activity indicators and risk indicators.

4.2.2. TRALI/TACO task force

One of the principal objectives of the TF was to describe the epidemiological characteristics of pulmonary oedemas (TRALI and hypervolemic oedemas).
Therefore, the 2007 declarations were subjected to a retrospective study and the 2008 declarations a prospective study. In all, 85 cases of TRALI were analysed and their imputability classified from 2 to 4. Certain cases examined could not be classified as lesion-related or hypervolemic oedemas, most often as a result of a lack of information in the declaration. The results demonstrate, in particular, that the rate of TRALI in relation to the type of LBP was much higher for single-donor FFPs and Aphaeresis platelet concentrates than for packed red blood cells. Very significant regional disparities were observed, but these require confirmation. The TF underlined certain weaknesses observed in the current system: lack of information in the declarations, somewhat unsatisfactory severity rating, denominator (number of transfused LBPs) difficult to obtain, anti-HLA antibody screening techniques not homogeneous throughout the entire territory.

In the short term, there remains the issue of preventing TRALI through donor selection and the benefit-to-risk ratio between TRALI and LBP unavailability. The TF feels that manufacturers could work to reduce the quantity of plasma when this is possible for certain products.

Furthermore, for the TRALI TF, the evaluation of a low risk is, in principle, difficult and the link between death due to a lesion-related oedema and transfusion must be specified: Indeed, as the severity of this adverse effect is closely linked to the clinical condition of the recipient, it is difficult to decide between the different possible causes of death. It should be noted that the upcoming e-FIT V2 programme will make it possible to improve the assessment of the cases, as it will take into account not only the severity of the adverse effect, as is currently the case, but also the patient's evolution.

4.2.3. Allergy task force

● In the course of its mandate, the Allergy TF conducted a statistical analysis of all the cases of serious allergies to plasma declared between 2005 and 2009 and a case-by-case analysis of the serious allergies to VIP-MB declared between 2008 and 2009. This analysis revealed that[38]:

- Regarding the serious RARs of imputability 2 to 4:
Between 2005 and 2009, 1,295,011 units of plasma (FFPs or VIP-SD) were transfused and 59 serious allergic events of imputability 2 to 4 were declared. Based on the hypothesis that the frequency of events was the same with MB-plasma, the expected number of events per 263,539 transfused units in 2008-2009 amounted to 59 x (263,539/1,295,011), i.e. 12.0. The number of declared events for MB-plasma (n=30) was significantly higher than the expected number based on the null hypothesis (Chi2 (1ddl) = 8.35, p<0.001).

- Regarding the serious RARs of imputability 3 to 4:
31 cases were declared over the 2005-2009 period with FFPs and VIP-SD. The expected number for MB-plasma in 2008-2009 was, with the same calculation as before: 31 x (263,539/1,295,011), i.e. 6.3. The observed number of events of grade 3-4 with MB-plasma (n=19) was significantly higher than the expected number (Chi2 (1ddl) = 6.38, p<0.01)
Finally, the difference remains significant if we only take into account the events for which the plasma was in first position in the list of transfused LBPs (for events 3-4: expected number=5.7, observed number=17, Chi2=5.6, p<0.0).

The initials conclusions that can be drawn from this study period regarding the link between serious allergic reactions and transfusions of VIP-MB are therefore as follows:
- The signal compared to other plasma is quite genuine;
- There really are allergic reactions to MB;
- To demonstrate cases linked to the inactivation process, it would be necessary to have access to VIP-MB for skin and in vitro tests, which was only possible on an exceptional basis.
- The analysis of the allergic reactions must be extended to all the LBPs.

● Based on the different allergy RAR forms, the TF drew up a data sheet specifying the mechanism, diagnostic elements and steps to be taken in case of hypersensitive reactions during LBP transfusion, as the international literature contains very little data on this subject.

● The Allergy TF also submitted an opinion to the Director General of Afssaps on the subject of serious allergic reactions associated with transfusions involving VIP-MB. It drew up a procedure for

[38] The results given below may differ from the results in chapters 2 and 3 of this report, the former being from the data analysed and reclassified by the TF experts and the latter from the "raw data" from the e-FIT database.

the investigation of cases intended to be adapted to regional conditions by the regional haemovigilance coordinators (RHC)[39].
In spite of the initial delay in implementing investigations (due to the withdrawal from the market in January 2009 of the Aguettant® methylene blue used in the tests), of the 34 cases declared and 30 cases retained (4 cases were reclassified as grade 1 or imputed to another LBP), 11 skin tests were performed (2 were positive for MB), as well as 4 in vitro tests (including 2 positive for MB): the continuous improvement of the data collected over the course of time made it possible in 7 other analysed cases to rule out the responsibility of MB based on the clinical data.

4.2.4. TTBI task force

● From 2007 to 2009, the TTBI TF assessed 297 declarations of bacterial infections liable to be linked to a transfusion. Based on the imputability table that they drew up[40], the experts retained 11 cases of imputability 3 or 4, including one death in 2008. In 3 cases, the microorganisms in question were found in the donors.
56 bacterial strains responsible for a transfusion-transmitted bacterial infection were centralised by Afssaps; 12 other strains are currently being transferred to this "culture collection".

● The TF is finalising two articles based on the processing of the data from the e-FIT database. One focuses on the epidemiological analysis of the TTBI of imputability 3 to 4 from 2000 to 2007 and the other on the analysis of TTBI of imputability 2 declared from 2000 to 2007.

● It monitored the introduction of the referring laboratories, drew up a data sheet and gave its opinion on the TTBI section of e-FIT version V2.

● The TF experts gave an opinion on the measures to be taken in the event of meningitis, when a donor or a "contact case" is a donation candidate[41]. They also approved the opinion of the Centre National de Référence (French National Reference Centre) and InVS issued following suspected cases of whooping cough in a college where a blood drive took place[42].

● Finally, discussions were held on the introduction of bacterial inactivation for all LBPs.

4.2.5. RCA task force

● The TF worked on the optimisation of the reading and analysis of the serious incident forms (SIF). It validated a thesaurus for use in e-FIT V2 and drew up a standard table for use in recovering the results of root cause analyses (RCA), irrespective of the method used. A training kit is currently being developed for use by the haemovigilance network.

● 440 SAEs (declared in 2009) were studied by the RCA group:
- more than half involved patient identification. This issue was therefore pinpointed as one of the key targets,

[39] Description of the procedure for the investigation of serious allergic reactions during transfusion involving VIP-BM in chapter 6.2
[40] TTBI imputability table in annex 8
[41] Comment: An LBP from an asymptomatic donor or a donor in contact with a patient is not liable to transmit the disease; the risk of transmission is exceptional and any preventive measures are for purposes of precaution.
[42] Opinion: "It is not necessary to provide for eviction or quarantine measures other than those relating to the donor's state of health".

- a large number involved transfused patient identification errors. The treatment of this issue by the group led to the introduction of a specific study with a capture/recapture-type methodology, making it possible to measure the exhaustive nature of these declarations,
- a certain number of incidents were linked to electronic information exchanges (within the same facility or between facilities)
- few declared SAEs were linked to blood donation. However, given the severity of these incidents, root cause analyses were performed.

The group began a specific study of cases associated with errors or near-errors in the transfusion of red blood cells to a patient who should not have received them, the objectives being:
- to estimate the incidence of these transfusion errors,
- to identify the transfusion chain barriers, their weaknesses and strengths.
- to identify factors associated with the failures (or successes) of these barriers

Furthermore, in order to optimise the conclusions of the analyses performed by the task force, this task force developed an "opinion form" that shall be appended to the minutes of the meetings and proposed, e.g.:
- rule and procedure evaluation tools,
- tools for feedback and the sharing of information from SI declarations with the transfusion participants...

● The issues of identification, identito-vigilance and electronic information exchanges (within the same facility and also between facilities), whose relevance extends beyond the scope of haemovigilance (stages of the transfusion chain), were therefore highlighted by the RCA task force, which agreed with other task forces (e.g. NHVN) and institutions on this fact and on the need to quickly look for solutions.

4.3. The new e-FIT V2 application

e-FIT has been continuously improved since its introduction in May 2004:

In 2007, a new RARF and user guide were published online.

In 2008, a complete overhaul of the electronic declaration system was undertaken, in order to integrate the modifications requested by the haemovigilance network, the NHC and the related task forces, as well as the Afssaps haemovigilance unit.
A first "test" version of e-FIT V2 (application without a database) was received by Afssaps in November 2009 and delivered to a group of 15 testers (BDF HVC, CHU HVC and RHC). It was followed in December by a 2nd version (full database). The definitive version of e-FIT V2 entered use in March 2010.

4.3.1. Amendments and upgrades to e-FIT V2

Many changes were included in e-FIT V2, including:
- A new approach to declarations regarding the reporting of the diagnosis(-ses), particularly i) the possibility of choosing 2 diagnoses with a level of certainty of diagnosis and ii) the initial reporting of the diagnosis, in the event of transfusion, irrespective of the causal link with the transfusion, as this link (or non-link) is determined following the enquiry using the level of imputability. This new diagnostic approach aims to limit to the strict minimum the diagnostic categories "diagnosis not listed" or "diagnosis not specified" (previously, the "unknown" category);
- A new approach to the completeness of the data regarding biological and clinical manifestations (figures before and after transfusion), e.g. temperature, blood pressure, haemoglobin concentration or platelet concentration;
- A new approach to "Bacterial infection" diagnosis with reference to the "responsible agent" when the LBP culture is positive, the identified microorganism and imputability 3 or 4;
- The introduction of the ICD 10 classification for reporting of the "principal/secondary pathology" item;
- The removal of the "after the end of transfusion" item and its replacement with the "after the start of the transfusion process" item in order to report the time to onset of the RAE; it is rounded off with the words "transfusion process in progress, closed";

- The introduction of the "ferritin increase" (>1,000 ng/mL) item in the "biological manifestations" part, and the highlighting of the DAT (Direct Antiglobulin Test);
- In the "diagnosis" part, addition of the new diagnoses (hypertensive reaction, hypotensive reaction, lesion-related pulmonary oedema, hypervolemic pulmonary oedema, transfusion inefficacy, dyspnoea not associated with an oedema, drepanocytic haemolysis, etc...) ; "associated pathology" has been removed from the "possible diagnosis" thesaurus as the "principal pathology" but remains in the "secondary pathology" thesaurus.
- The possibility of entering products either individually (in chronological order of their transfusion) or per group in the context part of the product. The preparing BE code and the "number" of LBPs have been deleted.

4.3.2. New RARF user guide and "help balloons"

e-FIT V2 also has 2 new features, intended to improve the quality of the data in the e-FIT database:
1° Online help via help balloons for each of the numbered sections of the RARF.
2° Three new data sheets:
- Allergy
- TRALI / TACOs
- and the "RCA" table

4.3.3. Correction of the incoherencies in e-FIT V1

e-FIT V2 also corrects certain incoherencies or ambiguities that had come to light after 4 years of use of e-FIT V1, particularly:
- deaths associated with intrinsically low-grade RAE (appearance of irregular antibodies, FNHTR);
- grade 0 RARFs including clinical or biological signs of adverse effects, not complying with their definition (isolated dysfunction without RAE);
- completed, unapproved RARFs;
- RARFs with the bacteriological enquiry still "in progress" after several years;
- confusions between the appearance of irregular antibodies and incidents of immunological incompatibility;
- high numbers of unknown RARs.

4.3.4. Recovery of data from e-FIT V1

The e-FIT V2 application recovered data from e-FIT V1, either in its entirety or by modifying it;
- Certain items, such as the HF service/department, allo-immunisations and immunological incompatibilities, etc., were reclassified based on the cross-classification tables;
- The grade-2 RARs were re-assessed based on the international classifications (European Community, ISBT);
- The erythema and bronchospasm items were added and the terms "erythrodermia" and "rashes" were reclassified as "erythema" when the data was recovered, with approval from the TF.

4.3.5. e-FIT V2 user training

Training sessions were held in December 2009 for a panel of users (BE HVC, CHU HVC and HVC), who themselves then become trainers for the HVCs on a local basis. To do so, they received coaching materials (training kit) in the form of a slide show in 4 parts: i) explanation of the new e-FIT design, ii) application screenshots, iii) help balloons and iv) RAE scenarios for the major categories of diagnoses.
Other forms of training, particularly e-learning, are being studied.

4.4. CNIT activity

● In 2009, the CNIT continued the monitoring and assessment of the regional LBP traceability projects (13 meetings, 15 regions),
It was therefore able to note that computerised traceability has been increasing, particularly for blood banks, since the entire EFS switched to using Inlog. However, a major issue remains: this relates to the lack of recommendations in terms of validation:

of exchanges of information between computer systems

of information systems in general and blood issue/relay bank information systems in particular.

This issue has also been revealed in certain declarations of serious adverse events and other events relating to bank software installation, qualification, calibration and monitoring defects.

● The CNIT has also continued its work on updating the AFNOR traceability message norms (norm XP X 97-536).

4.5. Papers and publications

● French haemovigilance data on adverse reactions related to platelet transfusion – 11th European Haemovigilance Seminar (EHS) in Rome, Italy, from 25 to 27 February, 2009
Béatrice Willaert, Mai-Phuong VO Mai, Cyril Caldani, Nadra Ounnoughene, Imad Sandid

● Analysis of the concordance of the opinions of 8 experts from the "Root cause analysis" (RCA) task force relating to declarations of Serious adverse events (SAE) – SFTS Conference, Strasbourg, June 2009
M.P. Vo Mai (1), C. Caldani (1), I. Sandid (1), D. Benhamou (2), Y. Auroy (3), C.N.D. Root cause think tank (1)
(1) Afssaps, Saint-Denis, France; (2) Bicêtre Hospital, Le Kremlin Bicêtre, France; (3) Hôpital Instruction des Armées (Army Training Hospital) – Clamart, France

● Serious adverse events (SAE): two years of experience – SFTS Conference in Strasbourg, June 2009
I Sandid, C Caldani, M-P Vo Mai, B Willaert, N Ounnoughene, for the "Root cause analysis" think tank of the National Haemovigilance Commission (D Benhamou; G Andreu; JP Aullen; Y Auroy; N Canivet; C de Lardemelle; F Desroy du Roure; A François; M Gruber; C Linget; B Loulière; M Perrin; D Rebibo; X Richomme; X Tinard

● Description of the haemovigilance data obtained from the national e-FIT database, regarding "recipient adverse effects" affecting patients under the age of 19 – SFTS Conference, Strasbourg, June 2009
N. Ounnoughene, M.P. Vo Mai, P. Breton, A. Girard S. Chèze, L. Hauser, A. Sailliol, S. Schlanger, P. Renaudier, C. Waller, C. Caldani

● Haemovigilance Newsletter n° 19 – 2009. The themes covered included:
- Provisional management of blood donations at the EFS, Bourgogne-France Comté
- RBC transfusion in aged subjects...
- Haemovigilance data: Description of RAR declarations in the e-FIT database: patients aged over 65 years old

4.6. Other work

4.6.1. Labile blood product (LBP) delivery document

The NHC was contacted in December 2008 by the CHU haemovigilance correspondents regarding their difficulty in applying paragraph 6. "Checking and delivery of LBP in chapter I. – Issue" of the guidelines relating to issue and distribution activities in the Decision dated the 6th November 2006, defining the principles of good practice provided for in article L. 1223-3 of the French Public Health

Code. This chapter specifies that "The delivery of LBPs to the person who transports these products can be based on any document (prescription, copy of the prescription, blood group card, transport bill, etc...) enabling the identification of the recipient. In vital emergencies and immediate vital emergencies, this requirement can be waived."

Firstly, the NHC sought the opinion of several experts. They unanimously felt that "the text does not appear to be applicable and could cause transfusion delays".
Secondly, the Director General of Afssaps demanded the creation of an ad hoc task force to look into this issue. This group, consisting of representatives of the BE, CHUs, RHCs, DHOS, DGS and Afssaps (haemovigilance unit and Human Body Product Inspection Unit), met on 30 September 2009 and submitted proposals to the Director General of Afssaps.

4.6.2. Participation in European and international works

- Annual summary report to the European Commission (1st report in July 2008, 2nd in September 2009). European electronic form;
- Participation in the European Commission "blood" task force workshops
- Participation in the IHN and ISBT task forces;
- Publications in the IHN conferences (see chapter 4.5.).

5. Measures taken and proposed improvements

5.1. Upgrading of e-FIT to e-FIT V2 beta

The occurrence of serious adverse events affecting blood donors led the Director General of Afssaps to decide to notably order the revision of the decisions from 2007 relating to SAEs and DSARs.

This revision shall have a direct impact on the specifications of the e-FIT V3 tool for the declaration of SAEs and DSARs. Under these conditions, in order to have a unique national database for SIFs and DSARFs that avoids multiple entries before the implementation of e-FIT V3, the specifications of an intermediary "e-FIT V2 beta" system for the electronic input of declarations of SAEs and DSARs were drawn up for implementation from the 1st quarter of 2010.
Firstly, the application was designed on a like-for-like declaration basis according to the 2007 decisions. It is solely intended to replace the paper declaration with an electronic declaration. Afssaps, EFS head-office, CTSA, the relevant BE and HF HVCs may therefore be informed by e-mail in real time of the creation and modification of a declaration form.

Regarding the DSARFs, secure access to input data using a health professional card is reserved for BE HVCs via an e-FIT menu.
Regarding the SIFs, the system is the same, though access is also possible for BE and HF HVCs. For the HF HVCs, access is also possible using a health professional card, as for the BE HVCs. There are also plans to propose access using the Finess number of the facility with an access code for HF HVCs who do not have a health professional card. In the latter case, the HVC must publish, sign and send its forms to Afssaps and the RHC as with the paper system.
Afssaps, EFS head-office, CTSA and the RHCs can each extract the data they respectively need from the database.

5.2. Upgrading of e-fit to e-FIT V3

e-FIT V3, which is set for release in 2011, shall constitute a single entry portal for haemovigilance declarations, irrespective of the process involved (RAE, SI, DSAR, PDI): the objective is to retain the same environment with which the participants in the haemovigilance network are familiar. Links between the declarations for the different processes must be provided for situations where at least 2 processes are involved.

e-FIT V3 must also enable the Afssaps haemovigilance unit to take action, directly if necessary, to correct the data in the database. Currently, the data in the database is only the data provided by the declarants (BE and HF HVCs). However, it has been observed that i) the content of the e-FIT V1 database for a given year differs depending on the extraction time and ii) when Afssaps forwards the substantiated opinions of the TFs of the NHC in order to modify the data in the database (essentially regarding diagnosis, the level of severity or level of imputability), they are not always taken into account or only after quite a long time. Therefore, with the implementation of the "Afssaps profile" process in e-FIT V3, the haemovigilance unit will be able to:
- "unlock" a form in order, for example, to add additional information;
- implement modifications, irrespective of the status of the approval of the form by the network's participants. The approval process becomes the Afssaps approval process (traced and open process) and includes a guarantee for the retention of the original declarations (declarations belonging to the HVCs) that are automatically published in PDF format at the time of locking. However, the data processing uses the data from the database after correction by Afssaps.

5.3. The principal points of the revision of the DSAR and SI decisions from May 2007

Three years after their publication and based on experience of the events, it appeared necessary to revise the Decisions regarding the declaration of DSARs and the declaration of SAEs, published in May 2007.
Indeed, the experts of the NHVN and RCA TFs proposed to redefine the following points:

5.3.1. Definition of the scope of declarations

Based on the current scope of declarations, the serious SI and DSAR events (chapter 3.5) have been successfully detected but only as weak signals. In other terms, their severity was successfully noted but not their systemic nature, as this type of event is very rarely declared (or even reported).

5.3.2. The issue of the annual report

The Decisions from 2007, in the absence of an electronic declaration tool and according to the spirit of Directive 2005/61/EC of the European Commission and Directive 2002/98/EC of the European Parliament and the Council, provided for the HFs or BE forwarding the SI and DSAR to it, either by way of an immediate declaration using the serious incident form (SIF) or the serious effect form (DSARF) or by way of a differed declaration in the annual report for SAEs having occurred in their facilities in order to ensure that the declarations are as exhaustive as possible. These annual reports, which only provide quantitative information (tables of figures without causal analysis) are, in practice, of no real use for haemovigilance and transfusion safety. This view, which is shared by the RCA and NHVN task forces, led the haemovigilance unit, after consulting the other departments and services of the Agency, to propose the cancellation of the recovery of the current formats of the annual reports in the revisions of the Decisions from 2007; other procedures for the recovery of the annual reports are being developed by Afssaps, particularly via the e-FIT tool, as is the case with recipient adverse effects.

5.3.3. DSAR declaration

The principal proposals focused on:
- the modification of the definition of the grades of severity in order to make the declaration of the adverse reactions recovered in situ by the BE staff enforceable;
- the modification of the list of adverse reactions to also comply with the international definitions (ISBT, IHN) and make certain diagnostic categories more visible;
- for DSARs occurring during or after Aphaeresis, specification of the medical instruments used;
- the modification of the deadline for the declaration of the adverse reactions in order to increase the responsiveness of the system (currently one month, as a general rule);
- addition of grade 4 (death);
- addition of the notion of DSAR evolution (with or without after-effects);
- tailoring of the declaration procedures to the implementation of e-FIT (online declaration) on the model of the current Decision for effects affecting recipients (RAE);
- the content of annex II (declaration form template) to the limited-service declarations (e-FIT failure); the content of the form shall be the same as the content of the online declaration, which will make it possible in the future to upgrade it and tailor it to requirements more easily, without issuing a new Decision.

5.3.4. SI declaration

It has been particularly proposed to:
- redefine the severity threshold beyond which the SAEs must be declared in order to clarify, in particular, incidents "likely" to cause serious adverse effects; this threshold could take into account the criticality of the transfusion chain stages, based on the works of the NHC task forces;
- specify that the haemovigilance correspondent may be asked to fill in a root cause analysis document, for which the template is supplied by Afssaps;

- reaffirm the role of the RHCs; firstly, in encouraging haemovigilance correspondents to declare either repetitive incidents on a regional basis, or incidents they consider to endanger the safety of transfusions on a regional or national level; secondly, in analysing and monitoring the implementation of the corrective measures by declarant facilities;
- tailor the declaration procedures to the implementation of e-FIT on the model of the current Decision for effects affecting recipients (RAE);
- reserve annex II (declaration form template) to the limited-service declarations (e-FIT failure); delete the words "without adverse effect" as the SI declaration procedures must be the same regardless of whether there is an adverse effect or not; the content of the form shall be the same as the content of the online declaration, which will make it possible in the future to upgrade it and tailor it to requirements more easily, without issuing a new Decision.

5.3.5. PDI declaration

Since its introduction in October 2002, the declaration of PDI to Afssaps has been based on an agreement between Afssaps, EFS and CTSA. To date, no specific Decisions on this declaration have been issued. The declarations are submitted in paper format (fax, letter) and are difficult to process. They also constitute only around 10% of the PDI reported by the BE.

In 2009, 2 preparatory meetings between Afssaps and EFS were devoted to PDI declaration and made it possible to set the content and format of this declaration:

● The proposed definition for the scope of PDI declaration to Afssaps covers:
- firstly, any information sent to the BE after the donation regarding LBPs having left the BE and casting doubt on the safety or quality or the donation and previous donations,
- and, secondly, any information sent to the BE after the donation liable to have an impact in terms of health & safety.

● The principles for the implementation of the RAR declaration process on e-FIT must apply to the PDI declaration process, notwithstanding a few exceptions.

● This declaration form consists of the following:
- general data: source of the information, date of birth and sex of the donor, chronology of the events (date of occurrence, of the donation in question, discovery, reporting to the HVC and date of declaration, which is a system date);
- PDI data: type of information liable to cast doubt on the safety or quality of the donation or previous donations, reporting method and existence, or not, of donations prior to the donation in question;
- blood products involved;
- remarks and administration: informing of the manufacturer and HF and consequences for the recipients, any remarks and conclusion by the HVC, status of the enquiry, recording of the declaration.

6. Assessment of previously-taken measures and follow-up of measures: opinions and recommendations

6.1. The occurrence of a DSAR of grade 4 and imputability 4 and its implications

The first elements of the enquiry were followed by the quick putting in place of an action plan for the EFS, Afssaps and the medical instrument manufacturers (see Speech by the Director General of Afssaps to the NHC dated the 4th December 2009)

6.1.1. Enquiry and subsequent corrective measures by EFS

An enquiry was conducted, on the site of the accident and at the head-office of EFS, by IGAS with Assistance from the Afssaps inspectors and local State services.
Its recommendations led EFS and Afssaps to put in place an action plan. They principally conSAEsted of improving the prevention of the risk of confusion and better dealing with incidents liable to occur during plasma donations. Therefore, a number of manufacturers of Aphaeresis machines, single-use kits and anticoagulant solutions held a materiovigilance meeting with Afssaps, in the presence of users (EFS and Armed Forces Blood Transfusion Centre), in order to discuss the measures that would make it possible to prevent the risk of inversion of anticoagulant and NaCl pouches during Aphaeresis procedures.
A consensual proposal was issued and the connection systems were secured with a view to using a specific connection kit for each type of solution used for plasmaphaeresis. The manufacturers were invited to put in place these new measures as quickly as possible. The selected solution was brought to the attention of the other competent authorities in terms of medical instruments. During the exchanges regarding the increased safety of the Aphaeresis systems, it appeared that other treatment procedures, using pouches of anticoagulants, are liable to cause the same risk of inversion of the connection between the anticoagulant and another solution. These different procedures are in the course of being pinpointed by Afssaps.

6.1.2. Increased monitoring

Until recently, the importance of the value of reporting DSARs, even minor, had not really been realised: the information provided generally gave a low risk for donations of blood and blood components. However, the events of 2009 underlined that these accidents are not always anodyne.

Following the serious accident in question and generally regarding the serious events affecting blood donors, feedback was reciprocally introduced between the BE and the Afssaps haemovigilance unit, including analysis of:
- the measures put in place locally immediately after the DSARs,
- the measures planned in the short and medium term,
- the measures to homogenise practices and manage events taken by EFS,
- the measures to increase the safety of the medical instruments proposed by the medical instrument manufacturers.

A monthly monitoring update on the preparation and implementation of the action plans by Afssaps has been provided since the end of 2009, with the participation of all the agency's relevant departments, under the aegis of the general directorate. In this respect, these events led to consolidation of the efficacy of the alert procedure (inter-departmental) already in place at the Agency that processes the alert signals received, irrespective of their origin.

Furthermore, under the aegis of the NHC, the creation of a multidisciplinary task force entrusted with studying adverse reactions affecting blood product donors will make it possible to better understand the nature of these adverse reactions and to put in place consensual measures in order to prevent their appearance.

To continue this work, Afssaps decided to entrust:
- this new task force with the task of studying adverse reactions affecting blood product donors, in order to better understand their nature, appreciate their criticality and plan for their prevention.
- the NHVN with the task of assessing the monitoring system, based on the definition of the cases by the RCA TF, as well as assessing based on the guidelines (specifications)

6.1.3. Revision of the decisions from May 2007

Upon the implementation of the two decisions relating to the declaration of DSARs and SAEs dated 7 May 2007[43], plans were made to review them after 3 years of feedback.

Based on the current scope of declarations, events were successfully detected in 2009 but only as weak signals. Their severity was successfully noted but not their systemic nature, as this type of event is very rarely declared (or even reported). Accordingly, the NHVN TF and RCA TF mentioned certain inadequacies inherent in the declaration system, particularly:
- inadequacy between the scope of declarations and the objectives of the declaration systems (unclearly defined definitions, confusion between serious events and critical events)
- definition of the cases (unclear concept of potentially serious events, absence of thesaurus, etc.)
- the complexity of the declaration system, particularly for SAEs (use of both immediate declarations and annual report, etc.)
- a lack of sensitivity for SAEs but above all for DSARs. The system does not make it possible to detect non-serious but frequent events,
- the existence of multiple systems, each entirely separate from each other.

Based on this fact, the revision of the decisions from 2007 has now become a priority for the Director General of Afssaps.

6.1.4. The introduction of an immediate electronic declaration system

See chapter 5.1

Currently, there are 3 separate SDAE databases, one at Afssaps, one at EFS and a third combining the HF-BE activity declarations to the RHCs. As these databases do not strictly reflect the same declarations, differences in interpretation between the facilities regarding the events that need to be declared to Afssaps appear in relation to the events processed internally by the facilities' risk management departments.

From the end of 2009, Afssaps decided to urgently put in place an upgrade of e-FIT V2: e-FIT beta. This new version of e-FIT V2 shall offer the haemovigilance network the possibility of immediate

[43] Decision dated the 7th May 2007 setting the form, content and procedure for the transmission of the forms declaring serious adverse reactions affecting a blood donor (DSARF)
Decision dated the 7th May 2007 setting the form, content and procedure for the transmission of forms declaring serious incidents (SIF)

responsiveness, via the simultaneous communication of information to all the participants. The declarants shall have direct access to the DSAR declaration forms for labile blood products but also to the transfusion chain SI forms.

6.2. Serious allergic reactions occurring during transfusions involving VIP-MB

6.2.1. Recommendations regarding serious allergic reactions occurring during transfusions involving VIP-MB

In 2009, with the participation of the Allergy TF, Afssaps sent:
- A letter to healthcare facility managers and transfusion safety and haemovigilance managers, informing them of the potential risk of serious allergic reaction with methylene blue virus-inactivated plasma (VIP-MB) and inviting them to conduct the necessary investigations if faced with any new cases (09/01/2009)
- Warning regarding the correct use of VIP-MB (02/06/2009)
- Procedure for investigation of serious allergic reactions (grades 3 and 4) during transfusion involving VIP-MB – 05/06/09

6.2.1.1. Letter dated 09/01/2009 to healthcare facility managers and transfusion safety and haemovigilance managers

Afssaps sent a letter to healthcare facility managers and transfusion safety and haemovigilance managers, informing them of the potential risk of serious allergic reaction with methylene blue virus-inactivated plasma (VIP-MB) and inviting them to conduct the necessary investigations if faced with any new cases.

VIP-MB undergoes pathogen inactivation treatment using a technique that combines methylene blue and illumination with invisible light. This plasma is intended to replace quarantined fresh frozen plasma (FFPs) which has been progressively stopped being dispensed.

The letter called on them to "maintain an active monitoring approach" as, at this stage, "the hypothesis of a significant risk of serious allergic accidents linked to VIP-MB remains presumptive given the reduction in the number of reports seen over the autumn and the analytical difficulties mentioned earlier". "As in the majority of cases, the reactions seen with blood products are benign; there is no exploratory protocol enabling confirmation of their allergic mechanism. It is therefore necessary, with each new case, to determine if it is really an allergic reaction and if it is really the methylene blue that is involved as, during a transfusion, a patient can also simultaneously receive red blood cell and platelet plasma".

6.2.1.2. Warning dated 02/06/2009 regarding the use of methylene blue virus-inactivated Fresh Frozen Plasma

The Warning on the use of methylene blue virus-inactivated Fresh Frozen Plasma (drawn up based on the assessments by a multidisciplinary group of experts chaired by Professor Dan BENHAMOU) was

intended to specify the indications of VIP-MB, which are the same as for other plasmas (VIP-SD, Leuko-depleted Amotosalen virus-inactivated fresh frozen plasma for Aphaeresis)[44].
It is therefore recommended that any information on the recipient linked with possible use of BM-VIP be included on the LBP prescription, in order to enable the blood transfusion facility (BE) to dispense on a reasoned basis, i.e.:
• Contraindications:
- known allergy to methylene blue
- prior allergic reaction to VIP-MB in the absence of explorations excluding its responsibility
- known or suspected G6PD deficit in adults or children (particularly in case of jaundice of non-determined aetiology)
• Precautions for use:
- prior parenteral contact with methylene blue
- thrombotic microangiopathies.
This document is available on the Afssaps website (http://afssaps.fr).

Afssaps also issued two other recommendations:
- Validation of the method for assaying the residual methylene blue in the methylene blue virus-inactivated fresh frozen plasmas (06/07/2009)
- Use of methylene-blue virus-inactivated Fresh Frozen Plasma (02/07/2009)
Also available on its website.

6.2.1.3. Procedure for the investigation of serious allergic reactions (grades 3 and 4) during transfusion involving VIP-MB – 05/06/09

This procedure cancels and replaces the procedure from December 2008: the Allergy think tank gave its opinion on various points:
- the examination of patients based on the protocol drawn up by the task force
- transfusion recommendations: see 6.2.1
- proposals submitted to the RHC for a common aetiological enquiry procedure

The investigation of serious allergic reactions during transfusion involving VIP-MB should feature 2 stages:

I. Immediate investigations:
These apply to any serious accidents suspected to be allergic, irrespective of the labile blood product (LBP) involved.

Table 46. Recipient samples for the assaying of histamine and tryptase:
3 samples are required:

Sampling deadline	< 30 mins	30 mins to 2 hrs	> 24 hrs
Type of assay	Histamine	Tryptase	Tryptase (base rate)
Type of tube	EDTA	EDTA or dry	EDTA or dry

II. Investigations after 6 weeks
These explorations are specific to VIP-MB.
It is important to store the pouch(-es) of VIP-MB involved at -20°C, disconnected according to the procedure set out in annex B of the "Transfusion-transmitted bacterial infections" data sheet dated January 2008. These products are intended to be used in the in vitro tests, but not for the skin tests due to the break in the chain of sterility. If no native plasma samples and no other pouches of VIP-MB

[44] Since 14 September 2007, Afssaps has authorised the distribution of fresh frozen plasma from aphaereSAEs, leuko-depleted and virus-inactivated with methylene blue and photon exposure (VIP-BM).

from the donor(s) are available, it is important to request a new donation from the donor(s) in order to obtain native plasma and new VIP-MB (with informed consent).

A procedure to investigate serious allergic reactions must be put in place by the RHCs in each region, particularly specifying the sampling systems and the performance of the secondary allergenic assessment.

6.3. Opinions and recommendations of the experts of the TTBI TF

6.3.1. Opinions of the TTBI TF following a PDI declaration (meningitis)

The experts of the TTBI TF were contacted following this PDI. Their opinion on the measures to be taken in the event of meningitis, when a donor or a "contact case" is a donation candidate is as follows: "a LBP from an asymptomatic donor or a donor in contact with a patient is not liable to transmit the disease; the risk of transmission is exceptional and any preventive measures are taken for the purposes of precaution".

6.3.2. Opinions of the TTBI TF following suspected cases of whooping cough

The experts also approved the opinion of the Centre National de Référence (French National Reference Centre) and InVS issued following suspected cases of whooping cough in a college where a blood drive took place: "It is not necessary to provide for eviction or quarantine measures other than those relating to the state of health of the donor".

6.3.3. Recommendations during investigation of suspected TTBIs

The analysis of the RARs by the group's experts showed that in the majority of cases, the direct examination (DE) of the sample(s) of the LBP suspected to be the cause of an adverse effect is only performed when the RAE is of grade 3.
However, as this is a significant examination in the diagnosis (as mentioned in DGS/DHOS Afssaps circular n° 581 dated the 15th December 2003), the experts recommend that this test be performed irrespective of the severity of the RAE and would like this recommendation to be broadly distributed to the participants in the Haemovigilance network during local and regional training courses.
The LBP storage procedures in case of occurrence of a suspected TTBI outside laboratory working hours are specified in the data sheet drawn up by the TF experts, available on the Afssaps website at the following address: http://www.afssaps.fr/.

6.4. Opinions of the TRALI TF on the use of single-donor LBPs sampled from non-nulligravida donors

In a memo dated 29 September 2009, Afssaps was informed of the decision by the EFS to take samples from female donors having had a maximum of two pregnancies in order to prepare therapeutic plasma in case of supply chain issues.

The position of the TRALI TF on this question is summarised below:
"Single-donor LBPs rich in plasma are the LBPs that most expose recipients to a risk of TRALI. The data from the 2007-2008 database suggested that the average incidence of TRALI linked to FFPs and APC varied between 3 and 8 per 105 products over the entire country. The extent of the regional variations showed significant under-declaration and suggested that these figures could be multiplied by 4 to reach the genuine incidence of TRALI. The risk linked to single-donor LBPs rich in plasma is therefore around 10-4. The data from foreign literature support this claim.
The role of anti-leukocyte antibodies is likely in 9 of the 10 TRALI of imputability 3 and 4 with a certain link with the transfusion of secured FFP in 2007-2008 in France. The role of the antibodies acquired during pregnancy is well established in the pathophysiology of TRALI. Therefore, a recent paper proposed an odds ratio of 15 for the development of a TRALI with LBP from a donor containing anti-

leukocyte antibodies compared to a LBP that contains none (Middelburg et al. Transfusion 2008; 48 :2167). The prevalence of these antibodies in female donors increases with the number of pregnancies. A recent major North American study showed that the prevalence of anti-HLA antibodies is 11%, 22.5%, 27.5% and 32.2% after respectively one, two, three and more than three pregnancies (Triulzi et al, Transfusion 2009; 49:1825). The risk of allo-immunisation is therefore highly significant from the first pregnancies. This study also showed that the immunisation remains after the pregnancy.

The TF therefore considers that the reintroduction to the LBP system of single-donor products rich in plasma from non-nulligravida donors exposes recipients to a risk of immunological TRALI, a serious complication that can occur in case of transfusion of LBPs containing anti-leukocyte antibodies, from the first pregnancy. The TF does not have access to the information required to assess and put a precise figure on this risk, but feels that a study and simulation must be performed. Furthermore, given the current state of knowledge, there is no data suggesting that the virus-inactivation processes used for a single-donor product reduce the immunological risk.

Under these conditions, the TF feels that the extension of Aphaeresis donations, for the preparation of single-donor LBPs rich in plasma to non-nulligravida donors must be backed up with measures for the screening of donors with anti-leukocyte antibodies. The TF considered that the introduction of preventive measures based on the screening on non-nulligravida doors is currently hindered by a lack of standardisation, on a national scale, of the techniques for screening for anti-leukocyte antibodies and identifying their transfusional importance, which is not the case for organ grafts. The TF therefore recommends the rapid implementation of a consensual definition of the methods of screening for antibodies and the transfusional significance thresholds. Furthermore, the logistical and technical procedures for such screening would need to be jointly defined with Afssaps, EFS, CTSA and biologists specialised in leuko-platelet immunology. "

This opinion was set out in a letter from the Director General of Afssaps to the Chair of EFS dated 3 December 2009.

7. Summary and prospects

7.1. Highlights of 2009

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

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

- The rate of transfused patients was 8.3 per 1,000 inhabitants; this varied significantly according to age. Except for the DOM-TOMs, this rate differed little from region to region. Furthermore, each patient received an average of 6 LBPs, though this figure varied from inter-region to inter-region.

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

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

1. Recipient adverse reactions (RAR)
- 7,808 RARs were declared in 2009, including 8 of imputability 2 to 4 resulting in deaths (3 TACOs, 2 immunological incompatibilities, 1 allergy, 1 TRALI and 1 post-transfusion purpura). Of these 8 RARs, 7 involved RBC and 1 SC-APC. 4 were of imputability 3 and 4. The RAR declaration rate per 1,000 distributed LBPs was 2.6 and the incidence rate of deaths of imputability 2 to 4 of 0.3 per 100,000 LBPs.

- 5,902 of the 7,808 RARs declared were of imputability 2 to 4: this was the highest level ever reached since the introduction of haemovigilance.

- Regarding allergic reactions in the event of transfusion of VIP-MB, 114 cases of imputability 2 to 4 were declared in 2009, i.e. a frequency of 1 per 1,797 distributed LBPs. However, for the most serious and most certain cases of grade 3 or 4 and imputability 3 to 4 (i.e. 8), the frequency fell to 1 per 25,602 transfusions.

2. Donor serious adverse reactions (DSAR)

The number of DSARs declared in 2009 was 475, i.e. a declaration rate of 15.5 per 100,000 donations. 76% were of grade 2 (adverse reactions requiring external consultation) and 23% of grade 3 (effects having required hospitalisation) and 1 of grade 4 (death).

Of the 3,071,238 million donations, women, donors under the age of 30, Aphaeresis donors and new donors appeared to present a higher risk of occurrence of donor serious adverse effects.

3. Serious adverse events (SAE)
440 SAEs were declared in 2009, distributed as follows: 33 SAEs associated with RARs, 176 SAEs with transfusion of LBP without RAE (declared in the RARF as grade 0) and 231 SAEs without transfusion of LBP.
The rates of declaration of these SAEs were respectively 1.1 per 100,000 LBPs, 5.9 per 100,000 and 7.8 per 100,000 LBPs distributed.
The SAEs were often the result of multiple dysfunctions. 75%, irrespective of their categories, were declared by healthcare facilities.

4. Post-donation information (PDI)
1,295 PDIs were declared in 2009, i.e. 4.8 PDIs per 10,000 samples.
PDIs can have an impact on the quality and safety of the blood products and therefore on the recipients. PDI is essentially information on transmissible disease markers, biological markers and clinical anomalies.

● National Haemovigilance Commission
The 1st mandate of the NHC comes to an end in March 2010. In the course of this mandate, 5 task forces operated under the aegis of the NHC since 2008:
1. NHVN (National Haemovigilance Network) TF
2. TTBI (Transfusion-transmitted bacterial infection) TF
3. TRALI / TACO TF
4. Allergy TF
5. RCA (Root cause analysis) TF
The assessment of these different TFs is summarised in chapter 4.2. It does not, however, exhaustively cover the measures taken. Their principal actions and opinions included:
- the dossier on allergies in the event of transfusion of VIP-MB. This dossier is particularly closely monitored, firstly by observing the precursory signals of any evolution of allergy-type RARs and, secondly, by closely monitoring the availability of alternative plasma therapies in the event of significant VIP-SD production issues.
- accidents affecting blood donors
- the structuring of the NHC and the organisation of the TFs
- the importance of feedback to the network and RHCs
- the upgrading of the e-FIT tool for haemovigilance event declarations
- projects for the international promotion of haemovigilance work.

7.2. Major trends

● Transfusion activity
Consumption of LBPs has continued to increase since 2000 at a rhythm of +1.2% per year. The progression has been greater for VIP (+14%) and PCM (+8%) than for the other products, particularly RBCs.
This change should be partially linked to the slight growth in the number of patients.

● Adverse events and serious adverse events

1. Recipient adverse reactions (RAR)

There has been a stable increase (+0.1%) in the number of declarations of RARs since 2001, with an average of 7,540 declarations per year. However, in relation to the number of LBP transfusions, the rate of declaration was slightly down (3.1 in 2000 and 2.6 in 2009).
Nearly 78% of RARs of imputability 2 to 4 recorded between 2000 and 2009 were declared as FNHTR, allergies and appearances of irregular antibodies.
Among the most serious and most certain diagnoses (grades 3-4 and imputability 3-4), there was an increase in TACOs, allergies and TRALI and, conversely, a decrease in immunological incompatibilities, FNHTRs and ABO incompatibilities. The rate of these serious RARs increased by 1.4 points between the 2000-04 and 2005-09 periods, increasing from 4.8 to 6.2 per 100,000 distributed LBP.

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

3. Donor serious adverse reactions (DSAR)
The declaration of DSARs started in 2006, on a voluntary basis, and 188 forms have since been sent to Afssaps. In 2009, the number more than doubled, reaching 475.

4. Post-donation information (PDI)
The number of PDI declarations has multiplied by 5 since 2003, reaching 1,295 in 2009. The rate of declaration during the last 4 years was 3.9 per 10,000 samples.

7.3. Prospects

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

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

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

8. Annexes

8.1. Key figures

8.1.1. Summary figures

Table 47. Key figures for 2009

General data: Number	Rate
Number of patients transfused: 538,506	Number of patients transfused per 1,000 inhabitants: 8,3
Number of donors: 1,773,374	Number of donors: 4.1% of the population from 18-65 years old
Number of collections: 3,071,238	Number of collections per donor: 1.7
Number of LBPs distributed: 2,979,117 Number of LBPs not traced: 24,388 Computerisation via pivot formats (number of HFs involved and number of LBPs): 147 HFs in 13 regions for 818,211 LBPs dispensed	Number of LBPs distributed per patient: 5.5 Rate of destruction of homologous LBPs: 1.5% Traceability rate: 99.2%%
Number of transfusing HFs: 1,520 of 2,191 HFs Number of blood banks: 668, including 180 issue	
Transfusion effects and incidents: Number	**Rate**
Number of RARs (excluding grade 0 RARF): 7,808 including: • 2,363 imputability 2, • 2,555 imputability 3 • 1,215 imputability 4 Number of deaths, imputability 2 to 4 – enquiry closed 8 including: • 4 imputability 2, • 3 imputability 3 • 1 imputability 4	Rate of RAE, all grades and imputability included, per 1,000 LBPs: 2.6 Rate of death of imputability 2-4 per 100,000 LBPs: 0.3
Number of SAEs: 436 including: • 231 SAEs without transfusion • 176 declared in the RARF as grade 0, • 33 RAR of grade ≥ 1 with dysfunction,	Rate of SAEs with LBP per 100,000 LBPs: • 7.8 for SAEs (SI without transfusion) • 5.9 for SAEs declared in the RAR as grade 0 • 1.1 for SAEs with associated RAR grade ≥ 1
Number of DSARs: 475	Rate of DSARs per 100,000 collections: 15.5
Number of PDIs: 1 295	Rate of PDIs per 10,000 collections: 4.2

8.1.2. Distribution of RARs per product and product family

		Diagnoses[45]												
Family of products	Type of product[46]	DIA	FNHTR	Allergy	Immunological incompatibility	Hyper-volemia	TRA-LI	Bacterial infection	Viral infection	Post-transfusion purpura	haem.	unknown	Other	Total
erythrocyte	RBC	1,652	1,284	376	164	249	26	2	2	2	1	343	41	4,142
	AUTO-RBC		1											1
	RB											3		3
	WB								1					1
	APC	55	88	570	72	9	11	4				89	7	905
platelet	APC-IA	2	1	17	2							2		24
	APC-SS	14	70	155	39		1	2				42	9	332
	PCM	12	6	10	5							6		39
	PCM-IA	3	6	9	2	1	1					3	2	27
	PCM-SS	53	36	55	30	2		2				26	1	205
plasma	FFPs	1												1
	VIP-SD	2	3	48		2	1					1		57
	VIP-MB	1	8	114	1	3	1					5	3	136
	IA-VIP		4	7								1		12
AGC		1	1				1							3
BP-GEN												1		1
NON-LBP												6		6
NS		4		1	1	1								7
Total		1,808	1,508	1,362	316	267	43	10	3	2	1	528	63	5,902

[45] Key: DIA: appearance of irregular antibodies, FNHTR: febrile non-haemolytic transfusion reaction, other: other immediate or delayed effects, haem: haemosiderosis
[46] Product declared to be the most likely to have caused the RAR during the transfusion process

Table 49. RARs of grade 3-4 and imputability 3-4, enquiry closed, according to the type of product and diagnosis in 2009

Family of products	Type of product[47]	Diagnoses									
		Hyper-volemia	allergy	TRALI	Immunological incompatibility	Bacterial infection	DIA	Post-transfusion purpura	unknown	other	Total
erythrocyte	RBC	72 (9)	10 (0)	13 (5)	6 (4)		1 (1)	1 (1)	2 (0)	2 (0)	107 (20)
platelet	APC	5 (1)	21 (3)	7 (4)	2 (1)	3 (3)			2 (0)		40 (12)
	APC-IA		2 (1)								2 (1)
	APC-SS		7 (1)						2 (0)		9 (1)
	PCM								1 ()		1 (0)
	PCM-IA				1 (0)					1 (0)	2 (0)
	PCM-SS		3 (0)			1 (1)			2 (0)		6 (1)
plasma	VIP-SD		4 (1)								4 (1)
	VIP-MB	2 (1)	8 (1)	1 (0)					1 (0)		12 (2)
AGC				1 (1)							1 (1)
NS		1 (0)									1 (0)
Total grade 3-4 and imputability 3-4		80 (11)	55 (7)	22 (10)	9 (5)	4 (4)	1 (1)	1 (1)	10 (0)	3 (0)	185 (39)

Reading: values between brackets = RARs of grade 3-4 and imputability 4

8.1.3. Organisational data per inter-region

Afssaps supplies a selection of data from 6 inter-regions, covering the 26 French regions. In addition to the tables provided in this report, the data is split into 6 themes: transfused patients, donors and donations, HF activity, BE activity, bank activity, network management... They supply an overview of the statistics for all the regions of Metropolitan France and the DOMs and add to the information already distributed by the RHCs for the regions and departments.

Table 50. Number of blood sites and transfusing HFs per inter-region in 2009

Inter-region	BE sites	Transfusing HFs*
South West	24 (14.5%)	210 (13.8%)
South East	44 (26.7%)	409 (26.9%)
North West	31 (18.8%)	272 (17.9%)
North East	32 (19.4%)	313 (20.6%)
Ile-de-France	30 (18.2%)	273 (18%)
DOM-TOM	4 (2.4%)	43 (2.8%)
Total	165 (100%)	1 520 (100%)

* Definition: see chapter 1.3, note 6, Data to be used with caution due to the existence of double entries and missing data

[47] Product declared to be the most likely to have caused the RAR during the transfusion process

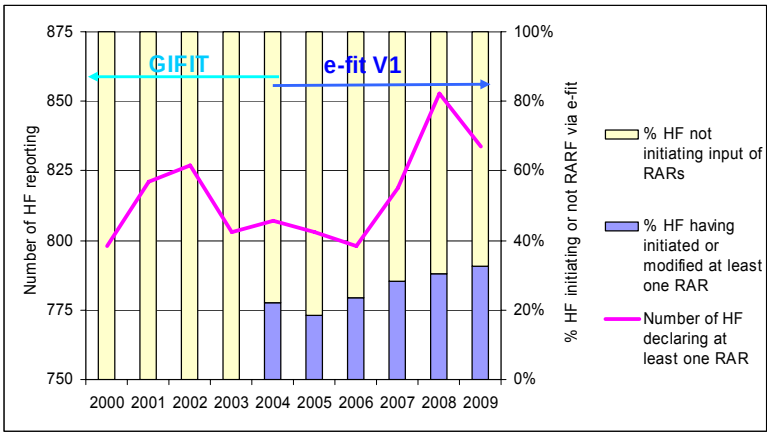
Table 51. Number of HF and BE haemovigilance correspondents and RHCs per inter-region in 2009

Inter-region	Number of transfusing HF HVCs*	Number of BE HVCs	Number of RHCs
South West	207 (14.6%)	24 (15.8%)	5 (17.2%)
South East	339 (23.9%)	38 (25%)	6 (20.7%)
North West	272 (19.2%)	27 (17.8%)	4 (13.8%)
North East	292 (20.6%)	27 (17.8%)	8 (27.6%)
Ile-de-France	268 (18.9%)	31 (20.4%)	3 (10.3%)
DOM-TOM	40 (2.8%)	5 (3.3%)	3 (10.3%)
Total	1418 (100%)	152 (100%)	29 (100%)

* Data to be used with caution due to the existence of double entries and missing data

8.1.4. e-FIT tool usage indicator

Figure 37. Number of HFs declaring at least one RAE according to the declaration system and process



Since 2004, the HF haemovigilance correspondents have had the possibility of electronically declaring RARs directly via e-FIT[48]. In 2009, there were 271 of them. Their declarations constituted 60% of all the RARs from the e-FIT database.

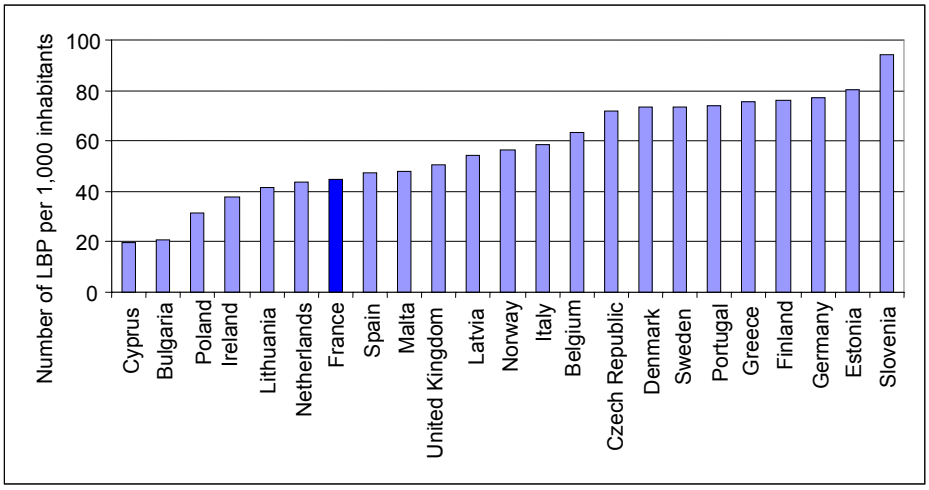
8.1.5. European Community data

Warning: the rates and incidences in this chapter were calculated based on the data extracted from the "SARE Annual activity report 2008" of the European Community dated 30/11/2009.
It should be noted that, although the member states of the European Union use the same standard declaration form, the content of the variables can sometimes differ somewhat from country to country. This content is progressively being harmonised through the introduction by the European Commission of the "Common approach" document for the definition of variables.

[48] The BE HVCs/BE sites have declared RARs electronically since 1994 (firstly via the GIFIT application, from 1994 to 2004, and subsequently via e-FIT).

8.1.5.1. Consumption of LBPs in 2008

Figure 38. Number of LBPs distributed per 1,000 inhabitants in 2008 per member state ("units issued")



The consumption per 1,000 inhabitants is not homogenous for the 23 member states, above. The ratio is 1 to 5, i.e. 20 LBPs issued per 1,000 inhabitants in Cyprus and 94 in Slovenia.

The mathematical average for these countries was 56 LBPs issued per 1,000 inhabitants (standard deviation of 19.9).

8.1.5.2. Recipient adverse reactions (RAR) or incidents without transfusion of LBPs (SI)

Figure 39. Incidence of deaths* of imputability 3-4 according to the type of LBPs issued in 2008

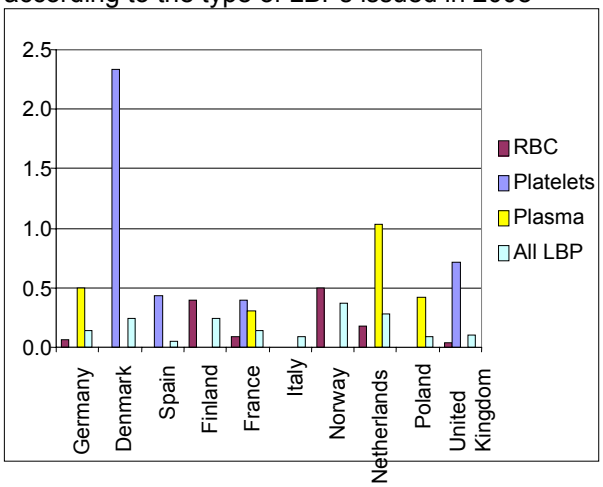
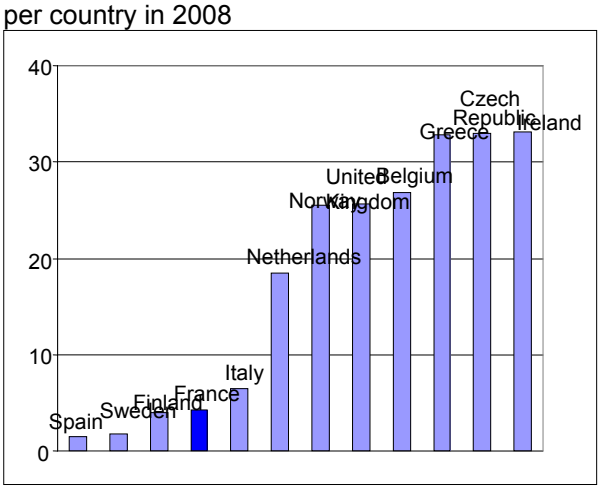


Figure 40. The number of SAEs without transfusion of LBPs per 100,000 LBPs distributed per country in 2008



*In 2008, Denmark, Spain and France declared 1 death of imputability 3-4 with platelets and Great Britain 2.

8.2. List of strains centralised since 2003

Table 52. The microorganisms isolated in the 22 TTBIs were:

Bacterial species	Number of strains
Bacillus cereus	4
Enterobacter cloacae	2
Enterococcus faecalis	2
Escherichia coli	7
Klebsiella pneumoniae	6
Proteus mirabilis	1
Serratia marcescens	4
Staphylococcus aureus	15
Staphylococcus epidermidis	9
Staphylococcus epidermidis + Staphylococcus hominis	2
Streptococcus dysgalactiae	3
Yersinia enterocolitica	1
Total	56

For each TTBI, 2 to 5 strains of microorganisms isolated from the LBP culture, haemoculture or any other specimen cultured during the investigation were centralised by Afssaps (i.e. 56 bacterial strains stored – 30th October 2009).

8.3. Definitions

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

The following definitions apply for the application of article R1221-23 of the French PHC:
1° Adverse effect: a harmful reaction affecting donors and related or likely to be related to the blood collection or affecting recipients, related or likely to be related to the administration of a labile blood product;
2° Serious adverse effect: an adverse event resulting in death or danger of death, resulting in disability or incapacity, or provoking or prolonging hospitalisation or any other morbid condition;
3° Incident: an incident related to the collection of blood, biological qualification of donations, preparation, storage, distribution, issue or use of labile blood products, due to an accident or error, likely to affect the safety or quality of the product and result in adverse events;
4° Serious incident: an incident likely to result in serious adverse effects.

8.3.2. Severity levels

8.3.2.1. Severity of RARs

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

8.3.2.2. Severity of DSARs

Grade 4: death
Grade 3: serious (requiring medical treatment)
Grade 2: moderate severity – prescription of external consultation by the BE doctor

Grade 1: minor severity with or without medical treatment

8.3.2.3. Severity of SAEs

There are no levels of severity defined for transfusion chain SAEs.
As a reminder, the SAEs currently declared in the RARFs as grade 0 correspond to one or more dysfunctions in the transfusion chain having resulted in the inappropriate transfusion of a LBP without any clinical and/or biological consequences being observed in the recipient at the time of the report. However, while awaiting the implementation of the electronic declaration of all SAEs, these SAEs in "grade 0" RARF continue to be declared using e-FIT in order to enable their analysis.

8.3.3. Imputability levels

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

8.3.3.1. Imputability of RARs

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

From March 2010, with the introduction of e-FIT V2, the definition of the imputabilities in Directive 2005/61/EC shall replace by the current definition in e-FIT V1.

Table 53. Equivalent levels of imputability: European Commission and France

DIRECTIVE 2005/61/EC		French regulations	
0	Excluded	0	Excluded
	Improbable	1	Doubtful
1	Possible	2	Possible
2	Probable	3	Likely
3	Certain	4	Certain

8.3.3.2. Imputability of DSARs

For each adverse effect declaration, a case-by-case analysis should make it possible to establish a causal 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 there is proof beyond doubt, making it possible to attribute the adverse effect to the blood or blood component donation;
Imputability 2: Probable: when the available assessment data gives strong encouragement to attribute the adverse effect to the blood or blood component donation;
Imputability 1: Possible: when the available assessment data does not give strong encouragement to attribute the adverse effect to either the blood or blood component donation or to other causes.
Imputability 0: Excluded or improbable: when there is proof beyond doubt, making it possible to attribute the adverse effect to causes other than the blood or blood component donation, or when the available assessment data gives strong encouragement to attribute the adverse effect to causes other than the blood or blood component donation.

Imputability NE: Non-evaluable: when the data is insufficient to assess the imputability.
N.B.: these are the levels defined in European Commission directive 2005/61/EC.

8.3.4. RARF investigation levels

Level 0: Cannot be performed
Level 1: In progress
Level 2: Closed
Level 3: Not performed

8.3.5. Distribution and issue definitions

Decree n°. 2006-99 dated 1 February 2006 art. 2 gives the following definitions:
1° Distribution of labile blood products: the supply of labile blood products by a blood transfusion facility to other blood establishments, to healthcare facilities that manage blood banks and to manufacturers of health products derived from human blood or from its components;
2° Issue of labile blood products: the issue of labile blood products on medical prescription for their administration to a given patient. When issue LBPs, it is essential to verify immunological compatibility, in compliance with the medical prescription and the implementation of haemovigilance rules.

8.3.6. Whole blood donation and Aphaeresis donation

Whole blood donation consists of collecting blood in a sterile pouch, by way of a venipuncture. The sampled volume cannot exceed 13% of the estimated whole blood volume of the donor nor exceed 500 ml. Blood donation is possible from 18 to 70 years old, 6 times per year for men and 4 times per year for women (Order dated the 12th January 2009 setting the selection criteria for blood donors).

Aphaeresis donation (simple or combined) makes it possible to obtain, from a single donor and using a separator, one or more blood products ready to be labelled, stored and distributed (platelets, plasma, red blood cells, granulocytes). The Aphaeresis sampling technique makes it possible to sample, separate the plasma from the cells and leuko-deplete at the same time. The blood components for sampling are separated by centrifugation and stored, whereas the non-sampled components are re-injected into the donor. The most common forms of Aphaeresis donation are plasmaphaeresis (plasma sampling) and cytAphaeresis (platelet sampling) but other types of donations using this technique are practiced ("double red", granulocyte sampling, etc...).

8.3.7. The different types of HBBs

1° Issue HBBs: HBBs that stores the labile blood products distributed by the referring blood transfusion facility and dispenses them to a patient hospitalised in a healthcare facility;

2° Emergency HBBs: HBBs that stores only the group-O red blood cells and group AB plasmas distributed by the referring blood transfusion facility and dispenses them in case of vital emergency to a patient hospitalised in a healthcare facility. The maximum number of units of labile blood products that can be stored and dispensed by an emergency bank is set in the agreement provided for in article R. 1221-20-2 entered into between the healthcare facility and the referring blood transfusion facility;

3° Relay HBBs: HBBs that stores the labile blood products dispensed by the referring blood transfusion facility in order to transfer them to a patient hospitalised in a healthcare facility.

An authorised issue HBB can perform the activities of an emergency HBB, as well as the activities of a relay HBB, without demanding additional permission from the regional health agency.

Reference: Article D1221-20, Modified by Decree n°2010-344 dated 31 March 2010 – art. 10

8.3.8. Definition of the inter-regions

Table 54. 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								

These departmental groups were inspired by the French telephone area codes groups.

8.3.9. List of LBP abbreviations

Table 55. List of abbreviations used

Type of LBP	Abbreviations	LBP definition
Homologous	WB	Whole blood
	RB	reconstituted blood
	AGC	Aphaeresis granulocyte concentrate
	RBC	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
	VIP-MB	Plasma Virus-inactivated with Methylene blue
	VIP-GEN	Virus-inactivated plasma
	VIP-SD	Plasma Virus-inactivated with Solvent detergent
	CTSA	CTSA plasma
Autologous	WB-AUTO	Whole blood
	RBC-AUTO	Packed red blood cells
	APC-AUTO	Aphaeresis platelet concentrate
	FFP-AUTO	Fresh frozen plasma
Others	GEN-R	Erythrocyte family
	BP-GEN	Generic blood product
Non-LBP	NON-LBP	Non-LBP

8.4. Glossary

AE: Adverse effect
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 health products safety agency)
ALI: Acute Lung Injury
AABB: American Association of Blood Banks
APO: Acute pulmonary oedema
ARDS: Acute Respiratory Distress Syndrome
ARS: Autorité de Sûreté Nucléaire (Nuclear Safety Authority)
BE: Blood Transfusion Facility
CDC: Centres for Disease Control and Prevention
CHU: Centre hospitalier universitaire (University hospital centre)
CMV: cytomegalovirus
APC: apheresis platelet concentrates
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)
DG SANCO: European Union Directorate-General for health and consumers
DGS: Direction Générale de la Santé (General Directorate for Health)
DH/DHOS: Direction des Hôpitaux / Direction de l'Hospitalisation et de l'Organisation des Soins (Hospitals Directorate / Hospitalisation and Healthcare Organisation Directorate)
DIA: Determination of irregular antibodies
DIC: Disseminated intravascular coagulation
Distributed LBPs: LBPs from the distribution records of the EFS or CTSA
DOM-TOM: French Overseas Department-Territory
DRASS: Direction Régionale des Affaires Sanitaires et Sociales (Regional Health and Social Affairs Directorate)
DSAR/DSARF: Donor serious adverse effect/donor serious adverse effect form
EC: European Commission
e-FIT: NHVN Internet application introduced on the 24th May 2004, only accessible by NHVN participants: HF HVC, BE HVC and blood sites HVC, RHC, Afssaps, CTSA and EFS
EFS: Etablissement français du Sang (French Blood Transfusion Organisation)
ENEIS: Etude Nationale sur les Evénements Indésirables liés aux Soins (National Study on Treatment-related Adverse Events)
EURORDIS: federation of associations of patients and individuals active in the field of rare diseases (www.eurordis.org)
EUSTITE: European Union Standards and Training for Inspection of Tissues Establishments
FNHTR: Febrile non-haemolytic transfusion reaction
FY: Duffy
GIFIT: Previous transfusion incident form computer management application
GVH: graft versus host reaction
HBV: Hepatitis B Virus
HCV: Hepatitis C Virus
HF: Healthcare Facility
HIV: Human Immunodeficiency Virus
HLA: Human Leukocyte Antigen
HVC: Haemovigilance correspondents
ICD 10: International classification of diseases.
IGAS: Inspection Générale des Affaires Sociales (General Inspectorate for Social Affairs)
IHN: International Haemovigilance Network
INTS: Institut National de la Transfusion Sanguine (French National Blood Transfusion Institute)
InVS: Institut de Veille Sanitaire (Health Monitoring Institute)

ISBT: International Society of Blood Transfusion
JK: Kidd
LBP: Labile Blood Products
MEDDEV: Vigilance and post-market surveillance guide for industrialists and competent authorities, describing the resources to be implemented in order to comply with the European requirements in terms of vigilance systems
http://ec.europa.eu/enterprise/sectors/medical-devices/documents/guidelines/index_en.htm
NA: Not assessable
NaCl: sodium chloride, a chemical compound with the formula NaCl
NCTA: Non-conventional transmissible agents
NHC: National haemovigilance commission
NHVN: National Haemovigilance network
NS: Not specified
PDI: Post-donation information
PHC: Public Health Code
PSPH: Private healthcare facilities participating in the public hospital service
RARF: Recipient adverse reaction form
RAEB: Refractory anaemia with excess of blasts
RH: Rhesus
RHC: Regional haemovigilance coordinator
RPOB: Recovery of peroperative blood
RSS: health & safety meeting for the permanent health watch system in accordance with the law dated the 1st July 1998 and the law dated the 9th May 2001
SARE: Serious adverse reactions and events
sCSTH: sub-commission responsible for transfusion safety and haemovigilance
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 vigilance and transfusion therapeutics society)
SAE/SAEF: Serious adverse events / serious adverse events form
TACO : Transfusion associated circulatory overload
TAD: Transfusion Associated Dyspnoea
TF: Task force
TRALI: Transfused-related acute lung injury
TTBI: Transfusion-transmitted bacterial infection
UNCAM: Union Nationale des Caisses d'Assurance Maladie (National Health Insurance Fund Union)
WB: Whole blood