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# 2002 Annual Report Haemovigilance Unit

# National Data

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## **Foreword**

As the previous report in 2001, the objective of the present "2002 Report" is to provide health care professionals and the public with an updated homogeneous information on the haemovigilance system in France. Such a procedure lies within a context of information exchange and submission between the great many actors of the system, either at national, regional, local or even international levels.

Most of the European states are now in the process of or have been developing a haemovigilance system intended to discard a certain number of risks related to transfusion. France is known for the efficacy of its system, which is the oldest in Europe and probably in the world too, and wishes to make its contribution to the development of references in the field of haemovigilance.

*The 2001 report is available on the site of the Afssaps at*

*<http://afssaps.sante.fr/pdf/5/hmv2001.pdf> or <http://afssaps.sante.fr/ang/indang.htm>*

*The 2002 report will also be available on the site of the Afssaps*

# 1. Introduction

## 1.1. Reminder of the main legal and institutional aspects

### 1.1.1. Organisation

Haemovigilance represents the system of vigilance relating to transfusion, applying from the transfusion of blood or blood components to the follow-up of recipients. In accordance with the Public Health Code:

- **Article R. 1221-16:**  
*"Haemovigilance is an element of transfusion safety. It implies for all prepared labile blood product unit:*  
  
*1° The statement of any unexpected or adverse event associated with or likely to be associated with the therapeutic use of the product;*  
  
*2° To collect, keep and give easy access to information relating to the blood product collection, preparation and use as well as to information relating to the events mentioned in 1°;*  
  
*3° the evaluation and use of such information in order to prevent any unexpected or adverse event from happening, related to the therapeutic use of these labile blood products.*
- **Article R. 1221-17:**  
*The French Health Products Safety Agency has ensured the implementation of haemovigilance. It defines the orientations of haemovigilance, leads and coordinates the actions carried out by the various participants and sees to the respect of the surveillance procedures organised by the present section. If the cases arise, it takes the appropriate measures in order to assure transfusion safety or refers to the competent authorities.*
- **Article R. 1221-18:**  
*The French Health Products Safety Agency and the Etablissement français du sang inform each other about any transfusion incident.*

The national haemovigilance system now gathers several thousands of health care professionals. The role of each one of them is specified in Articles R.1221-16 and further articles in the Public Health Code, that is to say Articles R.1221-27 (HCC), R.1221-23 (EFS), R.1221-36 (RHC), according to the following typology:

#### **At the local level,**

- The haemovigilance correspondents in BTCs and those in health care centers who carry out transfusions, that is to say more than 2,200 haemovigilance correspondents (more generally, the 8,000 staff of the Etablissement français du sang -EFS)
- 50,500 potential prescribers and nursing staff directly involved daily.
- the biologists and technicians particularly involved in immunohaematology and blood collection/storage.
- the staff involved in vigilance functions, that is to say almost 2,000 professionals.

There exists a close cooperation between the professionals at blood transfusion centers and those working at health care centers. In fact, haemovigilance consists in making the whole transfusion process safe, from donor to recipient. The liability engaged is that of the Etablissement français du sang (local transfusion site) from the donor (product collection) up to the act of distributing these products. From the management of the product after its distribution up to the transfusion, it is that of the health care center where the patient is hospitalized.

**At the regional level,** the 28 regional haemovigilance coordinators, doctors or hospital practitioners (or equivalent qualification)

**At the national level,** since July 1st, 1998, the date when the regulation concerning the

reinforcement of the public health surveillance and health safety control of blood products for human use was enforced, the Afssaps has ensured the implementation and coordination of the vigilance systems.

In particular, it centralises the directly or indirectly collected data relating to haemovigilance, reports to parent authorities such as the DGS and the DHOS and works in close collaboration with organisms such as the InVS and the INTS. The French Health Products Safety Agency (Afssaps) and the Etablissement français du sang (EFS) shall inform each other about any transfusion incident.

The health care center accreditation results these last years have shown that the haemovigilance network is one of the better structured and the most operational organisations among the public health surveillance networks. Indeed, as a result of a common awareness of the public health authorities and the professionals with a practical background, haemovigilance has contributed to improve the whole transfusion process quality, thus participating to avoiding the occurrence of serial events such as those known for last century.

### 1.1.2. Transfusion incident notification

Three articles of the Public Health Code principally specify the regulatory aspects about it:

- **Article R. 1221-40:**  
*Any doctor, chemist, dental surgeon, midwife or nurse who is informed about the administration of a labile blood product to one of their patients and who notices an unexpected or undesirable effect due to, or likely to be due to this product shall immediately notify it to the haemovigilance correspondent at the center where the product was administered. Failing that, he/she will notify it to any blood transfusion center or health care center haemovigilance correspondent who will transmit the information to the competent haemovigilance correspondent.*  
*The haemovigilance correspondent of the center in which the administration of the product involved took place carries out the appropriate investigations and examinations in the related department. He/she informs the haemovigilance correspondent at the blood transfusion center which distributed the product involved and, in collaboration with the latter, fills in a transfusion incident report form, a copy of which is added to the patient's medical records.*  
*If undesirable effects likely to be due to a labile blood product have appeared in a patient to whom blood-derived medicines were also administered, a copy of the transfusion incident report form is transmitted to the blood-derived medicine pharmacovigilance correspondent at the health care center in which these medicines were administered.*
- **Article R. 1221-41:** *The French Health Products Safety Agency, the Etablissement français du sang and the regional haemovigilance coordinator shall receive the transfusion incident report forms simultaneously.*
- **Article R. 1221-42:** *Following the advice given by the Etablissement français du sang, a technical directive of the French Health Products Safety Agency determines the transfusion incident report form layout and content and transmission conditions. This directive defines the cases and situations in which it is not necessary to transmit a report form.*

## 1.2. 2002 transfusion figures

### 1.2.1. Number of blood donations

In 2002, 2.5 million blood donations, among which 14.8% in new donors, were collected. This represents an increase of 1.2% compared to the year 2001. The donors' epidemiological data are itemized and analysed by the Institut national de veille sanitaire. Concerning the viral risk, for 2002, 36 donors were confirmed to be positive for HIV, 58 for HTLV, 289 for HCV and 433 for HBs Ag. Over the period 2000-2002, the residual risks were estimated before the use of the viral genomic detection (VGD) on each blood donation, in a proportion of 1/1,400,000 for HIV, 1/1,000,000 for HCV and 1/400,000 for HBV. Since the use of the VGD on July 31<sup>st</sup>, 2001, the serologically silent window was reduced to 12 days for HIV and 10 days for HCV, and the updated residual risk is 1/2,500,000 for HIV, corresponding to one blood donation per year, and 1/6,650,000 for HCV, corresponding to an average of one potentially contaminating donation in



three years. (InVS source)

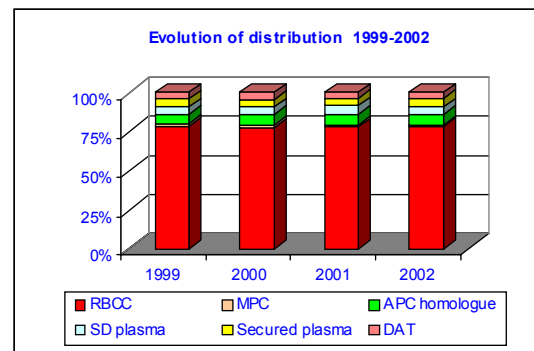
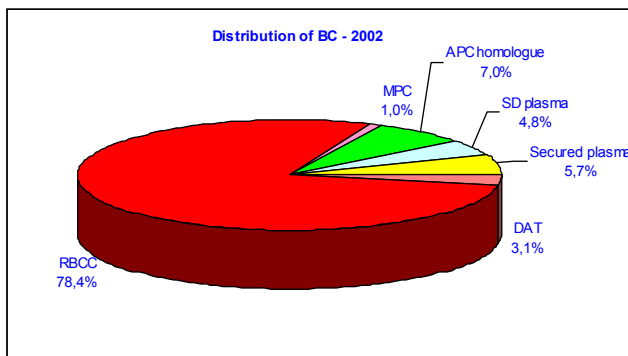
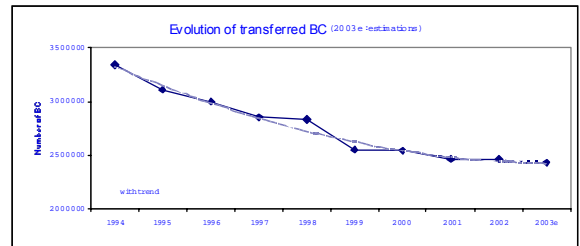
### 1.2.2. Number of distributed products

#### Number of blood collections and blood products transferred in 2002

Blood collections	2,543,416
Distributed BC	2,471,875

Source: EFS

In 2002, for the first time since several years, the BC transferred to blood transfusion centers is slightly increasing, whereas the evolution over the past ten years globally showed a consistent decrease, from 2 to 4% per year without distinction of products. The figure for 2003 is a projection calculated from the data of the past years.



Source: EFS

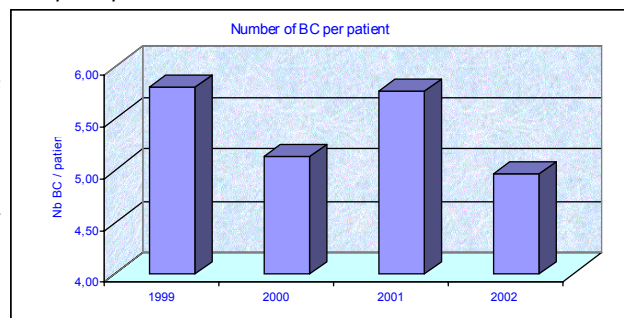
The product type distribution has been quite stable with a fresh plasma/red blood cell concentrate ratio in the order of 1/8. It is also to be reminded that the distribution of platelet concentrates is mainly represented by APCs (1 MPC for 7 APCs) and that the distribution of fresh plasma, donor retested, is slightly superior to the distribution of SD plasma.

### 1.2.3. Patients data

#### 1.2.3.1. Number of transfused products per patient in 1999-2002

The number of transfused products per patient still appears to be quite difficult to obtain and to evaluate, as well as the total number of transfused patients. The "RHC activity reports", which gather data from more than 1,500 health care centers carrying out transfusions, evaluate the number of patients in the order of 512,000 for 2002 (527,000 in 2001).

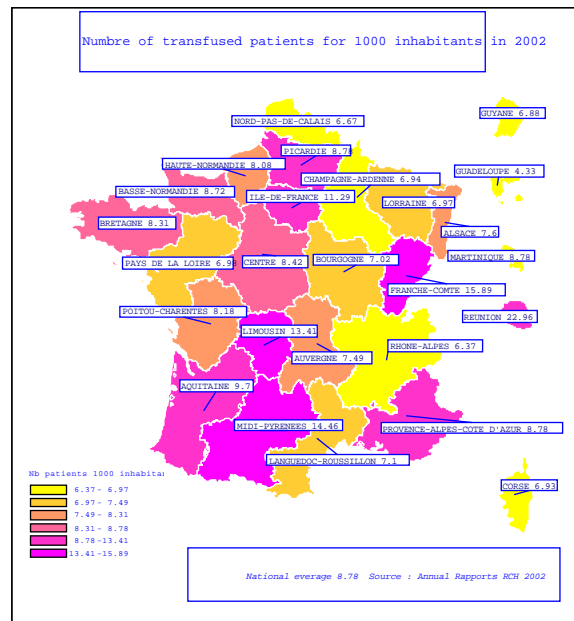
It is to be noted that a national investigation "Storage in HCC" conducted by the same RHC indicated a much lower figure, that is to say 400,000 patients transfused in 2002.



#### 1.2.3.2. Number of transfused patients for 1,000 inhabitants in 2002

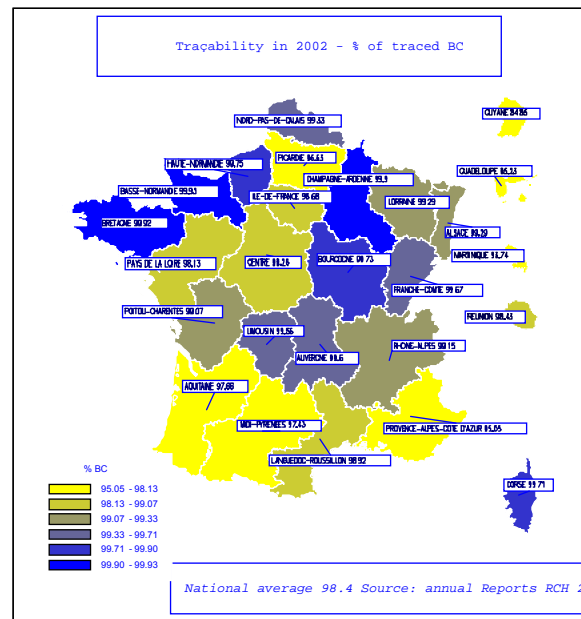
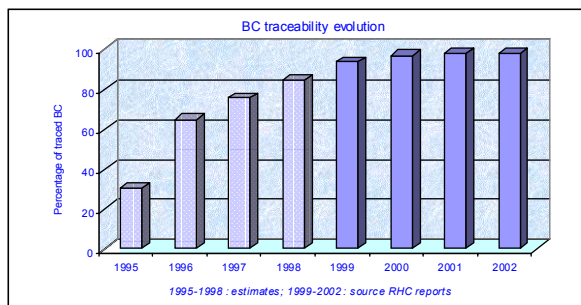
The national ratio is 8-9 transfused patients for 1,000 inhabitants (interval  $\pm$  a standard deviation [5.93;11.49]).

Source: 2002 RHC annual report



## 1.2.4. Traceability of distributed products by region in 2002

In 2002, the traceability of labile blood products reached 97.93% (for 22 regions, 4 regions out included). Therefore it is still slightly increasing compared to the last two years, the last percentage point hundredths being the most difficult to gain. However, implementing traceability computerization projects should help to complete the progression.



Source: 2002 RHC annual report

## 2. Haemovigilance context in 2002

### 2.1. Present preoccupations

#### 2.1.1. Alert notification

##### 2.1.1.1. Haemovigilance alerts

##### 2.1.1.1.1. Recipient incidents

The Afssaps haemovigilance unit receives approximately 100 alert Transfusion Incident report Forms (TIR) a week (new or modified) by fax or post, and between 150 and 250 TIR via the GIFIT database. These TIR are analysed daily by the unit doctors.

**Definition of alert TIRs: paper TIRs of grade 2 to 4 and grade 1 involving or likely to involve the safety of at least another recipient as well as grade 1 likely to be related to the transfusion equipment used.**

The year 2002 was characterized by a great many events, among which the following six:

### **Hyperphosphataemia**

A non-controlled hyperphosphataemia was notified in Ile de France in May 2002. It occurred with a female patient aged 67 with chronic renal failure after the transfusion of 14 SD plasmas. It was notified as a grade 1 incident with an imputability of 4, and was listed in the diagnosis category "other non listed immediate incident". No clinical sign was mentioned on the report form. This notification allowed the BTC to identify a high level of phosphate ions in the SD plasmas and was at the origin of a modification of the production process as well as a recommendation for the use of SD plasma ~~MA~~s.

### **ABO incidents**

24 ABO errors with imputabilities of 2 to 4 were notified in 2002. An average of 25 to 30 TIR have been established every year for 10 years now. For all the related actors, it is then fundamental to identify and analyse rapidly the various dysfunctions. The centralisation of all the investigations is carried out by the regional haemovigilance coordinator, who also ensures that the additional information report forms are correctly filled in. From that point, all the related actors can study together correctives and particularly preventive measures. If the dysfunction is the result of the BTC, the investigation expertise of the Afssaps can be requested. If it is the result of the HCC, the DDASS is the competent authority. Whatever happens, the initiation of an investigation is to be discussed for each case.

### **TIBC**

176 TIBC suspicion cases were notified to the Agence in 2002, among which 23 incidents with positive culture of the BC and imputabilities of 2 to 4. As for ABO type TI, for each TIBC suspicion case, the Afssaps haemovigilance unit, the EFS Vigilance unit and the RHC make sure that the BC derived from the same donation are held up and that the haemocultures and cultures of the BC are effectively carried out. A follow-up of the corresponding results is carried out and an additional information report form is then filled in. It is to be noted that the role of the RHC at the regional level is fundamental in the follow-up of each one of the transfusion incidents, and is indispensable to improve the quality and the reliability of the information gathered.

### **HIV**

29 HIV alert notifications were recorded in 2002, but only 1 case turned out to be actually positive with an imputability of 4. To be noted also the notification in 2002 of a one-off HIV contamination by transfusion of a blood donation collected within the very short serological window (10 days) but found negative with the VGD (the serum of the recipient now deceased was tested HIV positive). Since 1998, only 3 cases of HIV transmission with recent transfusions have been observed, which correspond to what had been theoretically planned using statistics.

### **Malaria**

Post-transfusion malaria is a very rare complication in France, since the last documented case was reported in 1993. In 2002 however, one case was notified. The affection was diagnosed fifteen days after transfusion in an elderly patient with a condition combining feverishness, thrombopenia, renal failure and consciousness disorders, and confirmed with a thick blood drop showing a parasitaemia superior to 15%.

The evolution of the illness became rapidly unfavourable due to the patient's general condition and the associated pathologies despite a treatment with Quinine IV. The investigation allowed us to identify a posteriori a donor originating from a malaria-infected country, however living in France for more than four years with no known clinical symptomatology, even formerly. Following this case, the EFS implemented a systematic detection of antimalarial antibodies on blood donations whenever donors originated from a malaria-infected area, and a modification of the exclusion criteria for donors coming from malaria-infected regions of the world could be proposed and implemented.

### **Alerts notified via the EHN (European Haemovigilance Network)**

In 2002, a haemovigilance/materiovigilance alert was recorded in Switzerland via the EHN - European Haemovigilance Network. It was a haemolysis of plasma derived from total blood. Two French alerts concerning hyperphosphataemia (cf above) and a defect in the watertightness of a blood collection kit were notified.

A website is now available: <http://www.ehn-org.net>

#### 2.1.1.1.2. Donor incidents

### **Post-donation information: beginning of the PDI report form pilot phase**

The PDI - post-donation information - can be defined as "any incident or piece of information provided by a donor or any other reliable source after a donation likely to challenge the safety of the products derived from this donation". The PDI report form was implemented within a pilot phase in October 2002. Before this date, the Afssaps would have received donor incident notifications which contained a partial information as incomplete very often and were submitted under various forms. The new report form now clearly identifies:

- 1) the origin of the incident,
- 2) the types of risks (markers of illnesses - HCV, HBV, HIV, minor infectious risks - anginas..., other risk factors - other viruses, transfusion..., clinical or biological abnormalities - neoplasia and others...; and ATNC risk - cornea transplant...
- 3) the involved blood products.

In 2002, post-donation notifications enabled to reveal the presence of transmissible positive markers such as HIV HCV, HBV in the donor, and gave rise to the question of the conduct to adopt as regards the previous donations.

#### 2.1.1.2. Alerts involving haemovigilance

##### 2.1.1.2.1. Q fever in the Rhône-Alpes region

On August 21<sup>st</sup>, 2002, the Afssaps was informed about the occurrence of an epidemic of Q fever in the valley of Chamonix, as a great number of influenza syndromes had been announced at the beginning of July. This influenza syndrome drew attention due to its occurrence in summer and some other elements such as serious headaches, an increase in transaminases and in some cases an alteration in the patient's general condition leading to hospitalisation. Nevertheless, recovery was spontaneous. Conservatory measures were implemented by the EFS, including the interruption of blood collections in the region with the quarantine or destruction of the BC resulting from previous blood collections in the same area. The blood donations from blood donors for whom a diagnosis of Q fever was confirmed were subjected to an investigation.

As a result, a donor was identified with a - non therapeutic - blood donation dating from May 29<sup>th</sup> and so was another one whose blood donation dating from July was transfused. Subsequent surveillance didn't enable to identify any undesirable effect in the recipients.

#### 2.1.1.2.2. West-Nile virus

In August 2002, the CDC of Atlanta informed the Afssaps and the InVS of a first case of interhuman transmission of the West-Nile virus. In this case notified on August 23<sup>rd</sup>, 2002, 4 people were transplanted organs and tissues from a female donor who was contaminated with the West-Nile virus when previously transfused after an accident on the public highway (at the origin of her death). The Agency formed a working group to follow the evolution of what happened in the USA and think about the impact that this could have in France on products derived from blood. The question of the donors who stayed in the USA was also mentioned.

A surveillance network for this illness has existed in France since 2000. It is to be reminded that animal cases occurred in Camargue in 2000 but no human transmission case was reported in France in 2002.

### 2.1.2. Organisational or regulatory evolutions

#### 2.1.2.1. *Good laboratory analysis practice (immunohaematology)*

A group of experts composed of representatives of the EFS, private pharmaceutical companies, the Afssaps, the DHOS and the DGS was formed in May 1999, in order to re-evaluate and reorganise the erythrocyte immunohaematology activity for better efficiency. The decree relative to the good laboratory immunohaematology analysis practice was published on April 26<sup>th</sup>, 2002. The principal modifications are summarised in the table below:

(<http://agmed.sante.gouv.fr/htm/10/filltrpsc/lp030202.htm>):

- gradual automation of the grouping techniques
- Rh Kell phenotyping performed with 2 reagents
- suppression of the A2 test red blood cells,
- suppression of the enzyme technique,
- the detection of fetomaternal blood group incompatibilities will no longer be carried out on the umbilical cord blood but on the veinous blood,
- the data safety is reinforced with the use of IT systems,
- the quality control is defined as daily,
- if issued, the blood type card will carry the results of the IAEAb including the identification of the antibodies if present.

Additionally:

- The blood group card (two determinations) must be issued by the same laboratory
- the old blood group cards are no longer valid...
- IHR data computerization

The IHR data computerization and transfer will probably bring about a better safety, "repeatability", a faster performance of examinations and a better quality control (no more copying out which was a source of errors, a unique list for IHR results on the national territory, homogeneous patient identification methods...).

#### 2.1.2.2. *Transfusion of homologous red blood cells: products, indications, alternatives*

Some recommendations and an updated leaflet concerning the indications relative to the various types of BC were produced:

. relative to red blood cell concentrates: (<http://afssaps.sante.fr/pdf/5/rbp/qlarq1.pdf>)

. relative to fresh frozen plasma: (<http://afssaps.sante.fr/pdf/5/rbp/tpfarq.pdf>)

. relative to the various types of platelets: (<http://agmed.sante.gouv.fr/pdf/5/rbp/plaqarq.pdf>)

. relative to granulocytes: (<http://agmed.sante.gouv.fr/pdf/5/rbp/granarq.pdf>)

#### 2.1.2.3. *Good practice in transport*

Defined by the decree dated April 24<sup>th</sup>, 2002 (O.B. no. 105 dated May 5<sup>th</sup>, 2002), the good

practice in transport ensures a better quality of transport of BC, especially in terms of deadline, respect of the hygiene rules by the personnel and respect of the environment. It also defines the BC packaging, transport and reception operations. All the operators (HCCs, military health care centres, BTCs and CTSA, LFB, as well as the Afssaps control laboratories) shall use it and provide themselves with the necessary technical and human means (article 2)

<http://www.legifrance.gouv.fr/WAspad/Visu?cid=310557&indice=2&table=JORF&ligneDeb=1>

#### 2.1.2.4. Re-evaluation of the final control cards at the patient by bed (FCPB)

The work achieved by the ad hoc working group in 2002 lead to the update (February 12<sup>th</sup>, 2003) of the note for guidance on "final control devices at the patient by bed - User information" in 2003. (<http://agmed.sante.gouv.fr/html/alertes/filalert/dv030207.htm>). The working group's objective was to analyse the devices' performance in terms of ability to authorize or forbid the transfusion of an erythrocyte unit, devices which are indispensable before any transfusion and contributing to transfusion safety. All the devices, which are now on the market, have been re-evaluated according to a protocol validated by the Commission Consultative d'Enregistrement des Réactifs (CCER) after consultation with the Syndicat de l'Industrie du Diagnostic in Vitro. They now need technical, clinical and design improvements to be made to them in order to include all the items defined in the evaluation criteria. In the case where a device would allow the testing of several erythrocyte concentrates for the same recipient, it was decided to limit the number of erythrocyte concentrates to 3 for each device and to keep these multi-bag designs for cases of massive transfusion.

#### 2.1.2.5. Miscellaneous

##### 2.1.2.5.1. Questionnaire "How to prepare for the medical interview"

The haemovigilance unit participated in the drawing up of the EFS questionnaire "How to prepare for the medical interview". Within this context, it asked that the risks of transmissible illnesses (HIV and hepatitis) were more clearly explained. On the front page, the questionnaire particularly reminds that: "The safety of transfusions depends on the performance of biological tests on each blood donation with the most reliable techniques to detect any potential presence of blood transmissible viruses and parasites which could endanger the lives of patients. It also depends on an assessment of your health condition and medical antecedents by the doctor."

##### 2.1.2.5.2. Access to the patient's medical records and impact on haemovigilance

The regulation dated March 4<sup>th</sup>, 2002, now authorizes the patient to have direct access to his medical records (Art. L 1111-7 of the Public Health Code). So, the patient now has direct access to all the formalized information concerning his health, which constitutes the records, both kept by HCCs and those kept by general practitioners. Previously, such access was necessarily authorized upon request by a doctor appointed by the patient.

It is to be reminded that Article R. 666-12 24 of the Public Health Code specifies that health care professionals must gather a certain amount of information concerning the administration of BC and, in case of undesirable effect occurring during or following the transfusion, they are obliged to notify it to the haemovigilance correspondent. These data shall be kept in the patient transfusion records. A copy of the TIR is added to the patient medical records.

##### 2.1.2.5.3. Other regulatory aspects

- Decree dated May 3<sup>rd</sup>, 2002, concerning dispensations from biological analyses and detections on blood donations for use in case of pressing therapeutically necessity only



in order to prepare labile blood products for autologous use, issued for the enforcement of Articles D. 666-4-1-III and D. 666-4-2 of the Public Health Code.

- Decree no. 2002-723 dated May 3<sup>rd</sup>, 2002, concerning biological analyses and detection tests relating to transmissible illnesses carried out on blood donations and their components, modifying the Public Health Code.

### 2.1.3. Congress

- **ISBT Congress in Vancouver - August 25<sup>th</sup>, 2002**

Doctor Pierre Robillard (DGSP - Quebec) and Doctor Bernard David (Afssaps - France) presented a comparison of all three English, Quebec and French haemovigilance systems at the ISBT Congress in Vancouver. The 4 tables below are from their presentation. The Quebec and French systems have very similar definitions and functioning. The British system, based on voluntary participation and selective information collection, is oriented towards the notification of near-misses.

<b>Organisation</b>			
Type of organisation	United Kingdom	France	Quebec
Type of TIR notification	Voluntary	Obligatory	Voluntary
Type of hospital service	Payable fees	Entitlement to reimbursement	Entitlement to reimbursement
Financing organism	Blood product professional organisation	Ministry of Health Hospital budget	Ministry of Health Hospital budget
Under the supervision of	Professional organisations	Afssaps	Ministry of Health

<b>information collection</b>			
Actors	United Kingdom	France	Quebec
Who notifies?	Hospital haematologists	Haemovigilance correspondents	Manager for the transfusion safety
Who to?	SHOT department or NBS or CDSC (infectious)	RHC, EFS, Afssaps	Ministry of Health, Héma-Québec
Report form	Original report form plus a detailed questionnaire	Transfusion incident report form	4-page report form
Methods of transmission	E-mail/fax	E-mail/fax and electronic transmission	E-mail/fax (2000) and electronic transmission

<b>Global data on labile blood products - 2002</b>			
BC	United Kingdom	France *	Québec **
RBCC	2,354,487	1,931,133	138,605
Platelets	217,725	195,390	15,975
Plasma	326,041	153,694	35,481
Total	2,898,253	2,380,217	190,061

\* transferred products \*\* transfused products

<b>Distribution of TIs by grades - 2000</b>			
Gravity	United Kingdom	France	Quebec
Grade 1 (little serious)	217 (68.9%)	5,475 (71.5%)	565 (86.4%)
Grade 2 (morbidity in the long run)	NR	1966 (25.7%)	30 (4.6%)
Grade 3 (major morbidity)	20 (6.3%)	181 (2.3%)	41 (6.3%)
Grade 4 (death)	42 (13.3%)	39 (0.5%)	16 (2.4%)
Non-determined	4 (1.3%)	ND	2 (0.3%)
Total	315 (100%)	7,661 (100%)	654 (100%)

ND : not documented

- **Toulouse Congress on December 12-14<sup>th</sup>, 2002**

In Toulouse, the Afssaps representatives gave a talk about the "Organisation and Reality of blood storage". Besides, the unit representatives presented a study about the "Analysis of ABO transfusion incidents" as well as two posters about the "Re-evaluation of bacterial incidents occurred since 1999" and "The determiners of grade 1 transfusion incidents" respectively.

## 2.2. **Latest improvements in the management of TIRs**

### 2.2.1. Latest improvements in the notification of TIs

Two new improvements were introduced in the notification of transfusion incidents in 2002: diagnosis of TRALI and grade 0.

### 2.2.1.1. Transfusion Related Acute Lung Injury (TRALI)

Transfusion Related Acute Lung injury (TRALI) is a rare but sometimes fatal transfusion complication. Clinical diagnosis of TRALI lies on a symptomatology occurring generally between 1 and 6 hours after transfusion, including dyspnoea, hypoxemia, hypo tension and fever (with no sign of heart failure) associated with radiological signs of lung injury (bilateral interstitial syndrome). The biological confirmation of TRALI shall be sought in the form of antigranulocyte (PNA ...) or class I or II anti-HLA antibodies in the donor and the recipient, but is not always achievable in practice.

Since September 2001, TRALI can be notified via the GIFIT computer database system. Indeed, often mistaken for overload volume incidents, it is now individualized in the TIR to better identify it and enable a comparison with the international data. **It shall be reminded that oxygen saturation is a simple examination, which enables us to differentiate it from an overload volume: In this very last case, the O<sub>2</sub> saturation is not modified.**

The severity of the first notified TIs was severe (7/8 cases of grade 3 and 1 death) with imputabilities >= 2. They occurred after the transfusion of platelet concentrates but also red blood cell concentrates and fresh frozen plasma. In all cases, they were accompanied with pulmonary signs (acute pulmonary oedema and/or dyspnoea) and sometimes the following clinical signs appeared:

**Incidence of clinical signs - TI with TRALI or suspicion of TRALI from 2000 to 2002\***

Vascular signs	Digestive signs	Chill Fever	Pulmonary signs	Other signs
37,5%	25,0%	50,0%	100,0%	62,5%

**Notified TIs with TRALI or suspicion of TRALI from 2000 to 2002\***

Incriminated products ranking 1 to 4	Number
APC	3
RBCC APC	1
RBCC Plasma APC	1
RBCC Plasma	2
Plasma	1
<b>Total</b>	<b>8</b>

\* retroactive effect for the notification of 1 TI

### 2.2.1.2. Grade 0 transfusion incidents

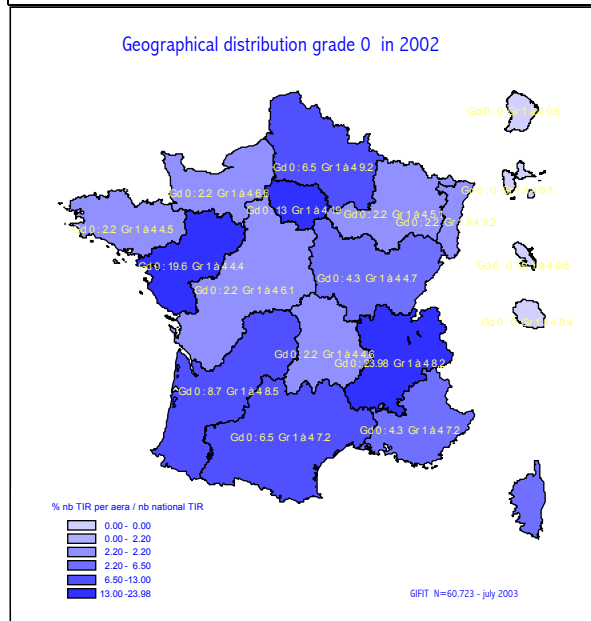
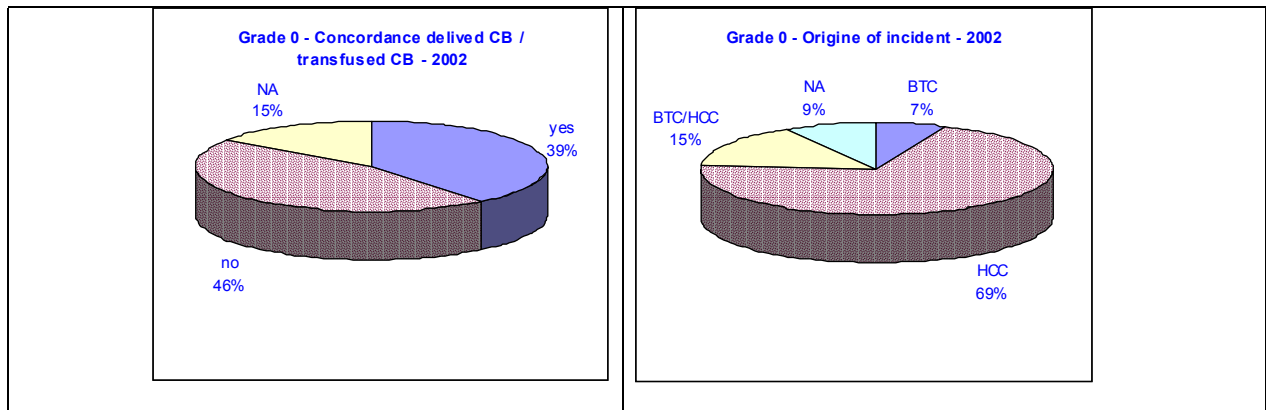
Following patient HIV contamination in January 2002, the Afssaps encouraged the notification, through the haemovigilance network, of any dysfunction leading to the transfusion of inappropriate products to a patient, *with no biological or clinical measurable effect though at the moment of patient observation*. Therefore, grade 0 incidents started being notified in November 2002 with a retroactive effect back to the beginning of the year both on the GIFIT electronic database and the paper copy. On July 1<sup>st</sup>, 2003, the GIFIT database included 46 grade 0 incidents for the year 2002, 42 of which occurred following RBCC transfusion. This figure seems to be increasing on a constant basis.

In terms of quality, the highest figure represents DELIVERY ERRORS (see analysis chart below). 40 report forms out of 46 correspond to a dysfunction notified as involving a product which was partly or totally transfused. **This doesn't include the notifications of abnormalities without transfusion**, especially the labelling error noticed - and the product held up - at the final control stage. These delivery errors with inappropriate transfusion wouldn't be previously notified, and their number is still probably being underestimated. This new type of notification certainly deserves a great deal of attention and a quasi-prospective examination in order to take the most adequate preventive measures.

**Grade 0 transfusion incidents in 2002**

Year month	RBCC	Platelets	Plasma	Other prod.	Total
2002 01	2				2
2002 02	1				1
2002 04	1				1
2002 05	3				3
2002 06	2			1	3
2002 07	4				4
2002 08	3				3
2002 09	6				6
2002 10	4	1	1		6
2002 11	8		1		9
2002 12	8				8
<b>Total</b>	<b>42</b>	<b>1</b>	<b>2</b>	<b>1</b>	<b>46</b>





The geographical distribution\* of grade 0 TIRs is slightly different from that of other grades, as can be seen from the map herewith.

\* Source: BTC

1<sup>st</sup> figure: number of grade 0 TIRs per BTC / national number of grade 0 TIRs;  
 2<sup>nd</sup> figure: number of grade 1-4 TIRs/ national number of grade 1-4 TIRs;  
 This heterogeneous distribution is probably related to the starting phase.

### 2.2.1.3. ABO incident analysis criteria - supplementary to the TIR

An "ABO incident" report form was drawn up for this type of incident to be more precisely documented. Similar work relating to the collection of additional information on "Bacterial incidents" is being undertaken and the resulting analysis criteria will be available some time in summer 2003.

### 2.2.2. Analysis of the GIFIT data

The two investigations relative to the harmonisation of the GIFIT databases carried out in 2001 with the BTC correspondents and RHC were updated in 2002. The objective of these investigations was to measure the number of discrepancies, to identify the nature of these discrepancies and eventually to work out a national database including quite exhaustive data, validated if possible, with a view to migrating the GIFIT system to the future "e-fit" application in 2004.

### 2.2.2.1. Quantitative investigation - Comparison of the BTC, RHC, EFS and Afssaps databases

The comparison of the BTC, RHC, EFS and Afssaps databases in May 2002 led to the identification of 148 local GIFIT databases, 18 regional BTC databases and 24 regional RHC databases, without mentioning the Afssaps and the EFS headquarters' databases. The BTC databases included 50,569 TIR, the RHC databases 51,194 TIR and the Afssaps database 51,100 TIR.

#### Quantitative control results

Date	Number of discrepancies	% number of TIRs	Number of EFS TIRs
May02	2 356	4,7%	50 569
Dec 01	3 526	7,6%	46 255

Date	Nature of the discrepancies	Number of TIRs	Nature of the discrepancies	Number of TIRs	Nature of the discrepancies	Number of TIRs
May02	A(-)	899	E(-)	1 406	C(-)	879
Dec 01	A(-)	1318	E(-)	1789	C(-)	1573

Key: A(-): missing TIRs in the Afssaps database, E(-): missing TIRs in the BTC databases, C(-): missing TIRs in the RHC databases

Compared to 2001, the number of discrepancies has decreased by almost 50%, falling from 3.526 to 2.356. Actually, they involved a larger number of TIRs due to the compensation effect of the cumulated "added and subtracted" quantities. The missing TIRs in the Afssaps database most often correspond to TIRs which were to be transferred or were transferred to some recipients only. Among the TIRs missing in the BTC databases, 978 were not recorded in the regional BTC databases due to a delay in information collection at the level of the local databases.

At the end of these two investigations, the local actors were asked to harmonise their databases. This operation is planned to be repeated at the end of 2003 in order to evaluate the result of such a readjustment before the transfer of the GIFIT system to the e-fit system and the recovery of the data by the new system.

### 2.2.2.2. Qualitative investigation - Consistency control carried out by RHCs

In 2002, BTCs via RHC were asked to control data consistency. This was done in 4 steps achieved in February, April, September and November. The objective was to have for their use a reliable database with regard to the principal items in the TIR: with **1)** the 6 TIR items which must necessarily be completed; **2)** certain inconsistencies, such as the absence of product code on the TIR, the absence of information relating to the clinical signs when the general item is documented, the absence of diagnosis, double or multiple diagnoses on one single TIR, the dysfunction box not being ticked for an ABO incident, as well as medical inconsistencies (for example grade 1 or 2 TIs with shock, haemorrhage syndrome, anuria...); **3)** inconsistencies in dates were also noticed. Such a consistency control is also to be applied to paper TIRs sent to the Afssaps and which weren't keyboarded into the GIFIT within a period of 3 months.

#### Qualitative control results

Sections	Feb 02	Apr 02	Sept 02	Nov 02	%
Missing principal items in the TIR	129	91	93	90	0,2%
Missing dates or errors in dates					
Missing dates	77	54	55	55	0,1%
Dates of notification/birth/occurrence if later than today's date	137	136	132	131	0,2%
Inconsistency in the dates of notification and occurrence	130	80	97	90	0,2%
Inconsistency in the dates of birth and occurrence	36	34	25	27	0,0%
Missing time limit and/or type of time limit	462	442	395	388	0,7%
Investigations in progress or not undertaken	681	700	726	698	1,3%
Serology date	342	348	360	359	0,7%
Medical inconsistencies					
Shock of grades 1 and 2	151	154	163	155	0,3%

<i>Oligoanuria of grades 1 and 2</i>	82	85	90	94	0,2%
<i>Diffuse haemorrhage syndrome of grades 1 and 2</i>	16	16	13	14	0,0%
<i>Convulsions of grades 1 and 2</i>	21	21	20	22	0,0%
<i>Quincke's oedema - laryngeal stenosis of grades 1 and 2</i>	45	47	49	49	0,1%
<i>Bacterial infection (positive culture) imputability&gt;0</i>	144	147	141	143	0,3%
<i>Other missing information</i>					0,0%
<i>TIR without product code - grade 1, 2 or...</i>	195	201	187	183	0,3%
<i>TIR with non-documented clinical signs</i>	119	123	89	93	0,2%
<i>TIR without diagnosis</i>	25	11	13	13	0,0%
<i>TIR with autologous products</i>	40	43	44	47	0,1%
Dysfunctions	126	126	150	129	0,2%
Incidents with double or multiple diagnoses	130	131	135	127	0,2%
Total number of inconsistencies or errors	3088	2990	2977	2907	5,3%
Total number of TIRs - GIFIT database	48776	50151	53260	54499	100,0%

At each stage, 2,900 to 3,000 TIRs were the subjects of requests for additional information or corrections. Most inconsistencies were errors in dates (60%) and medical data inconsistencies (15%). It is to be noted that 8 regions showed less than 5% errors and inconsistencies, contrarily to 3 other regions where the percentage was over 10% in each one of them respectively. This correction work intended to make the GIFIT database more reliable is one more factor guarantying the quality of the GIFIT database. It could be achieved thanks to the collaboration of all the actors participating in the network.

### 2.2.2.3. Percentage of completed TIR items

One of the risks using a database of the size of the GIFIT is the "guyère" effect. In order to evaluate its completeness and supplement the computerized controls described above, the Haemovigilance unit decided to evaluate the percentage of completed TIR items for each variable. It appears that the items relating to the patient are completed in 94% of cases and the items relating to the "incriminated BC" are filled in 98% of cases. Almost all of the TIRs identify one - and one only - diagnosis and only 130 have a double or multiple diagnosis. Concerning clinical signs, 73% of incidents are documented: most often, the delayed incidents don't involve any clinical sign. An absence of the date of birth is noticed for 51 TIRs (0.10%) and the sex item is not documented in 82 TIRs (0,15%).

**External advice:** 2 experts - a statistician and an epidemiologist at the InVS - were consulted to obtain their advice on the GIFIT database, its quality and the use with an epidemiological aim, which is made of it at present. In this regard, they were provided with a disk containing all the data available up to 2002. The result of this expertise is that the GIFIT database undoubtedly has a certain epidemiological value, with a rich anteriority - judged as fundamental: the editorial concertation between haemovigilance correspondents is a guarantee of quality and reliability. Besides, the possibility given to co-authors to give their advice on the value of the documented information is considered as being essential because it represents an automatic appraisal of the data transmitted (example: the "incomplete data collection" item concerning the "transfused products" and the "finished or unfinished investigation" concerning the status of the investigation relating to the TIR).

However, considering the number of inconsistencies and errors still noticed (7-10%), the implementation of additional automatic controls at keyboarding was suggested. However, while contributing to the improvement of the data quality, this operation could make data management heavy or even result in reducing notifications. To sum up, the GIFIT inconsistency rate can be considered as acceptable in the present state of little knowledge of the points of uncertainty.

## 2.3. Studies and work

### 2.3.1. Work conducted with the experts

#### 2.3.1.1. *Incidents reported with peri-operative autologous transfusion (POAT)*

An incident in a girl aged 12 following POAT reported in March 2002 was the occasion to remind the absence of good practice and regulatory framework surrounding with transfusion practice. This technique, which consists in recovering the patient's blood in the operation area to reinject it to the patient during and following surgery, is carried out under the responsibility of the doctor who performs it (Administrative circular DGS/DH/AFS no. 97/57 dated January 31<sup>st</sup>, 1997). The product thus obtained is reinjected to the patient but is not considered as a BC as it doesn't appear in the list defined by the Ministry of Health on March 30<sup>th</sup>, 1998. A RHC/Afssaps working group was formed in April 2002 in order to especially study the risks related to this type of product, practice and incident (bacterial incident or haemolysis...) and will be in charge of drawing up an investigation document. The POAT final status, the drawing up of a good practice and the management of surveillance and incidents are still being discussed. The Afssaps and the ANAES will probably be assigned to work jointly on this subject.

#### 2.3.1.2. *Incidents due to identification or delivery errors*

Incidents due to identification or delivery errors remain a major haemovigilance preoccupation as they are always related to one or several human errors. Despite training and prevention actions, these errors persist even though the total number has slightly decreased. A new text defining the act of transfusion at the patient bed is being elaborated in collaboration with the various departments at the Ministry of health (Direction de l'hospitalisation et de l'organisation des soins, DHOS and the Direction générale de la santé - DGS). At the same time, a prospective and analytical study of the final control devices at the patient bed has been conducted by the DEDIM in order to make their use more homogeneous and increase their efficiency. It was also at the origin of the issue of recommendations for manufacturers and enabled the withdrawal of some devices considered as non-complying from the market.

#### 2.3.1.3. *Incidents due to the bacterial contamination of BCs*

Incidents due to the bacteriological contamination of BC are being studied by a group of experts in charge of validating the incidents suspected of being of bacterial origin, in some cases using the existing specific report forms. In 2002, more than 60 reports were reviewed, leading to the reclassifying of about 45 of them. In addition, another working group updated the recommendations for the information of the haemovigilance correspondents and personnel of bacteriology laboratories conducting germ detection and those of health care centres.

Re-examination of TIs with positive culture per year of occurrence (imputability  $\geq 2$ )

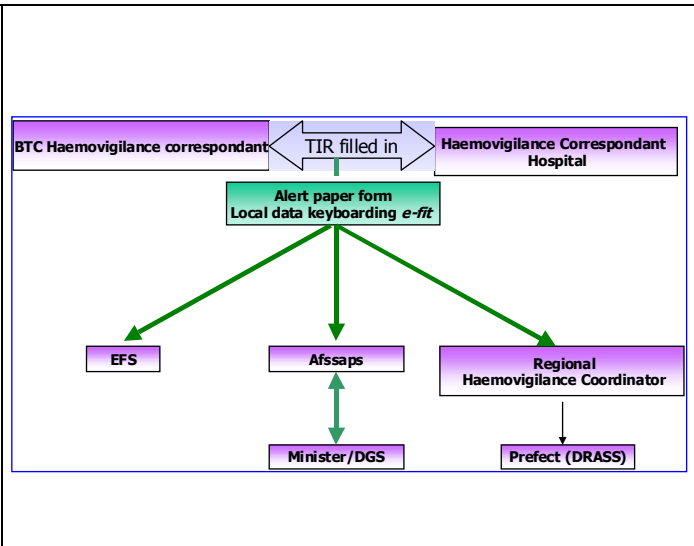
	1999	2000	2001	2002
GIFIT TIRs with suspicion of TIBC	72	48	33	15
GIFIT TIRs with positive culture	38	26	19	23
...and finished investigation	35	23	18	23
Examined TIRs	1	9	29	60
Re-evaluated TIRs	1	9	24	45

#### 2.3.1.4. *Afssaps centralisation of the strains of bacteria isolated after transfusion incidents*

Pursuant to Articles L. 5311-1 and R. 666-12-1 to 3 of the Public Health Code, the centralisation of the strains of bacteria is in accordance with the missions assigned to the Afssaps. This project aims at improving the knowledge of the bacterial risk in blood transfusion. The centralisation of the strains of bacteria identified via haemovigilance will especially contribute to better identifying the properties of the bacteria involved in order to prevent the occurrence of other TIs.

### 2.3.1.5. Computerized TIR e-fit

Since 2000, a global revision of the incident notification system has been undertaken. As a result, the *e-fit* electronic transmission system project was born and it is now being finalized. It is a major project enlarging the electronic transmission network to include all of the 2.200 haemovigilance actors of Blood transfusion centres and health care centres and RHC using the secured access system for health care professionals. This system will also enable us to better manage the French haemovigilance database. Its implementation is scheduled for the first half of 2004.



## 2.3.2. Work associating the regional haemovigilance coordinators

### 2.3.2.1. Main topics

In 2002, five times, the Haemovigilance unit gathered the regional haemovigilance coordinators (RHC) for meetings at the Afssaps. During these meetings lasting two days each, various topics were discussed. The following are among the principal:

EFS assents  
 blood storage site assents  
 RHC annual activity report  
 NCTC annual activity report  
 transfusion incident notification  
 accreditation and haemovigilance  
 the European Directive

blood donor haemovigilance  
 follow-up of transfused patients  
*e-fit* project  
 good practice in transport  
 questions concerning the distribution of BCs  
 revision of the good transfusion practice  
 good practice recommendations concerning  
 the transfusion of RBCC and plasma products

Various working groups were also formed on the following topics:

- transfusion incidents by bacterial contamination of BCs,
- post-transfusion examinations,
- blood donation analysis criteria user guide,
- RHC database...

Finally, as in 2001, every regional haemovigilance coordinator wrote an activity report (as defined by Art. R.666-12-20 of the Public Health Code). The 24 reports, which were about the year 2001, were used as the basis for a synthesis by the Haemovigilance unit of the Afssaps during the second half of 2002. The synthesis of the RHC 2002 activity reports will also be available on the Afssaps website.

## 2.3.2.2. More about a few topics

### 2.3.2.2.1. BC traceability computerization

The projects were conducted by the RHC as requested by the Afssaps and working meetings were held in this respect, gathering especially the national computerisation and traceability committee (NCTC) appointed in January 2001. A specific working group was also formed for the verification and revision of traceability standards approved by the AFNOR. A tool verifying the compliance of the softwares with the standards is made available for regional projects, as well as a standard and codification implementation electronic document. At the end of 2002, 14 metropolitan regions had projects at different progress stages, 5 projects are in an experimentation phase of message exchange between the HCCs and BTCs and 3 projects are in a phase of routine.

### 2.3.2.2.2. Serological follow-up of transfused patients

The follow-up of pre- and post-transfusion examinations had been recommended by: 1) Administrative circular DGS/DH no. 609 dated October 1<sup>st</sup>, 1996, concerning the analyses and tests carried out on BC recipients and 2) Administrative circular DGS/SQ no. 98-231 dated April 09<sup>th</sup>, 1998 concerning the information of patients relating to the risks related to labile blood products and blood-derived medicines

As no evaluation of the enforcement of these measures has been carried out up to date, the Afssaps appointed a working group as requested by the DGS. It is composed of 2 RHC and representatives of the DGS, DHOS, EFS and InVS. The results of their work is presented in the following table:

#### Investigation summary "Follow-up of transfused patients"

The investigation included 1,633 BTCs. The results for 1,394 of them (85.4%) have been keyboarded. The percentage of returned questionnaires is 100% in 7 regions, the other ones showing percentages between 91% and 97%; in one region, the portion of returned questionnaires corresponded to 52%. The survey part of the investigation included 1,224 BCs randomly drawn.

Results:

##### Health care centres

- 80% of all HCCs answered the questionnaire and among them 83% have a pre-transfusion follow-up procedure (the figure is declaratory).
- 95% of HCCs carry out pre-transfusion biological tests (viral markers such as HIV, transaminases). 23 HCCs specified that they have a serological reference storage room (in liquid nitrogen).
- 84% of HCCs have a post-transfusion follow-up procedure (HIV, HCV, HBV in 86% of cases, IAEAB in 66% of cases).

Procedure result feedback exists in one HCC in 2 and 16% of transfused patients get a follow-up.

##### Patients

- estimation of the number of transfused patients: about 400,000, when the previous estimations were in the order of 500,000.
- actual traceability (with information feedback to the BTC) and BTC/ HCC patient identity data analogy are estimated to be 96.25%.
- the BCs destruction rate is of 4.3% ± 2%.
- the percentage of patient death at six months is 35.7%.
- the percentage of deaths in transfused patient during their stay in hospital is 16.55% that is to say

For the patients non-deceased at six months in the post-transfusion phase, 30.5% were submitted to HIV and HCV serological detections; 67% presented no serology.

Only 19.54% of non-deceased patients would have been submitted to pre- and post-transfusion detections. It appears that detection, as recommended at present, is only used in its totality in 19.54% of the transfused population. When these tests were carried out, 73% of patients were subjected to pre-transfusion HIV and HCV detections, and 20% of them had their serological sample stored in the serological reference storage room before transfusion.

82% of patients were offered to be subjected to post-transfusion HIV and HCV detections and in this case, the HCC was informed of the result for 16% of the patients only.

The cost of all the exams carried out in pre- and post-transfusion phases is estimated to be 2,200,000 euros per year, that is to say approximately the cost for the VGD.

The practice differs according to the various regions. In some regions, up to five more pre-transfusion tests are carried out than in others. The transfused are 2.5 times more likely to be subjected to these tests in an HCC, which has more than 300 beds. On the contrary, when the HCC uses more than 5,000 BCs a year, the probability for a patient to be subjected to a complete set of tests is divided by 2.

However, an analysis deviation is to be noted. It concerns the random selection of samples, which over represented the polytransfused patients, hence an over evaluation of some parameters and an under evaluation of others.

As a conclusion, the risk of HIV contamination by blood transfusion is much inferior to that occurring in the general

during their stay in hospital is 16.55%, that is to say 76,000 deaths, regardless of the imputability.

Concerning HCC patients, 58.5% were subjected to pre-transfusion HIV and HCV serological detections; 35.8% showed no particular serology. For 32.4% of the transfused, a sample is stored in the serological reference storage room.

population and if the patient is well identified, he is managed efficiently. It is however necessary to analyse the cost/efficiency ratio of the system too.

### 2.3.2.2.3. Investigation on the peri-operative autologous transfusion (POAT)

In July 2002, the Haemovigilance unit received the notification of an incident of severity 1 with bacterial contamination of the recuperator tank with washing. The occurrence of this incident revived the question of the insufficiently defined use of POAT and lead the Afssaps to conduct an investigation with the collaboration of 6 RHCs (Alsace, Bourgogne, Franche-Comté, Limousin, Lorraine, PACA, that is to say 83 health care centres.)

It is to be reminded that perioperative autologous transfusion (PAT) consists in recovering the blood poured out in the operation area in aseptic surgery and reinjecting it to the patient during surgery, either with a blood recovery system or with a device connected to a Redon type drainage tube. Another technique consists in diluting the patient's blood before surgery in order to diminish the consequences of bleeding; it is the "normovolaemic haemodilution". The concerned blood is subjected neither to storage nor to biological qualification and remains at a near distance from the patient within the operating theatre. The blood bags to be transfused are prepared by the hospital personnel who see to the right functioning of the devices involved.

POAT products do not correspond to the definition of labile blood products since they consist in a red blood cell recovery carried out under the responsibility of the hospital personnel. (see Administrative circular DGS/DH/AFS no. 97/57 dated 31/01/97).

### Investigation results:

- **It was noticed that:**

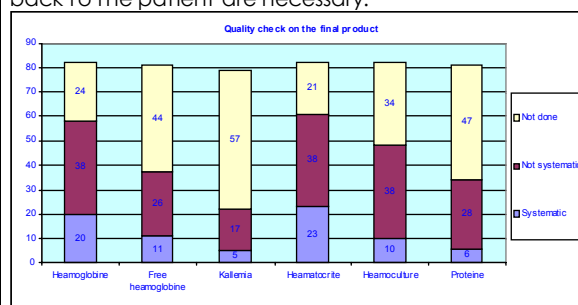
1. POAT techniques are more and more used in surgery, sometimes as a complement of BC transfusion, even though the actual needs are difficult to determine.
2. There is a geographical heterogeneousness in the methods of surveillance of these techniques.
3. The use of these products appears to be insufficiently defined, especially with regard to the controls to be performed on the products and on the patient.

- **Conclusion:**

Further thought appears to be necessary to:

- Define the status of surgery recovery products and specify who is competent to control pre- and post-surgery transfusion.
- Conduct a global evaluation of all the practices and especially \* identify the points which require thinking over and the questions that necessarily need answering, \* elaborate specific recommendations.

Pursuant to the administrative circular dated 1997, some quality controls on recovered blood before transfusion back to the patient are necessary:



- free haemoglobin,
- haematocrit,
- bacteriology,
- protein determination when the technique used is a technique with washing.

### 2.3.2.2.4. Blood storage site

On this subject, 2 items shall be mentioned:

- **Blood donation analysis criteria user guide,**



The task of the regional haemovigilance coordinator working group "Blood storage" was to revise the analysis criteria and elaborate a user guide, taking into account the question of the evolution of distribution in France. So, they based their work on a qualification document and another report written by the EFS Alpes Méditerranée. Consequently, 3 documents were created:

1. specifications for positive temperature storage sites,
2. a device compliance control procedure based on the above specifications,
3. (high and low temperature) storage site operational validation document.

- **blood storage site functioning on the basis of the data transmitted by the RHCs**

The objective of this investigation was to better understand the functioning of blood storage sites with a view to a possible national survey. A questionnaire was sent to 3 RHCs in the summer 2002. The questions related to the premises, equipment, personnel as well as the transfer procedure of labile blood products, performance of the IHR and computerization.

	Aera n°1	Aera n°2	Aera n°3
BC distributed by aera	158 367	97 006	86 867
Number of blood storage sites	20	20	33
BC distributed by blood storage	18 345	2 245	23 497
Average number of BC distributed by blood storage sites	592	112	712
% BC distributed by blood storage sites	11,58%	2,31%	27,05%
% BC thrown out	5,60%	2,60%	2,60%
% BC thrown out after passage by blood storage sites	2,50%	1,90%	0,50%
% conform BC retaken after passage by blood storage sites	19,00%	NA	4,60%

The information collected via this questionnaire show:

- interregional discrepancies, especially regarding the proportion of emergency storing on top of O+ or O- RBCC stock, storage of BC already assigned by the BTC, storage sites containing non assigned BC as well as the staff assigned to the functioning of these storage sites.
- The results were compared with the data provided by the RHCs in their annual activity report for the year 2001.
- A heterogeneous BC transfer design via blood storage sites.
- Discrepancies in the availability and training of the personnel assigned to the functioning of blood storage sites. Heterogeneous computer liaison between blood storage sites

In general, the discrepancies noticed seem to be related to the fact that the functioning of blood storage sites is not identical from one region to another, undoubtedly due to BC delivery history, the EFS and HCCs' choices and because in some cases the transfer of blood products via blood storage sites was thought over at the regional level in collaboration with the public health planning. As a result, a national survey including all the 723 blood storage sites identified in France appeared necessary and was initiated in 2003.



### 3. Transfusion Incidents – with all imputabilities

#### Warning:

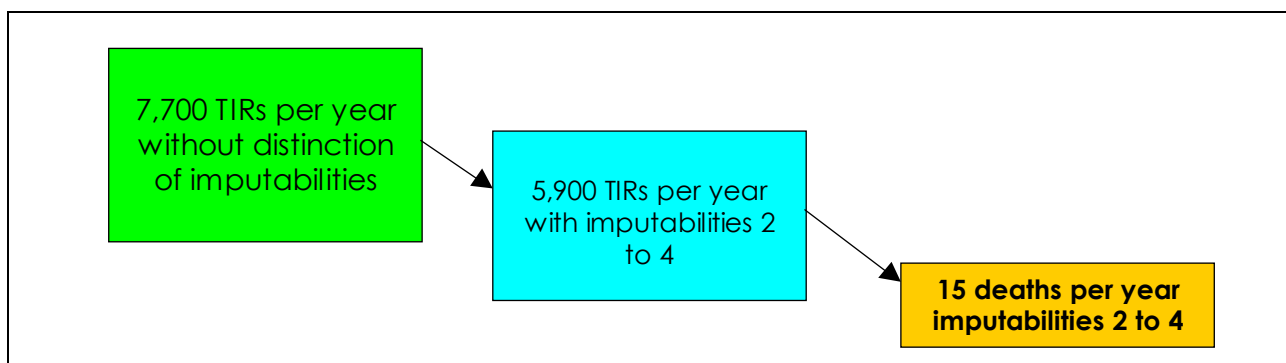
- The TIR data are transmitted by the haemovigilance correspondents and shall be corrected or completed by themselves only. They concern all the incidents, without distinction of imputabilities, including null and uncertain imputabilities after investigations; Some report forms are old and incomplete, particularly between 1995 and 1997, and could not be corrected. The data relative to the said years shall be analysed with care.
- The haemovigilance data presented hereafter were sometimes the basis of publications in other media such as the weekly haemovigilance bulletin which uses all the TIRs received by the Afssaps (paper + GIFIT TIRs) and is issued in-house at the Afssaps, the insert in the haemovigilance bulletin (available at present on the Afssaps website) which shows the TIRs keyboarded in the GIFIT, the statements sent to the RHCs... The data presented are thus likely to match up. Studies were also conducted (ABO, TIBC, immunologic incidents, TRALI, serologies, allergies...) at various organisms' request or with a view to national or international congresses. So, quantitative differences with other documents might be noticed. **The data presented in the present report reflect the database managed by the Afssaps on July 1<sup>st</sup>, 2003.**

### 3.1. Principal epidemiological data

#### 3.1.1. Number of TIs per year

In France 7,700 transfusion incidents were annually notified over the period 2000-2002. Among these incidents, 5,900 (or 76.7%) have possible, probable or certain imputabilities. The severity of a large proportion of these incidents is graded 2 to 4. More than 1,800 people presented an unexpected or undesirable effect related or possibly related to the transfusion with possible long-term morbidity, immediate life threat or death.

#### Number of transfusion incidents reported per year: 2000-2002 average



Key:

Grade: 0: with no biological or/and clinical effect; 1: absence of life-threatening reaction; 2: long-term morbidity; 3: immediate life-threatening reaction; 4: death.

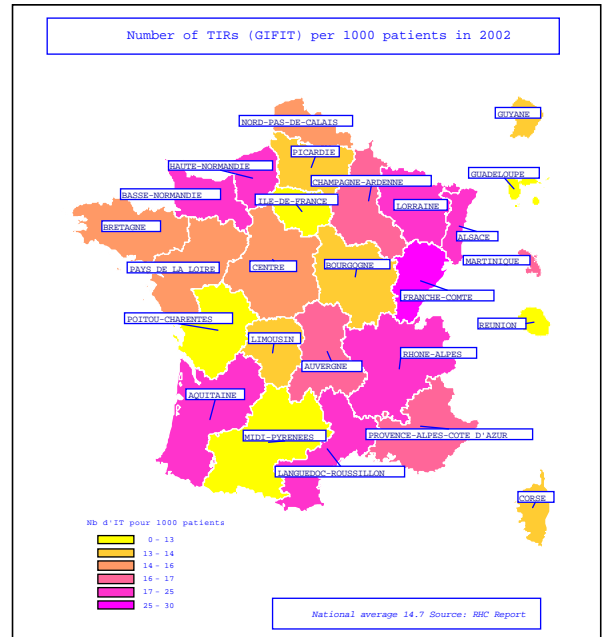
Imputability: 0 - excluded; 1 - uncertain; 2 - possible; 3 - probable; 4 - certain.

The number of transfusion incidents has been quite stable for five years now. However, (geographical and chronological) heterogeneous reporting persists, which is characterized by a larger number of notifications - which had been left pending - at the end of the year, overflowing on the following year. So, as in the past years, the number of transfusion incidents for 2002 cannot be estimated with precision and a minimum period of six to ten months is necessary when the delay in keyboarding and the time necessary to close all the investigation dossiers are taken into consideration.

### 3.1.2. Principal indicators

#### 3.1.2.1. Incident / 1,000 patients ratio

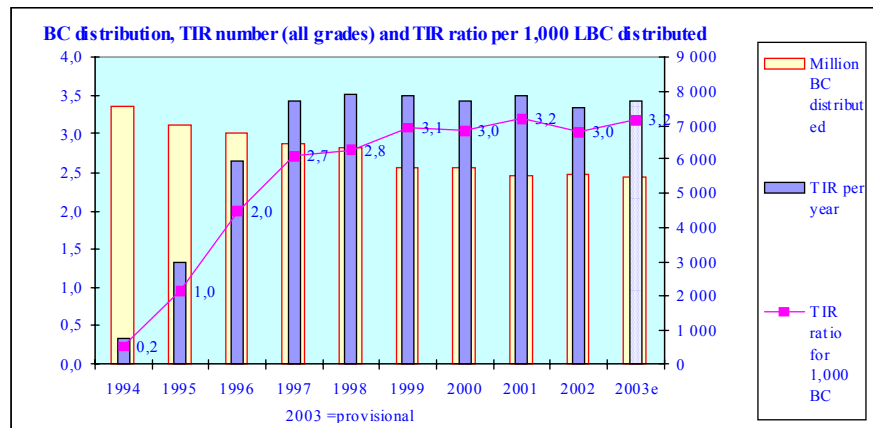
- The map opposite is presented for information only as the data relative to the transfused patients are sometimes questionable. Indeed, in some regions, the figure presents no distinction between the number of patients and the number of transfusion acts. With these reserves and considering the difference sometimes in definition from one BTC to another, it is possible, with all the necessary cautiousness, to put forward an approximative incidence (or annual number of new incidents) in the patient population of 15 in 1,000 in 2001 and 2002 with mean deviation intervals of [11.09; 19.30] and [11.45; 18.0], respectively. Furthermore, this figure also varies from one region to another since it also depends on characteristics other than the aspects purely related to transfusion, such as the population of transfused patients.



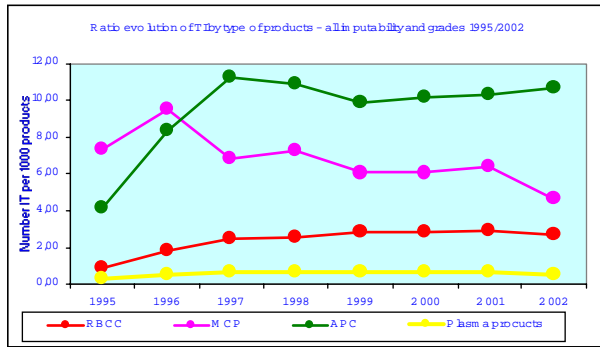
#### 3.1.2.2. Incident / distributed products ratio

##### Global ratio

Every year, the number of incidents per 1,000 distributed products in France ranges from 2.7 to 3.2, without distinction of severity. The ratio has now been steady around 3 ‰ for more than four years.

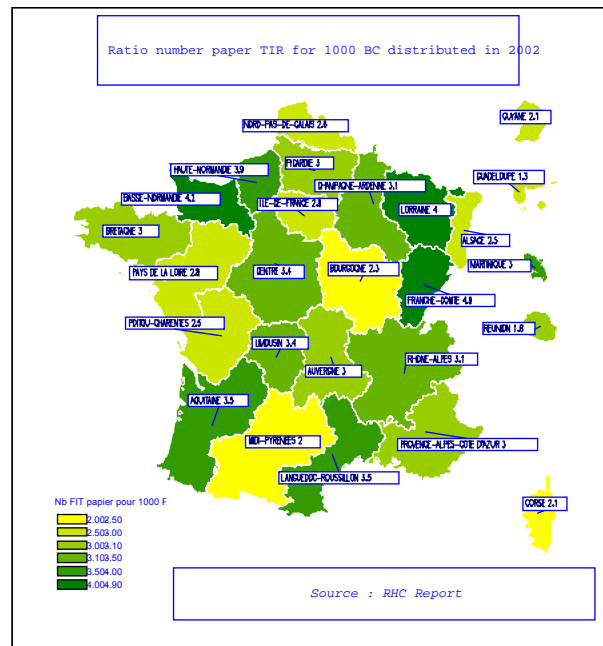


### Ratio by type of products



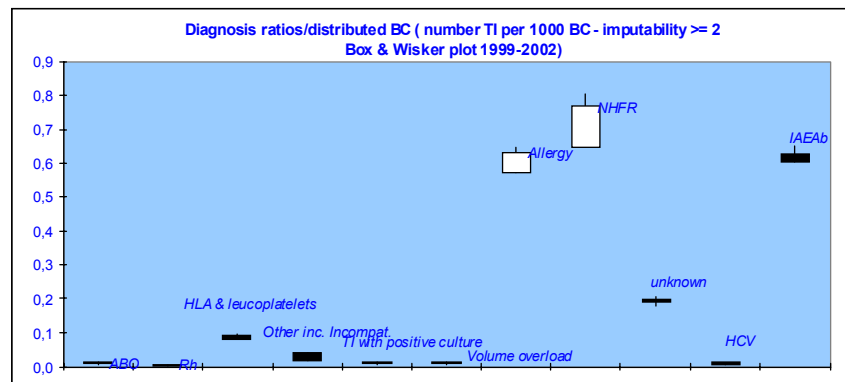
Excepted for two metropolitan regions, a grouping of the ratios of TI notifications per 1,000 BC between 2.5 and 5 is to be noted.

### Ratio by region



### 3.1.2.3. Diagnosis / 1,000 BC ratios

The term "diagnosis / BC ratio" is the number of types of diagnoses per 1,000 transferred BCs. Only TIs with imputability  $\geq 2$  diagnoses are taken into account. The incidence of NHFR, allergies and IAEAb comes clearly first.



## 3.2. Alert and GIFIT computerized data collection

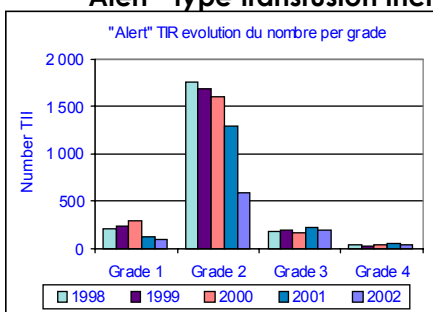
Every incident possibly related to the transfusion of labile blood product shall lead to specific notification. At the national level, these notifications enable us to collect data, which reflect the consequences of transfusion acts. At present, the Afssaps Haemovigilance unit uses a three-stream collection system: the first type is used for the Alert type TIR data, the second one for computerized data via the GIFIT database and the third type for the data extracted from the RHC activity reports. "Alert" TIRs are defined as paper TIRs of grade 2 to 4 or grade 1 involving or likely to involve the safety of at least another recipient as well as grade 1 likely to be related to the transfusion equipment used. These TIRs are transmitted by post or fax within 48 hours following their occurrence.

### 3.2.1. "Alert" type TIR collection - paper TIRs

The annual number of paper TIRs - about 1,600, new or updated TIRs (incidents of grade 2, 3, 4 and grade 1 where the incident can involve other recipients) - is decreasing compared to the previous years due to a modification in the receipt of this kind of TIRs. Indeed, since 2001, grade 2 incidents related to the appearance of anti-erythrocyte antibodies no longer have to be

notified to the Agency by post or fax, but only via computerized database.

### "Alert" type transfusion incident report forms between 1998 and 2002



	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
"Alert" TIR 1998		208	1747	179	38	2172
Pourcentage		9,6%	80,4%	8,2%	1,7%	100,0%
"Alert" TIR 1999		231	1695	190	30	2146
Pourcentage		10,8%	79,0%	8,9%	1,4%	100,0%
"Alert" TIR 2000		295	1598	168	44	2105
Pourcentage		14,0%	75,9%	8,0%	2,1%	100,0%
"Alert" TIR 2001		0	0	0	0	0
Pourcentage		0,0%	0,0%	0,0%	0,0%	0,0%
"Alert" TIR 2002		0	0	0	0	0
Pourcentage		0,0%	0,0%	0,0%	0,0%	0,0%

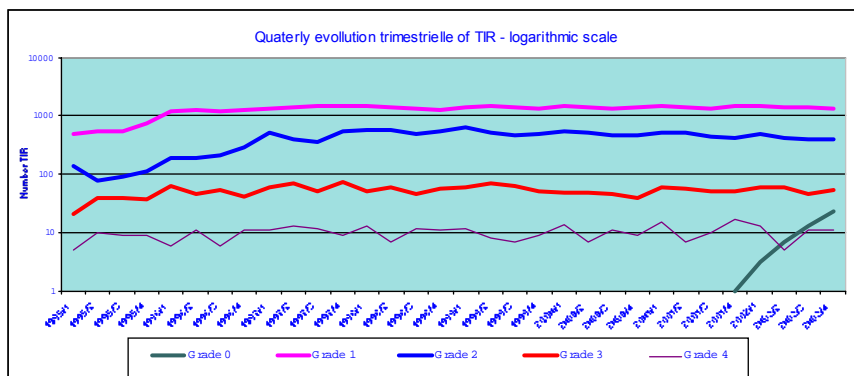
### 3.2.2. GIFIT TIR collection

**Note: Although compulsory, the transfusion incident notifications in the GIFIT database are not exhaustive. Incidents have to be notified within 15 days following their occurrence.**

At the end of 2002, the GIFIT database included 60,723 TIRs. Since 2000, about 7,700 TIRs are recorded every year, among which about 4,800 are grade 1 TIRs, 1,500 are grade 2 TIRs, 180 are grade 3 TIRs and 36 are grade 4 TIRs. The charts and tables below show the evolution of the GIFIT TIRs since 1995.

#### 3.2.2.1. Number of quarterly incidents

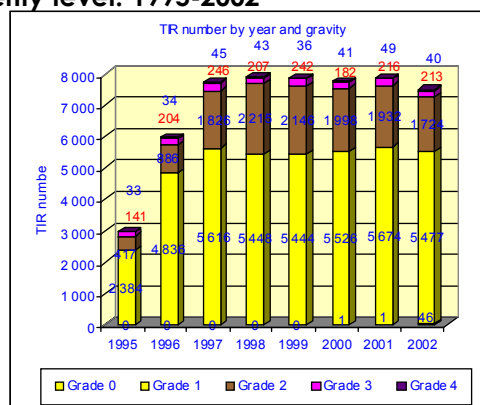
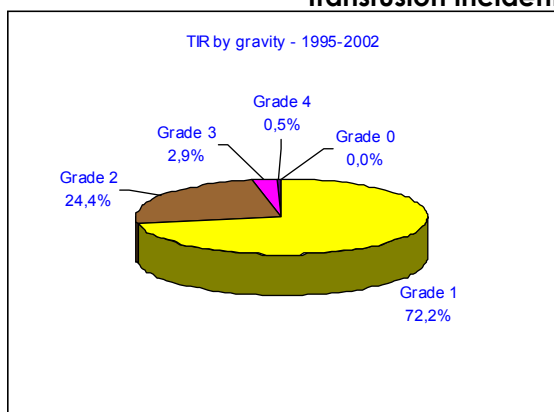
Over the period 1995/2002, the average number of quarterly TIs was 1,737 with a mean deviation interval of [1427;2046]. The figure for grade 3 and 4 TIs is 31 with a mean deviation interval of [10;52].



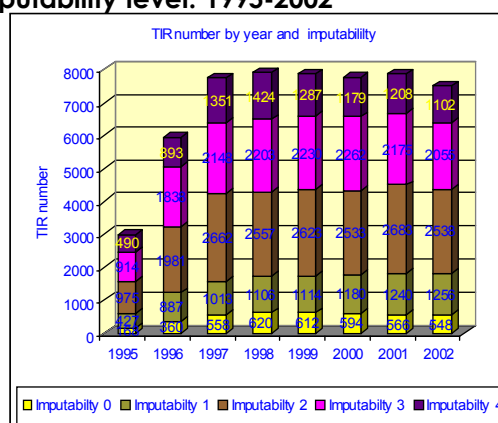
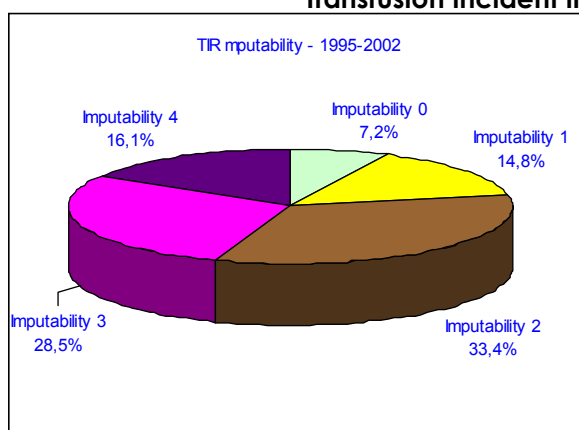
#### 3.2.2.2. Number of incidents by grades and imputabilities

The following charts show the incidence and the evolution of the TI by grades and imputabilities.

### Transfusion incident severity level: 1995-2002



### Transfusion incident imputability level: 1995-2002



### Global severity and imputability cross table – all years

As you can see it in the table below, grade 1 TIs are rather associated with imputabilities 2 and 3 and grade 2 TIs with imputabilities  $\geq 2$ . As regards TIs of high grades (3 and 4), the imputability distribution is not as categorized. It is to be noted that 53% of deaths are associated with low imputabilities such as 0 or 1.

Distribution of TIs by grades and imputabilities – without distinction of years - 60,723 TIRs

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	%
Imputability 0	7	2 612	1 404	204	106	4 333	7,1%
Imputability 1		8 092	489	255	86	8 922	14,7%
Imputability 2	3	16 530	3 730	369	88	20 720	34,1%
Imputability 3		12 236	4 379	528	40	17 183	28,3%
Imputability 4	95	3 999	4 977	441	43	9 555	15,7%
Not documented		9	1			10	0,0%
<b>Total</b>	<b>105</b>	<b>43 478</b>	<b>14 980</b>	<b>1 797</b>	<b>363</b>	<b>60 723</b>	<b>100,0%</b>
%	0,2%	71,6%	24,7%	3,0%	0,6%	100,0%	

Note: The percentages presented above are slightly different from those in the previous charts as they were calculated using all the data in the GIFIT database.

### 3.2.2.3. Number of incidents per year of occurrence

#### On the basis of the year of notification of the incident

To know the year of notification of all the TIs, which occurred in the year X, refer to the table

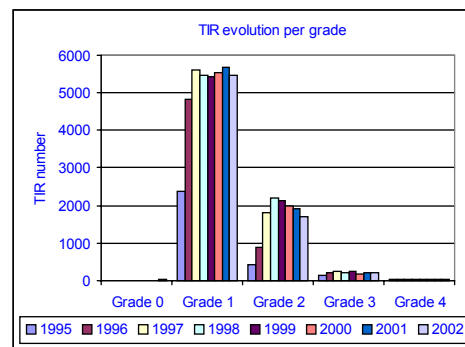
below. Most TIs, which occurred in the year y, were notified in the same year y, but for various reasons (investigations in progress, delay in keyboarding), there is sometimes a delay in the recording. As an example, 7,872 TIs occurred in 2001 but only 7,703 were notified the same year. Such a delay in the notification often leads to qualify the analysis of the risk factors noticed for the TIs of a same year, while waiting for exhaustive notification results.

#### Incident notification year according to the year of occurrence – 1995/2002

		Incident by notification year										
		Other years	1994	1995	1996	1997	1998	1999	2000	2001	2002	For all years
<b>o</b>	Other years occurrence	3 408	9	29	149	195	190	149	85	113	69	4 396
<b>u</b>	1994	1	500	52	26	31	57	38	26	15	12	758
<b>c</b>	1995	5		2 698	101	49	41	46	17	10	8	2 975
<b>c</b>	1996	7			5 635	175	64	37	16	14	12	5 960
<b>u</b>	1997	25				7 384	241	36	21	15	11	7 733
<b>r</b>	1998	4					7 659	173	39	23	15	7 913
<b>r</b>	1999	3						7 625	185	39	16	7 868
<b>e</b>	2000	6							7 569	162	11	7 748
<b>n</b>	2001	5								7 703	164	7 872
<b>c</b>	2002	128									7 372	7 500
<b>e</b>	For all years	3 592	509	2 779	5 911	7 834	8 252	8 104	7 958	8 094	7 690	60 723

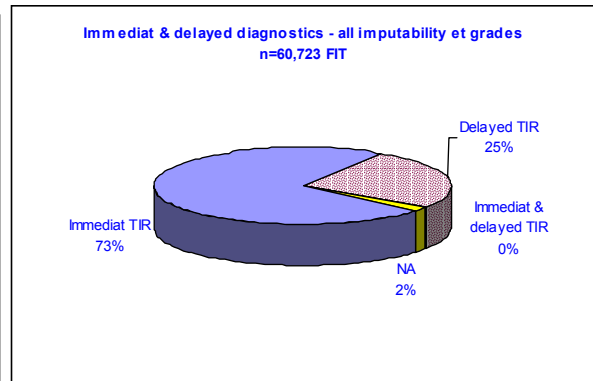
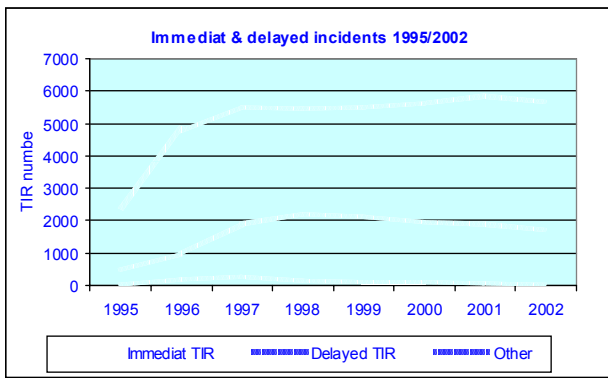
#### According to the severity of the incident

The evolution of grade 2 incidents has shown a decrease since 1995, which mainly reflects the decrease in the risks of transmission of viral affections as well as a reduction in the notification of irregular anti-erythrocyte antibodies.



#### According to the category of the incident

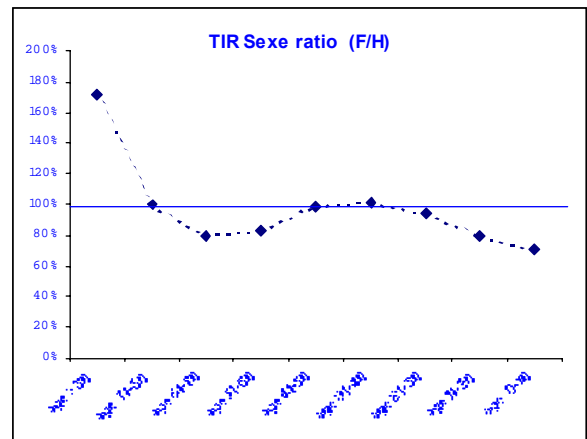
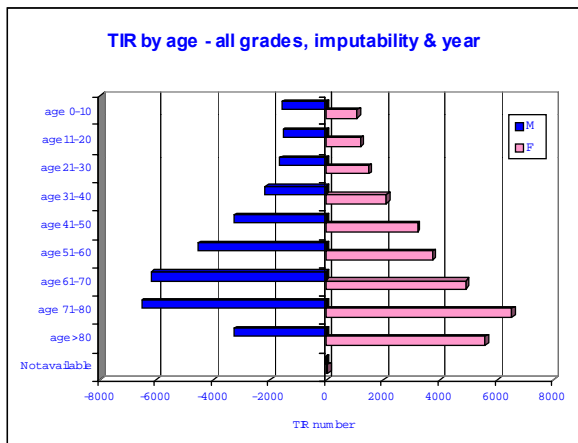
The following charts show that immediate incidents go on increasing slightly contrarily to delayed incidents. The former (immediate incidents) represent approximately 73% of the TIs in the GIFIT database and the latter 25%. In the second category, diagnoses are mainly IAEAAb (65.6% of delayed TIs) and positive serologies (27.7%).



Key: other TIs = TIs with double or multiple diagnosis or with non-documented diagnosis item

In general, since 1998, we have observed a great stability in the notification of transfusion incidents, which could lead us to believe that maybe this is not due to insufficiently efficient haemovigilance but to a non-reducible risk despite all the prevention measures taken. However, it is more probable that the improvement of the BC intrinsic safety and the improvement of the haemovigilance network and the notification system are the joint cause of this stability. The relative increase in mild incidents (grade 0 and 1) seems to be favouring this hypothesis.

### 3.3. Patients' characteristics

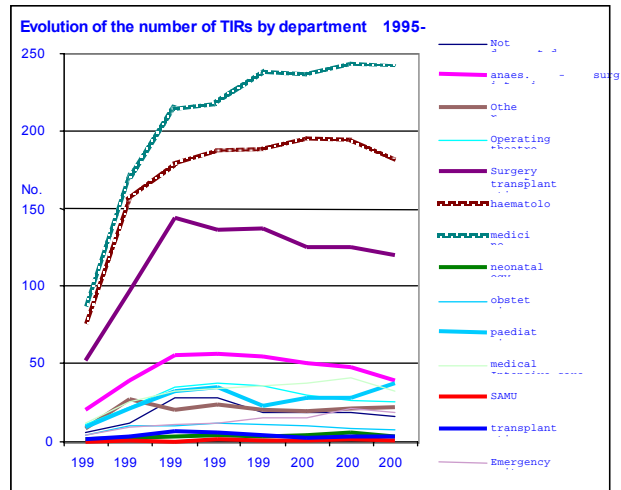
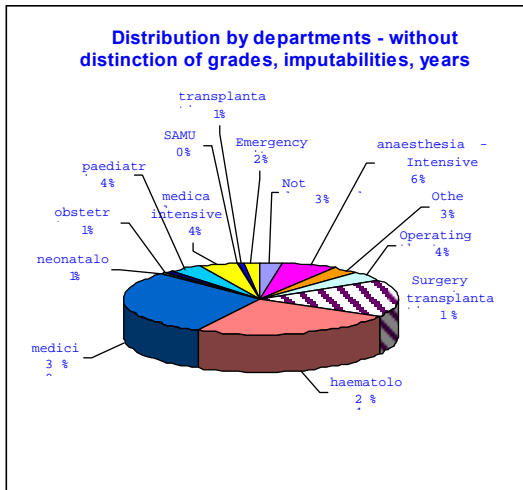


A comparison of the male and female populations shows that there are more transfusion incidents in women aged 31 to 40 and over 70 than in men.

The 2<sup>nd</sup> chart confirms the results in the 1<sup>st</sup> chart: the variations depending on sex differ according to the age of patients.

### 3.4. Origin of TI reporting

As regards volume, 2 departments, haematology and general medicine, represent more than half of the transfusion incidents (24 and 30%) and the operating theatre and surgery except transplantation represent 21%. As regards their evolution in time, an increase is noticed in the departments of general medicine, paediatrics and emergency units, while the decrease in anaesthesia units and operating theatres will be associated with a reduction in the use of BC by these departments.



### 3.5. Products incriminated in TIs

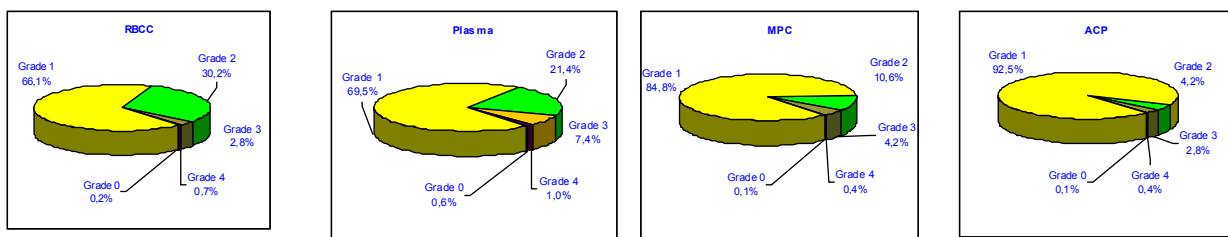
#### 3.5.1. Period 1995/2002

##### 3.5.1.1. Distribution by grades

Grade 1 TIs represent between 66 and 92% of all the incidents recorded in the GIFIT depending on the class of BCs. These incidents are associated with an absence of immediate or long-term life-threatening reaction, which means with an absence of death, immediate life threat or long-term morbidity. Platelets (MCP and APC) represent the majority of products at the origin of these grade 1 incidents.

Concerning grade 2 TIs, the largest proportion (32%) is associated with RBCCs and is represented by the expected occurrence of anti-erythrocyte antibodies or positive post-transfusion serology with negative or unknown pre-transfusion serology. On the contrary, the high proportion of grade 2 incidents observed with plasma products seems to be linked with HCV post-transfusion serologies (80% of grade 2 incidents). This finding has been unexplained but is associated with old incidents, which occurred before 2000.

Ti distribution by products and grades – without distinction of years - 60,723 TIRs



The proportion of grade 3 and 4 TIs appears to be larger with plasma products. Grade 3 represents an immediate life threat and is mainly associated with clinical signs presented by the recipient jeopardizing his immediate vital prognosis and requiring intensive care acts. As for grade 4, it is associated with death certified to have occurred during or following transfusion. Grade 4 incidents will be analysed later in section 4.6.

##### 3.5.1.2. Distribution by transfusion contexts

###### 3.5.1.2.1. TIs - all incriminated products

As already mentioned (Chap. 1.2 - incident / type of distributed product ratio), the distribution of



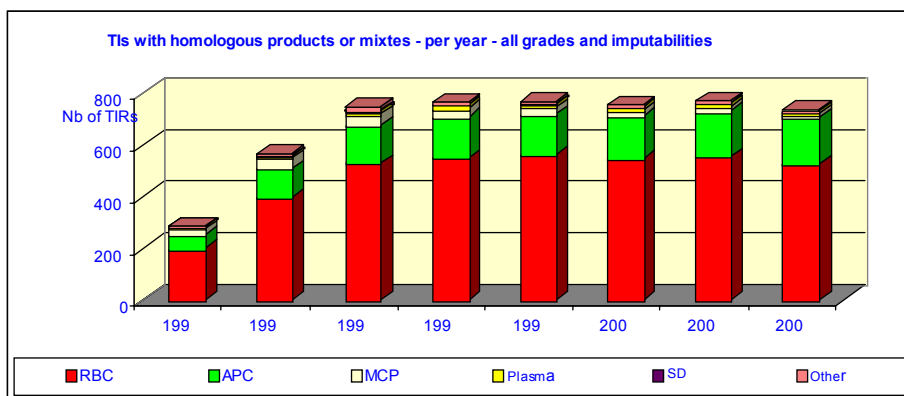
incidents by transfused products has been steady in time.

**TIs in the major categories of products (homologous and autologous)**

	1995	1996	1997	1998	1999	2000	2001	2002
RBCC	2068	4166	5451	5644	5742	5599	5650	5340
APC	540	1115	1524	1607	1569	1675	1794	1840
MCP	245	418	394	338	256	197	162	113
Other plasma	68	104	130	143	144	134	128	112
SD plasma	7	17	30	23	26	29	38	24
Other	47	140	204	158	131	114	100	71
<b>Total</b>	<b>2975</b>	<b>5960</b>	<b>7733</b>	<b>7913</b>	<b>7868</b>	<b>7748</b>	<b>7872</b>	<b>7500</b>

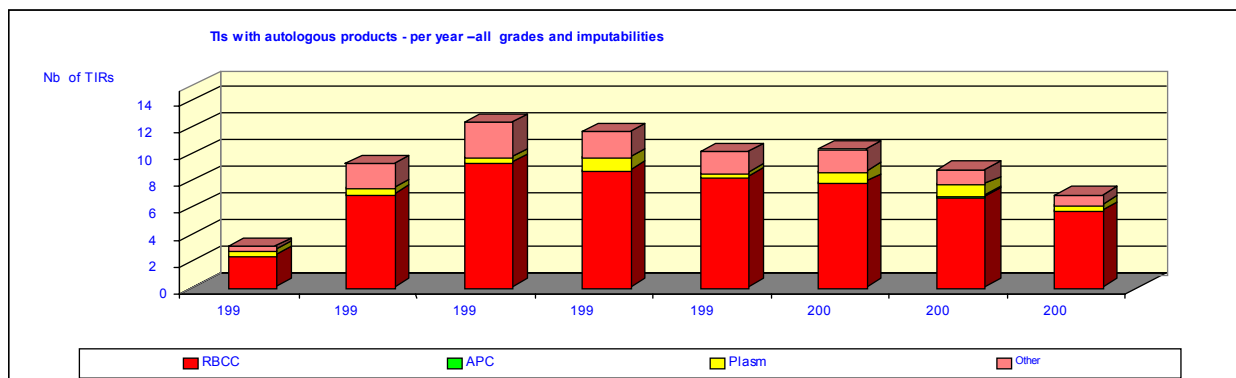
3.5.1.2.2. TIs with homologous products

TIs with homologous products represent the majority of TIs, 97%. This proportion is the same concerning the number of distributed units (homologous/autologous).



3.5.1.2.3. TIs with autologous products

Incidents in relation with the transfusion of autologous products tend to be decreasing, parallel to the number of products used. They can expose some other recipients to risks due to non-exceptional delivery errors while depriving the patients of the benefit of autologous transfusion. They occur in a large proportion with the use of RBCCs (76% to 84% of incidents, see chart below). Haematopoietic stem cells (others) are largely represented.

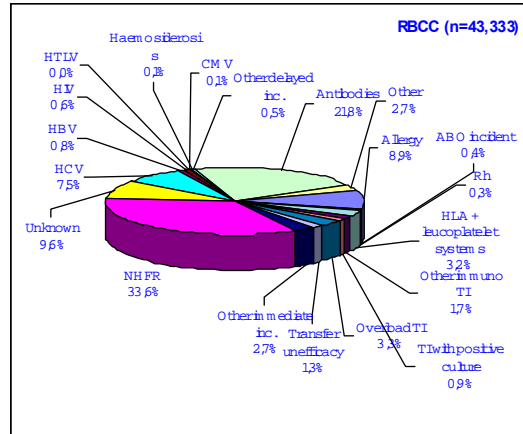


	1995	1996	1997	1998	1999	2000	2001	2002
RBCC	24	70	93	88	83	79	68	58
APC	0	0	0	0	0	0	1	0
Plasma	4	4	4	9	3	8	8	4
Other	3	18	26	19	15	16	11	7
<b>Total</b>	<b>31</b>	<b>92</b>	<b>123</b>	<b>116</b>	<b>101</b>	<b>103</b>	<b>88</b>	<b>69</b>

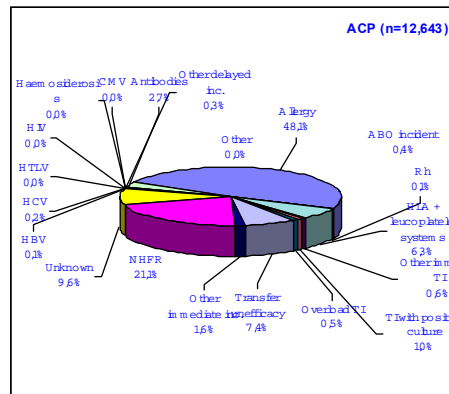
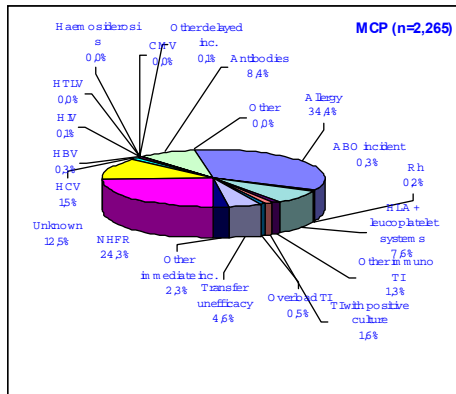
3.5.1.3. Distribution by diagnoses

### 3.5.1.3.1. "RBCC" incident diagnoses

In the whole number of TIs where RBCCs are involved, three main diagnosis categories can be observed. First of all, NHFR (33.6%), then IAEAb (21.8%) and finally allergies (8.9%). The cause of 10% of the incidents, which occurred with RBCCs, is still unknown; this ratio appears to be identical for the other products, except for MCPs with 13%. In the long run, the objective is to reduce this type of notification, especially by crossing the various data available in the TIR and making sure that the investigations and examinations relative to the pathogenic agents are effectively being conducted.



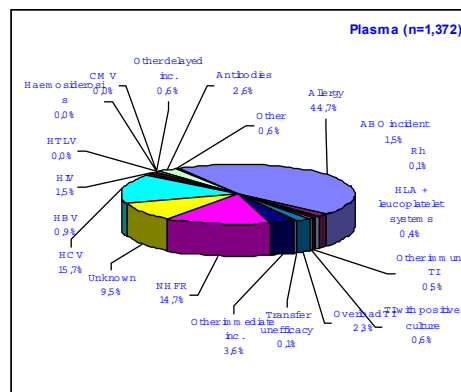
### 3.5.1.3.2. "Platelet concentrate" incident diagnoses



The expression of diagnosis categories by types of transfused products, for the whole database, without distinction of severity, grades or imputabilities, shows a similar distribution for aphaeresis platelet concentrates and standard concentrate mixtures, substantially represented by allergic reactions (48% with APCs) and febrile or unknown reactions (37% with MCPs). A clear predominance of the induction of alloantibodies with MCPs (8.4%) versus APCs (2.7%), probably related to residual red blood cells, shall be pointed out.

### 3.5.1.3.3. "Plasma concentrate" incident diagnoses

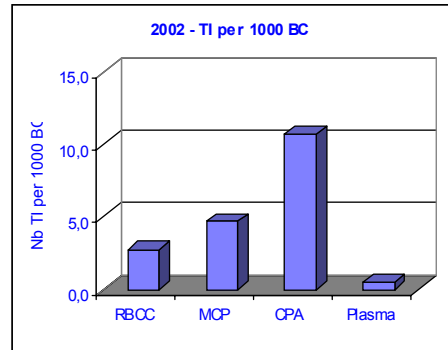
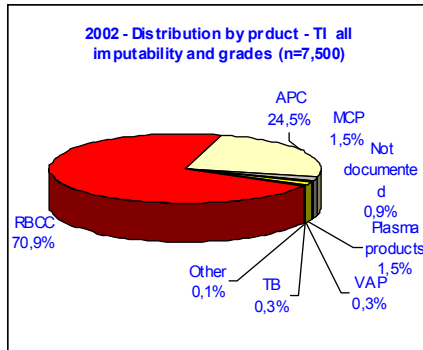
Allergic reactions appear to be as frequent with plasma products as with platelet concentrates, but far more numerous than with with RBCCs. HCV seroconversions seem to be over represented (16%). TRALI hasn't been identified so far.



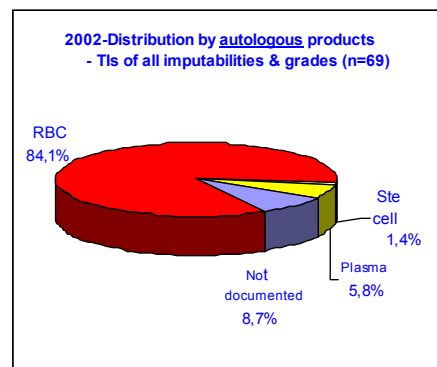
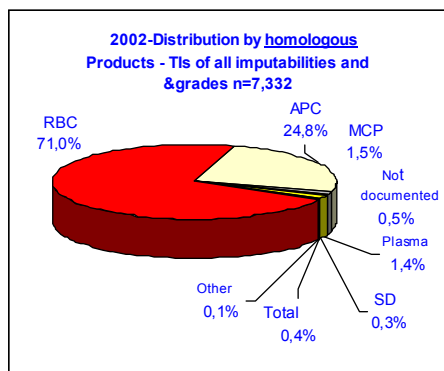
## 3.5.2. Year 2002

### 3.5.2.1. All products

Most TIs are attributable to RBCCs (70.9%) but RBCCs represent 78% of all distributed units. As in the previous years, the incident / 1000 BC ratio appears to be much higher (almost 1%) with APCs, however associated with a very large majority of minor allergic incidents with mild severity. Plasma products, especially SD plasmas, are associated with a very low percentage of incidents per 1,000 BCs.



### 3.5.2.2. Homologous/autologous products in detail



It is to be noted that the global incidence by distributed products in 2002 was 0.9 incident per 1,000 distributed autologous products, which is much lower than the ratio with homologous products.

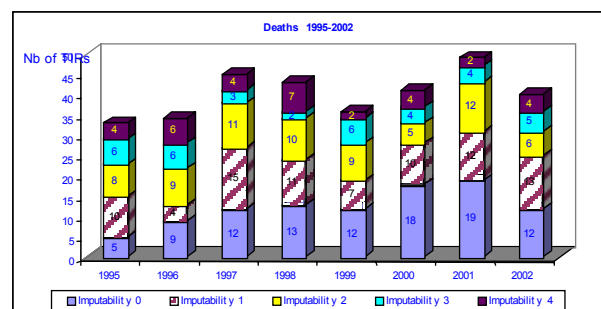
## 3.6. Deaths

Reminder: Deaths occurred during or following transfusion are defined as grade 4 transfusion incidents.

### 3.6.1. Deaths between 1995 and 2002

#### 3.6.1.1. Evolution by TI imputabilities

As previously mentioned, the number of deaths in the past 8 years without distinction of imputabilities was about 41 a year, with a mean deviation interval of [37;46]. Among them, imputabilities  $\geq 2$  represent 17 TIs [16; 19].



### 3.6.1.2. Incriminated products

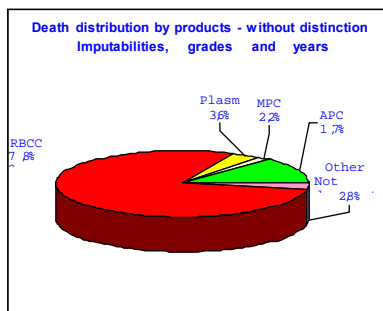
78.8% of grade 4 TIs occur in relation with RBCCs. It shall be reminded that these products globally represent 76.8% of all distributed BCs.

#### Deaths between 1995 and 2002

	Number of TIRs	%
RBCC	286	78,8%
Plasma	13	3,6%
MPC	8	2,2%
APC	46	12,7%
Other or not documented	10	2,8%
Total	363	100,0%

Number of deaths = 0.6% of all TIRs

GIFIT database - without distinction of grades and imputabilities - 60.723 TIRs

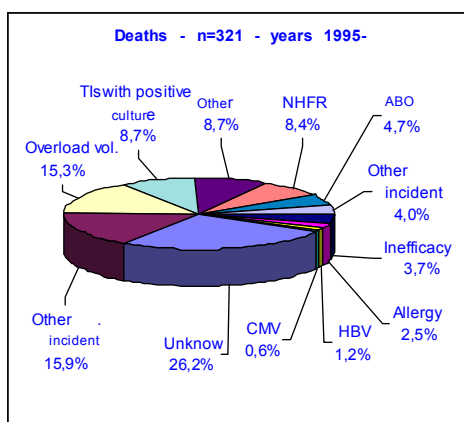


### 3.6.1.3. Main causes of death

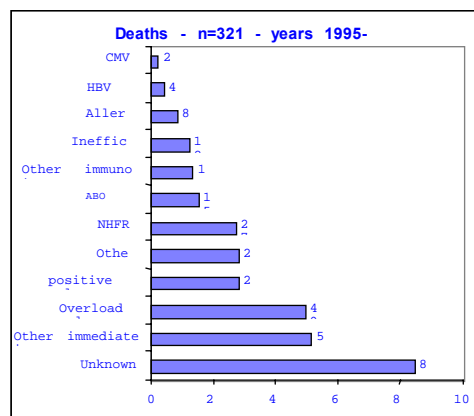
Globally, immediate reaction diagnoses represent 89.4% of death cases.

#### Deaths: Immediate and delayed TIs - 1995/2002

Years 1995-2002	Number	%
Immediate TIs	287	89,4%
Delayed TIs	28	8,7%
Immediate & delayed TIs	2	0,6%
Non-documented TIs	4	1,2%
Total	321	100,0%



The analysis of the death diagnosis categories significantly shows five main causes apart from the "unknown" category: overload volume, bacteriological contamination incident, NHFR, ABO error and other immunologic incompatibilities.



### 3.6.1.4. Imputability level for diagnoses with death

Some diagnoses appear to be principally associated with imputabilities 2 to 4 (more than 85%). It is the case for allergies, ABO errors and overload volume: the nature of the risk itself explains it all. Conversely, NHFR reactions or reactions of unknown nature are associated with excluded or doubtful imputabilities for approximately ¾ of them. Grade 4 TIs with positive culture are situated in an intermediate position with 61% of cases associated with imputabilities >= 2.

#### Immediate diagnoses - 1995/2002\*

1995-2002	Allergy	ABO	TI with cult.	Overload volume	NHFR	Unknown

#### Delayed diagnoses - 1995/2002\*

1995-2002	HCV	HBV	HIV	CMV	Malaria	IAEAB
Imputability 0	2	3				

Imputability 0			6	4	5	26
Imputability 1	1	2	5	3	15	39
Imputability 2	4	2	4	21	6	13
Imputability 3	2	3	4	17	1	
Imputability 4	1	8	9	4		

1995/2002\*: *years of occurrence*

Imputability 1		1			1	
Imputability 2				1		
Imputability 3				1		
Imputability 4						

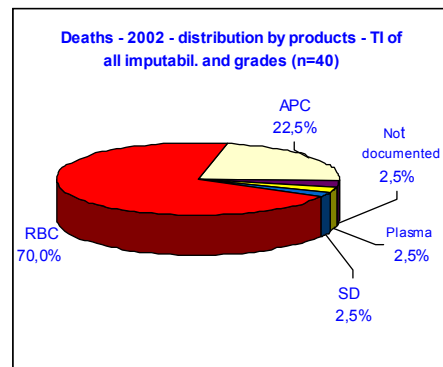
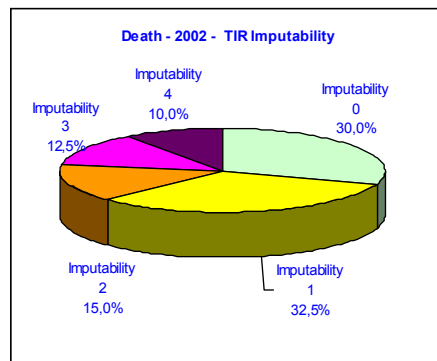
1995/2002\*: *years of transfusion, except for IAEAb with years of occurrence*

*Definition: positive serology TIs are presented according to the year of the transfusion. It is calculated using two pieces of information in the TIR: the year of occurrence and the time period since transfusion when documented.*

### 3.6.2. Deaths in 2002

In 2002, the GIFIT database recorded 40 deaths versus 45 in 2001 - without distinction of imputabilities. It seems that the GIFIT database exhaustivity concerning the year 2002 hasn't been achieved at the end of July 2003. Nevertheless, it appears that the mortality ratio is 1.6 per 100,000 distributed BCs (2.0 in 2001).

#### 3.6.2.1. Distribution by imputabilities and by products

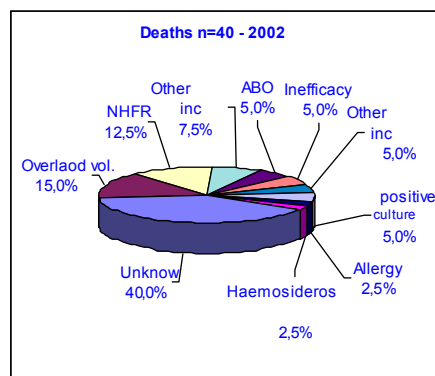
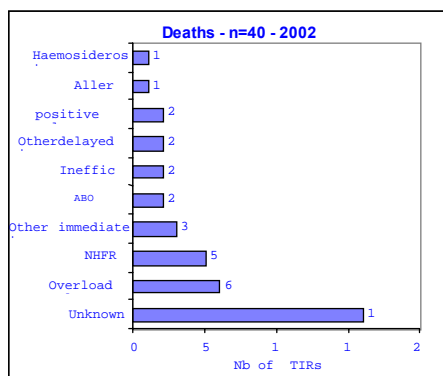


It shall be reminded that in terms of products, RBCs represent 78.5 % of all distributed BCs and APCs 7.0 %.

#### 3.6.2.2. Principal diagnoses

The distribution of diagnoses in 2002 didn't differ from those observed over the period 1995/2002.

In fact, overload volume, NHFR reactions and immunologic incompatibilities have become major transfusion risks, apart from "unknown" causes. In 2002, in 40 deaths recorded, 6 cases of overload volume, 5 cases related to NHFR reactions, 2 ABO errors, 2 incidents with positive culture of the BCs and 3 other immunologic incompatibilities were observed.

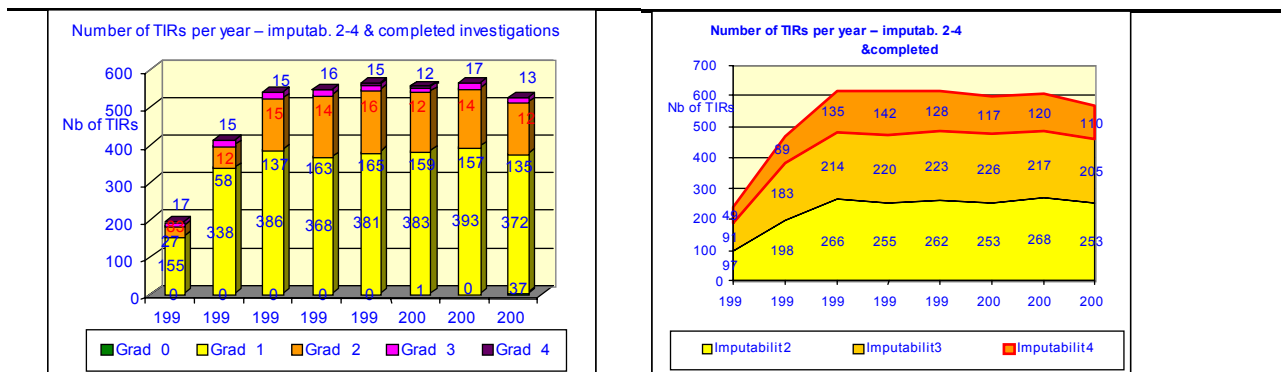
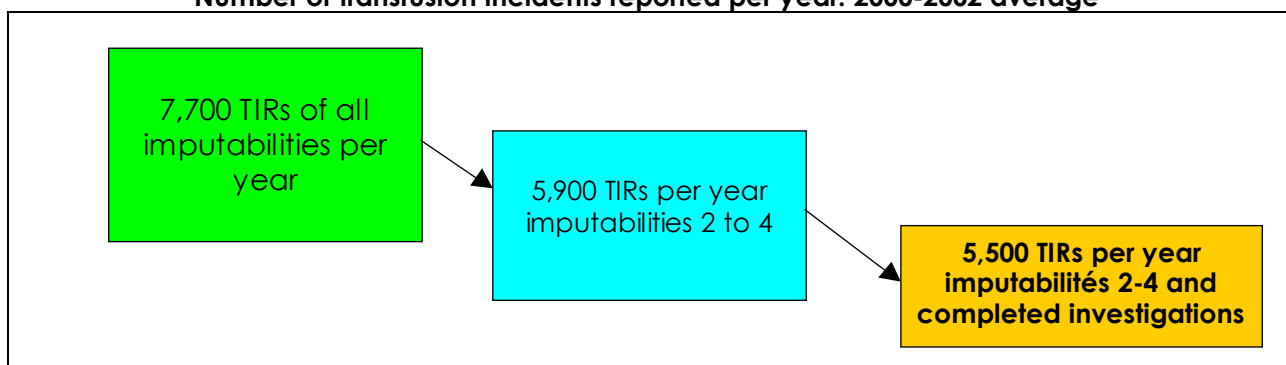


## 4. Transfusion incidents with imputabilities 2 to 4 and completed investigations

Foreword: The data showed in this chapter are relative to incidents with which the transfusion imputability of which is certain, probable or possible (imputabilities 2 to 4). Incidents with an excluded or uncertain imputability (imputabilities 0 or 1) were not analysed, so as to enable comparison with data from other haemovigilance systems at the national and international levels.

Globally, TIs with imputabilities 2-4 represented 76.7% of all TIs over the period 2000-2002, or an average of 5,900 TIs out of 7,700 per year. Nevertheless, the severity of these TIs has slightly decreased.

**Number of transfusion incidents reported per year: 2000-2002 average**



Key: Grade 0: with no biological or/and clinical effect; 1: absence of life-threatening reaction; 2: long-term morbidity; 3: immediate life-threatening reaction; 4: death.  
Imputability: 0 - excluded; 1 - uncertain; 2 - possible; 3 - probable; 4 - certain.

### 4.1. Presumed dysfunctions and non-matching BCs

#### 4.1.1. Definition

Among the dysfunctions the imputability to transfusion of which is certain, probable or possible (imputabilities 2 to 4), a category is drawing our attention more particularly: it is the category of those which are most often identified in health care centres, which can sometimes have fatal consequences as regards to the transfusion aspects and can occur at any moment in the transfusion process:

- Sample collection and labelling by ABO grouping: non-respect of the time interval between 2 collections, tube-labelling error...

- Product receipt: absence of recipient identity control, patient error...
- Transfusion act
  - error on final control at the patient bed: technical error, wrong interpretation, control carried out long before the transfusion act...
  - Outflow too rapid
  - Personnel absent at the beginning of transfusion act...
- Storage of products outside the storage areas laid down in the regulations (non-transfused products, stored and forgotten about in the usual storage area, then taken by error and transfused to another patient)...

But also errors identified in BTCe, mainly delivery errors.

As these errors or dysfunctions aren't all mentioned in the TIR, it appears that it is necessary to remind the criteria which led to the selection of the TIs included in the following paragraph.

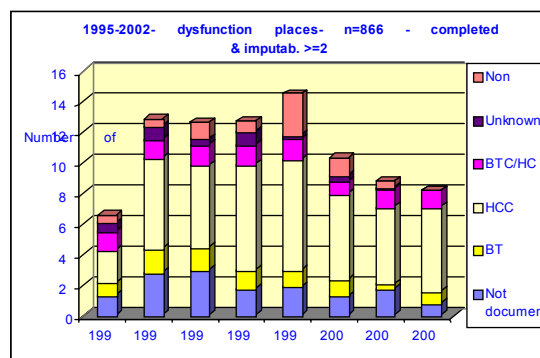
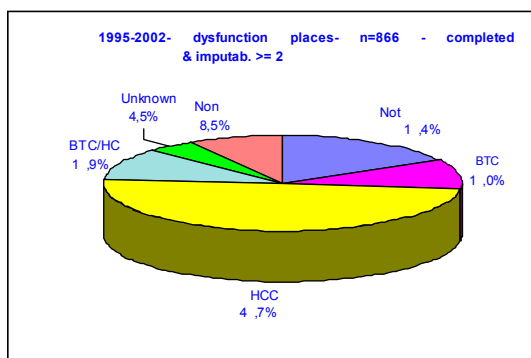
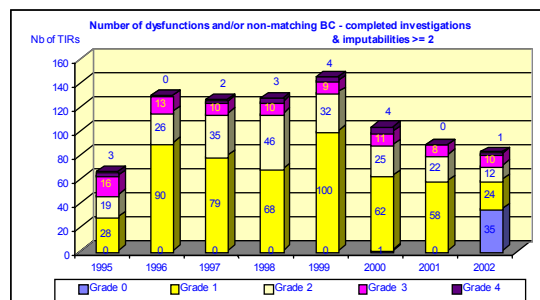
Definition: are considered as dysfunctions, incidents reported by correspondents as presumed dysfunctions (dysfunctions occurred in the BTCs or HCCs or both) and/or "non-matching" distributed and transfused BCs (items in the transfusion incident report form). The analysis is conducted regardless of the incident diagnosis category.

#### 4.1.2. Period 1995/-2002

Dysfunctions (imputabilities 2 to 4, completed investigations, 1995-2002)  
 Mean value: 108 dysfunctions per year, CI95% [85.1;131.4]  
 Risk of  $\approx 1$  dysfunction for 26,900 BCs, CI95% [19,400;34,500]  
*IC95%: 95% confidence interval*

A constant decrease has been observed for 4 years. The evolution remains to be confirmed. The training efforts shown by all the actors are maybe at the origin of this trend.

Dysfunctions and non-matching distributed / transfused BCs							
1995	1996	1997	1998	1999	2000	2001	2002
66	129	126	127	145	103	88	82



#### 4.1.3. Dysfunctions in 2002

A decrease in the number of reported incidents with dysfunctions has been noted for years

2000 to 2002, without satisfactory explanation. As in previous years, the origin of the majority of dysfunctions is at the level of health care services since 86% of the dysfunctions identified are partially or totally imputable to HCCs. A slight change in the distribution of incidents with dysfunctions in 2002 occurring with the appearance of grade 0 (43%) shall be pointed out. In view of the data collected in the first six months of 2003, it is probable that this trend will be confirmed.

**Distribution method – completed investigation and imputability >=2**

Storage		Nominative delivery: <b>yes</b>	Nominative delivery: <b>no</b>
Medicalized storage site: <b>yes</b>	Emergency storage site: <b>yes</b>	0	0
Medicalized storage site: <b>yes</b>	Emergency storage site: <b>no</b>	3	19
Medicalized storage site: <b>no</b>	Emergency storage site: <b>yes</b>	0	0
Medicalized storage site: <b>no</b>	Emergency storage site: <b>no</b>	57	3

Considering the number of BC, which passes in transit through blood storage sites (about 30%), passing through (emergency or non-emergency) storage sites doesn't seem to be a factor favouring dysfunctions (27%).

## 4.2. Principal diagnoses

### 4.2.1. Immediate / delayed incident distribution

Transfusion of labile blood products induces two types of reactions: immediate & delayed reactions

#### 4.2.1.1. Immediate incidents

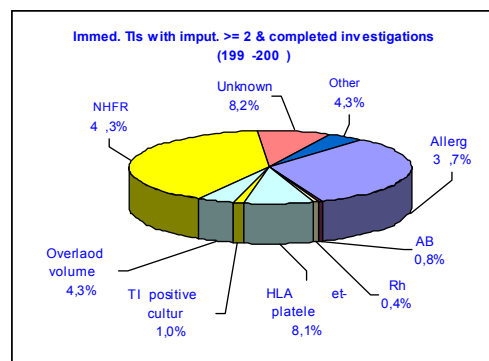
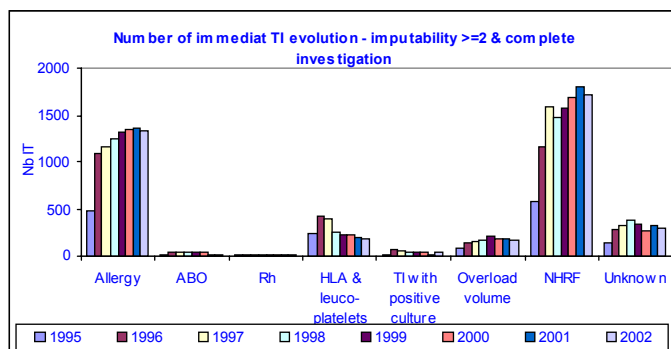
... which appear within 8 days and are - for about 90% - of 3 types:

- allergy,
- identified immunologic incompatibilities (ABO, Rh, HLA...),
- NHFR non-haemolytic febrile reactions (immediate incidents occurring during of following the transfusion act without signs of acute haemolysis)

The other observed immediate incidents are:

- overload volume caused by a large supply in blood products  
Two populations are substantially concerned: adult patients over 50 (almost 85 %) and children under 10 (2.4%).
- unknown type incidents
- incidents with BC positive culture

### Immediate incidents





Year of occurrence	1995	1996	1997	1998	1999	2000	2001	2002
Immunol. causes among which:								
Allergy	474	1089	1154	1252	1315	1345	1368	1330
ABO	19	27	33	30	36	29	19	21
Rh	13	16	15	15	10	13	16	14
HLA and leuco-platelet systems	239	427	390	252	213	213	188	177
Non-immunol. causes among which:								
TI with positive culture	20	58	48	35	35	23	18	23
Overload volumes	66	127	152	155	202	177	173	161
NHFR	584	1166	1578	1476	1565	1676	1790	1711
Unknown category	136	280	317	380	328	264	313	289

Except for NHFR (increasing), a relative stability in the distribution of diagnoses is noticed in view of the diagnosis category data.

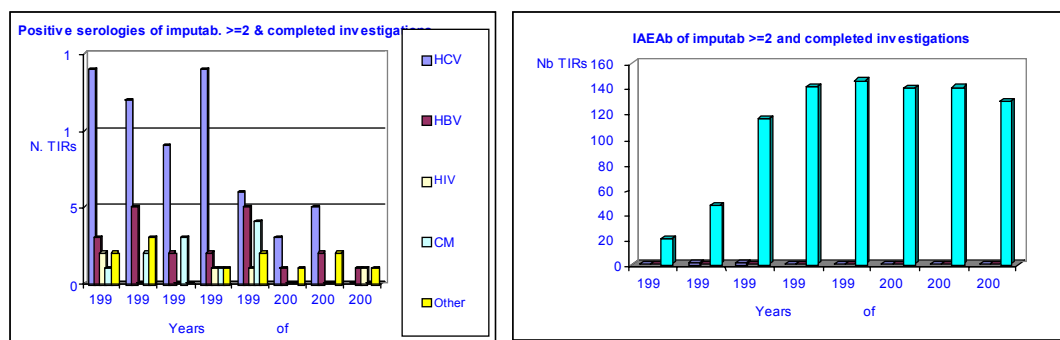
#### 4.2.1.2. Delayed incidents

The diagnosis categories are principally of 4 types:

- \* irregular anti-erythrocyte antibodies IAEAb
- \* suspicion of viral transmission
- \* suspicion of bacterial transmission
- \* suspicion of parasitic transmission

However, the most frequent categories are IAEAb and viral transmission.

#### Delayed incidents



Globally, a reduction in the number of delayed incident notifications is noticed and is particularly noticeable for HCV seroconversions and, to a lesser extent, IAEAb in 2002.

#### 4.2.2. ABO immunologic incompatibilities

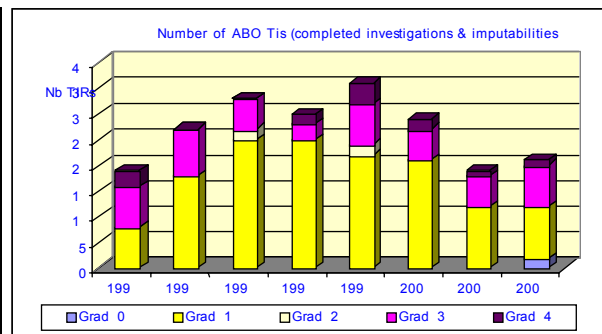
Criteria: ABO-type immunologic incompatibility reported on the transfusion incident report form. This diagnosis category doesn't take into account delivery errors which don't include ABO or Rh incompatibilities (incorrect blood component transfused from the Anglo-Saxons).

##### 4.2.2.1. 1995-2002- Evolution of the number of ABO incidents

ABO type TIs (incompatibilities 2 to 4, completed investigations, 1995-2002)  
 Mean value: 27 TIs per year, CI95% [21.3;32.2]  
 Risk of ≈1 TI for 107,600 BCs, CI95% [82,800;132,500]

Since 1999, a decrease in the number of notified ABO incidents has been observed. The large training actions taken by the whole haemovigilance network at the level of all the actors, as well as the systematic analysis and examination of each reported incident have probably contributed to such evolution. However, the year 2002 was marked by a slight increase in the number of ABO incidents. This increase is maybe due to the notification of grade 0 incidents which didn't exist in the previous years. Such evolution calls for the maintenance of our undivided attention to this type of incidents. Detailed analysis showed the progressive interference of deviations in operating procedures among a personnel who is used to transfusion acts and is appropriately trained though

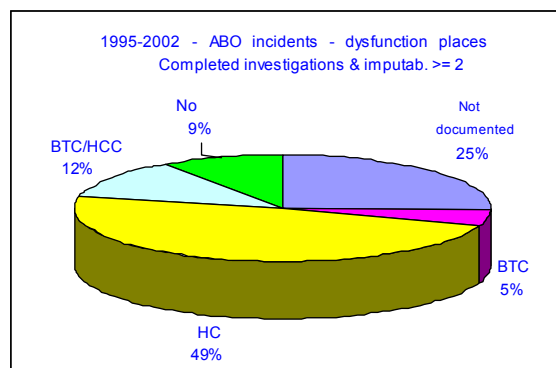
	1995	1996	1997	1998	1999	2000	2001	2002
Number of ABO TIRs	19	27	33	30	36	29	19	21
... With autologous products		2	1	2	1		1	



In total, 7 ABO-type incidents were reported with the use of autologous blood products. These incidents seem to follow the same evolution as the rest of ABO incidents. However, their incidence is difficult to assess considering the low total number.

#### 4.2.2.2. Dysfunction localisation - 1995-2002

Health care services represent almost 65% of TIRs when the dysfunction place is documented. Distribution errors in BTCs are rarely involved alone (7%).



#### 4.2.2.3. 2002 - ABO TIs

In 2002, 21 immediate incidents were recorded, for which the ABO immunologic incompatibility diagnosis category was ticked. High severity incidents (1 death and 8 grade 3 incidents) are related with RBCC transfusion.

Grades - completed investigation and imputability >=2

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Imputability 2		1				1
Imputability 3		4		1		5
Imputability 4	2	5		7	1	15
Total	2	10		8	1	21

IT by BC - completed investigation and imputability >=2

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
RBCC	1	1		8	1	11
APC		7				7
MCP	1	1				2
Plasma		1				1
Total	2	10	0	8	1	21

6/21 TI ABOs (28.6%) are in relation with a distribution from a storage site of blood (against 5/17 TI ABOs is 29.4% in 2001). This characteristic can constitute a factor developing the mistakes of delivery, while

Distribution method - completed investigation and imputability >=2

Storage site		Nominative delivery: yes	Nominative delivery: no
Medicalized storage site: yes	Emergency storage site: no	2	4

throwing out some particular gates of computer security (manual distribution frequently recovered in the commentaries of these incidents).

Medicalized storage site: no	Emergency storage site: no	15	
------------------------------	----------------------------	----	--

#### 4.2.3. "Allergy" diagnosis category Tl

**Definition:** allergy is a state of anaphylaxy in a patient who reacts with violence to transfusion. Such phenomenon is the consequence of a conflict between the allergene-resulting antigene (allergic substance) and antibodies. "Allergy" type incidents are identified with a specific item in the GIFIT database.

##### 4.2.3.1. 1995-2002- Evolution of the number of allergies

Allergy type TIs (imputabilities 2 to 4, completed investigations, 1995-2002)  
 Mean value: 1166 TIs per year, CI95% [918.2;1413.5]  
 Risk of  $\approx 1$  TI for 2,700 BCs, CI95% [1,366.4;4,058.65]

"Allergy" reactions represent 34.2 % of immediate TIs with imputabilities  $\geq 2$  and completed investigations. Nevertheless, they are a frequent apheresis platelet concentrate transfusion complication.

**Number of Allergies – completed investigation and imputability  $\geq 2$**

Year	1995	1996	1997	1998	1999	2000	2001	2002
Number	474	1089	1154	1252	1315	1345	1368	133

##### 4.2.3.2. 2002 - Allergy diagnosis category TIs

The "allergy" risk was 0.5 per 1,000 distributed BC in 2002. As in 2001, the 2002 data confirm that "allergy" diagnosis category TIs are mainly associated with grade 1 (97.6% of TIs with completed investigations and imputabilities  $\geq 2$ ). In 2002 no death was recorded (reminder: 2 in 2001).

**Number of Allergies – completed investigation and imputability  $\geq 2$**

	Grade 1	Grade 2	Grade 3	Grade 4	Total	%
Imputability 2	399		2		401	30,2%
Imputability 3	717		16		733	55,1%
Imputability 4	182	2	12		196	14,7%
<b>Total</b>	<b>1298</b>	<b>2</b>	<b>30</b>		<b>1330</b>	<b>100,0%</b>
%	97,6%	0,2%	2,3%		100,0%	

**Number of Allergies – completed investigation and imputability  $\geq 2$**

Products	Grade 1	Grade 2	Grade 3	Total	%
RBCC	377		5	382	28,7%
APC	828	1	20	849	63,8%
Granulocytes	1			1	0,1%
MCP	38			38	2,9%
Plasma	38	1	5	44	3,3%
SD PLASMA	9			9	0,7%
Not documented	7			7	0,5%
<b>Total</b>	<b>1298</b>	<b>2</b>	<b>30</b>	<b>1330</b>	<b>100,0%</b>
%	97,6%	0,2%	2,3%	100,0%	

In 2002, APC transfusion appears to be the greatest "allergy" type incident risk factor with a ratio of 4.93 incidents per 1,000 distributed APCs, whereas the ratio was 1.57 with MCPs and only 0.17 with plasma products and 0.20 with RBCCs.

On the whole, it can be reminded that allergic reactions are rarely serious and in 60% of cases the patient is immunodepressed.

#### 4.2.4. NHFR, Non-haemolytic febrile reactions

NHFR (imputabilities 2 to 4, completed investigations, 1995-2002):  
 Mean value: 1,444 NHFR per year, CI95% [1,112;131.4]  
 Risk of  $\approx 1$  NHFR for 2,190 BCs, CI95% [1,086.1;3,288.9]

**Definition:** TIs with non-haemolytic febrile reactions are defined as TIs where chill and/or fever and an "unknown" type diagnosis are recorded. This new category constitute an attempt to carve up the "unknown" diagnosis category in the GIFIT database, in the perspective of a comparison with haemovigilance data from other

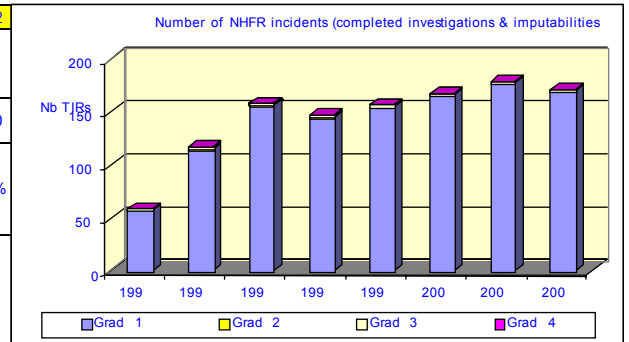
systems.

#### 4.2.4.1. 1995-2002- Evolution of the number of non-haemolytic febrile reactions

At the end of 2002, the analysis of the haemovigilance data on NHFR in transfused patients enabled us to notice the large number of NHFR reactions notified. Between 1995 and 2002, 26.7% of 43,311 declarations (11,550) are associated with these symptoms.

##### NHFR – completed investigation and imputability >=2

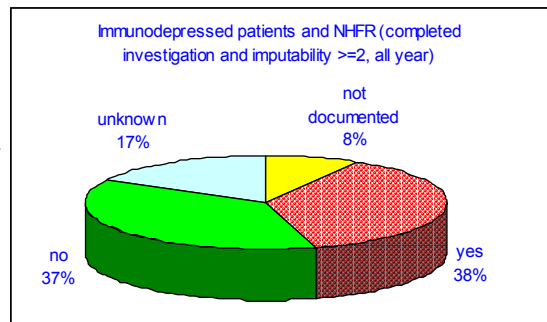
Year	1995	1996	1997	1998	1999	2000	2001	2002
Number of NHFR reactions	584	1166	1580	1477	1566	1676	1790	1711
unknown type TIs	720	1446	1895	1856	1893	1940	2103	2000
NHFR among the "unknown" type TIs	81,1%	80,6%	83,4%	79,6%	82,7%	86,4%	85,1%	85,6%



NHFR reactions are mainly mild incidents: 98% of NHFR are grade 1 incidents.

#### 4.2.4.2. NHFR and immunodepressed patients

The patient immunodepression status occurs in 40% of cases where this item is documented. Immuno-depression appears as a factor favoring the occurrence of non-haemolytic febrile reactions but a comparison with the status of all transfused patients shall be made.



#### 4.2.4.3. 2002 - TIs with non-haemolytic febrile reactions

Most often, NHFR reactions are associated with RBCCs and APCs. In 2002, the risk was estimated to be 0.68 per 1,000 distributed RBCCs (and 0.69 in 2001) and 1.98 per 1,000 distributed APCs. For MCPs, the ratio is 0.87 per 1,000 products. Therefore, APC transfusion presents a greater risk of NHFR than RBCC transfusion.

##### 2002 NHFR TIR severity – completed investigation and imputability >=2

Imputability	Grade 1	Grade 2	Grade 3	Grade 4	Total
Imputability 2	1325	1	6		1332
Imputability 3	343		8	1	352
Imputability 4	27				27
Total	1695	1	14	1	1711

##### By incriminated products

Products	Grade 1	Grade 2	Grade 3	Grade 4	Total
RBCC	1304	1	13	1	1319
APC	340		1		341
MCP	21				21
Plasma	19				19
Other	11				11
Total	1695	1	14	1	1711

#### 4.2.5. TIs with positive culture

TIs with BC positive culture (imputabilities 2 to 4, completed investigations, 1995-2002):  
 Mean value: 32 TIs per year, CI95% [20.5;44.5]  
 Risk of ≈ 1 TI for 96,850 BCs, CI95% [65,894.3;127,806.0]

The bacterial contamination of a labile blood product, which is a fearful incident, is followed by the multiplication of the bacteria during storage and can lead to a bacteraemic shock or an endotoxinic shock in the transfused patient. 17 lethal cases with imputabilities  $\geq 2$  (completed investigations) were reported in the GIFIT database between 1995 and 2002. Two major causes can be put forward: non-detected risk factors in the donor (fever, particular infectious context or transitory asymptomatic bacteraemia) and contamination related to the equipment, methods of collection used (cutaneous disinfection). Contamination during the storage phase occurs more rarely and is less often detected in investigations.

**Definition:** TIs with positive culture (request issued for TIRs with positive culture and identified germ). This examination doesn't concern suspicion cases of bacterial incidents, some of which have not been confirmed, particularly when the culture of the BC has proved negative.

#### 4.2.5.1. 1995-2001 - Evolution of the number of TIs with positive culture

**TIs - completed investigation and imputability  $\geq 2$**

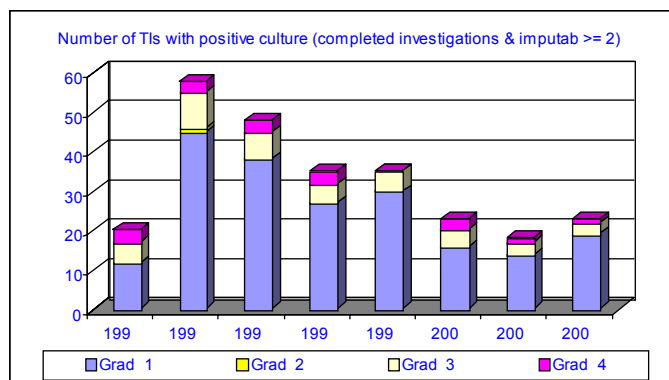
	1995	1996	1997	1998	1999	2000	2001	2002
TIBC suspicions	35	263	59	52	60	42	33	15
% TI	1,8%	6,4%	1,1%	0,9%	1,1%	0,8%	0,6%	0,3%
<b>Positive culture</b>	<b>20</b>	<b>58</b>	<b>48</b>	<b>35</b>	<b>35</b>	<b>23</b>	<b>18</b>	<b>23</b>
% TI	<b>1,0%</b>	<b>3,0%</b>	<b>2,5%</b>	<b>1,8%</b>	<b>1,8%</b>	<b>1,2%</b>	<b>0,9%</b>	<b>1,2%</b>
Negative culture	101	585	595	473	480	413	434	800
% TI	5,2%	30,2%	30,7%	24,4%	24,8%	21,3%	22,4%	41,3%
Culture in progress	2	31	21	18	16	14	9	11
% TI	0,1%	1,6%	1,1%	0,9%	0,8%	0,7%	0,5%	0,6%
total TIs with imputabilities 2 to 4 and completed investigations	1935	4116	5411	5483	5650	5563	5672	5265

It shall be pointed out that within the context of transfusion incidents the symptomatology of which can evoke bacterial contamination, an BC examination is very commonly carried out. The number of notified BC negative cultures thus doubled between 2001 and 2002.

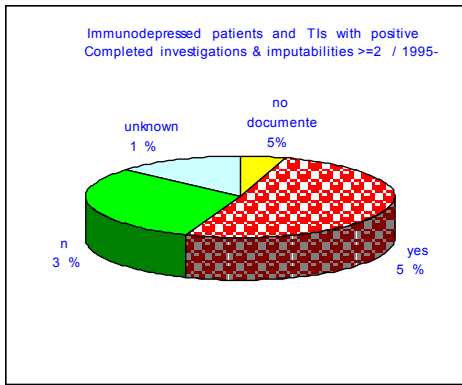
#### 4.2.5.2. 1995-2001- Distribution according to severity

1) Since 1996, a decrease in the reporting of TIs with positive culture has been noticed. However, it is advisable to check that the years 1996 and 1997 do correspond to overreporting concomitant with 1996-1998 BACTHEM study. This decrease was not reproduced in 2002.

2) There is a high number of grade 1 TIs, for which a BC culture is positive. In fact, between 1995 and 2002, 0.9 % of grade 1 incidents had a positive BC culture. This can be taken as a justification for the notification and investigation of mild transfusion incidents.



#### 4.2.5.3. TIs with positive culture and immunodepressed patients

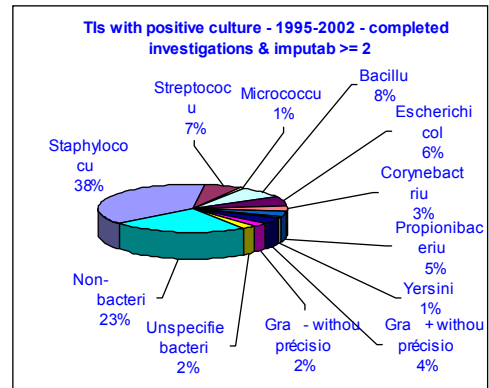


The immunodepression status is found in 51% of incidents of such type for which the patient status is known.

Transfusion of autologous products doesn't exclude the risk of bacteriological contamination. In the 260 incidents with BC positive culture (1995-2002), 9 incidents could be related to the use of autologous blood products (except stem cells): 1 in 1995, 2 in 1996, 3 in 1997, 1 in 1998 and 2 in 1999.

#### 4.2.5.4. TIs with positive culture – Types of germs - 1995-2002

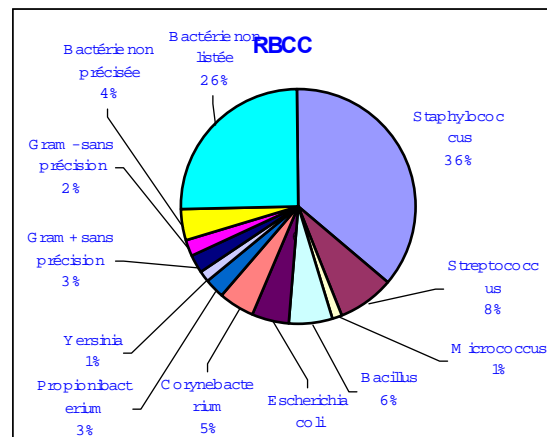
	1995	1996	1997	1998	1999	2000	2001	2002
Staphylococcus	6	25	12	14	11	11	8	12
Streptococcus	2	3	1	4	3	2	1	1
Micrococcus								2
Bacillus	4	4	1	2	6	2	2	
Escherichia coli	1	6	4		2		1	1
Corynebacterium	1	1	3	1	3			
Propionibacterium			3	4	1	2	1	1
Yersinia			1		1			
Gram + without precision	1	2	3	3	1			1
Gram – without precision	1	2	2			1		
Unspecified bacteria		4	1					1
Non-listed bacteria	4	11	17	7	7	5	4	5
Total	20	58	48	35	35	23	18	23

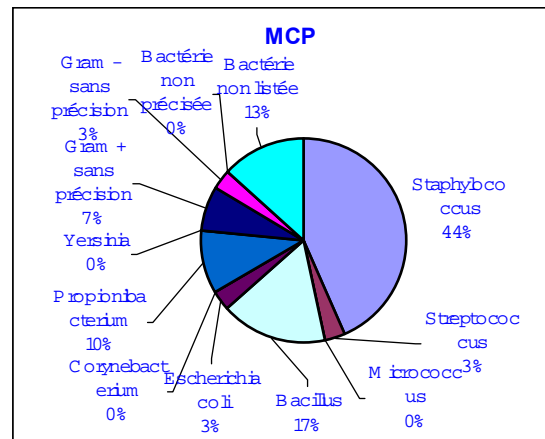
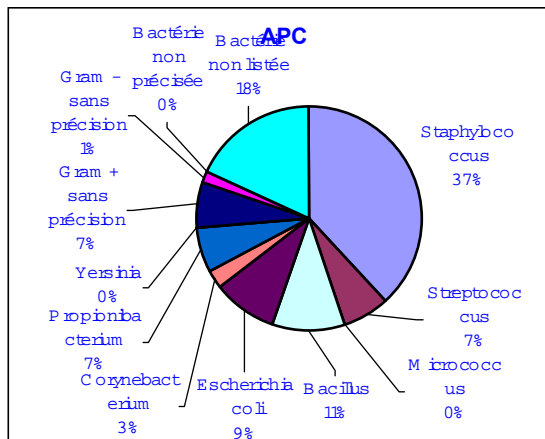


#### 4.2.5.5. TIs with positive culture – Types of germs by types of BCs

Transfusion incidents with positive culture in 1995-2002 – Completed investigation & Imputability >=2

Analysis of the identified germs comes across, in majority and in a similar manner with all three types of products, the staphylococcus family. The distribution didn't vary over the 1997-2002 period.





#### 4.2.5.6. TIs with positive culture in 2002

In 2002 as in 2001, half of the identified germs are staphylococcus, that is to say 12 cases in 23 (52%), the etiological study showing high imputability results (grade 3 or 4). As in the previous years, it appears that platelet concentrates, and APCs due to their use in majority, represent a high risk factor of the occurrence of these incidents with BC positive culture (about 1 for 17,000 APCs and 1 for 182,000 RBCCs).

**2002 TIBC TIR severity**  
**Completed investigation and imputability >=2**

Imputability	Grade 1	Grade 2	Grade 3	Grade 4	Total
Imputability 2	12		1		13
Imputability 3	2		1		3
Imputability 4	5		1	1	7
<b>Total</b>	<b>19</b>		<b>3</b>	<b>1</b>	<b>23</b>

**2002 TIBC TIR incriminated products**  
**Completed investigation and imputability >=2**

Products	Grade 1	Grade 2	Grade 3	Grade 4	Total
RBCC	9		2		11
APC	8		1	1	10
MCP	2				2
<b>Total</b>	<b>19</b>		<b>3</b>	<b>1</b>	<b>23</b>

**Germs – completed investigation and imputability >=2**

Germs	Grade 1	Grade 3	Grade 4	Total
Staphylococcus	11		1	12
Streptococcus	1			1
Micrococcus	2			2
Escherichia coli		1		1
Propionibacterium	1			1
Gram + without precision	1			1
Unlisted bacteria	3	2		5
<b>Total</b>	<b>19</b>	<b>3</b>	<b>1</b>	<b>23</b>

#### 4.2.6. Overload volumes

Overload volume type TIs (imputabilities 2 to 4, completed investigations, 1995-2002):  
 Mean value: 152 TIs per year, CI95% [117.5;185.8]  
 Risk of ≈1 TI for 20,550 BCs, CI95% [11,087.5;30,012.5]

**Definition:** TI with overload volume as diagnosis category documented in the form.

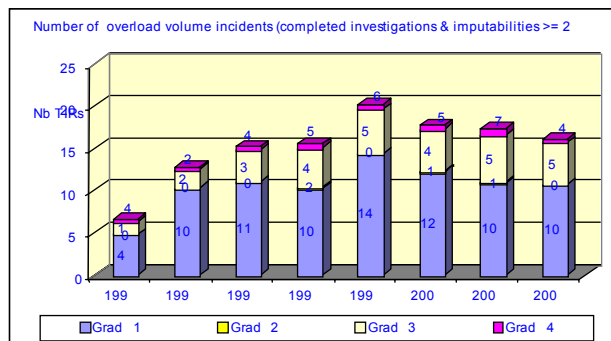
##### 4.2.6.1. 1995-2002 : Evolution of the number of overload volume cases

An average of 6 to 7 incidents with overload volume per 100,000 BC were notified each year over the period 1995-2002 (TIs with imputabilities 2 to 4 - completed investigations). These incidents are well known by transfusion professionals. Their incidence and severity especially are

now well known thanks to haemovigilance data. Since 1995, the overload volume diagnosis has been reported 1,213 times for 43,311 TIs, corresponding to a percentage of 2,8 % on average. These incidents are often little serious since 69.6% are grade 1 incidents, that is to say without immediate life threat. However, these overload volume cases can also be serious: 27% of incidents were notified as grade 3 incidents (immediate life threat and necessity for intensive care acts to be performed) and 3.1% as grade 4 incidents. A study on the circumstances favouring this type of incident conducted in Strasbourg hospitals (Hôpitaux de Strasbourg) in 1999 showed the presence of heart or lung antecedents in more than 85% of cases.

**Number of overload volume cases – completed investigation and imputability >=2**

Year	1995	1996	1997	1998	1999	2000	2001	2002
Number of overload volume cases	66	127	152	155	202	177	173	161
Total no. TIs	2 379	4 712	6 161	6 184	6 140	5 974	6 066	5 695
% ex. blood vol. / total TIs	2,8 %	2,7 %	2,5 %	2,5 %	3,3 %	3,0 %	2,9 %	2,8 %



#### 4.2.6.2. 2002 - TIs with overload volums

Incidents due to overload volume substantially remain associated with the use of red blood cell concentrates. In 2002, the vital prognosis was jeopardized in 50 cases (31%) with high imputabilities (3 and 4) in 92% of cases. Four deaths were reported, most often with a multiple pathology associated with them.

Overload volume has however remained the first cause of death directly imputable to transfusion since the implementation of the haemovigilance system. The recent individualised reporting of TRALI, sometimes included in overload volume cases, is likely to modify this transfusion incident diagnosis category in the future.

**2002 overload volume TIR severity – completed investigation and imputability >=2**

Imputability	Grade 1	Grade 2	Grade 3	Grade 4	Total
Imputability 2	26		4	2	32
Imputability 3	57		31	2	90
Imputability 4	24		15		39
Total	107		50	4	161

**2002 overload volume TIR Blood components – completed investigation and imputability >=2**

BC	Grade 1	Grade 2	Grade 3	Grade 4	Total
RBCC	94		46	4	144
APC	9		2		11
Plasma	3		2		5
SD plasma	1				1
Total	107		50	4	161

#### 4.2.7. Delayed incidents

##### 4.2.7.1. Post-transfusion positive serologies

The post-transfusion risk exists with various viruses:

- Hepatitis B and C
- HIV
- CMV (cytomegalovirus)
- Other viruses

The continuous decrease in these incidents is in large part due to the evolution detection tests in terms of antibody detection sensitivity. The impact of viral genomic detection for HIV and HCV post-transfusion positive serologies enforced on July 31<sup>st</sup>, 2001 will have to be evaluated with the benefit of hindsight.



Definition: positive serology TIs are presented per year of transfusion. It is calculated using two pieces of information in the TIR: the year of occurrence (= year of finding of the positive serology) and the time period since transfusion when documented.

- **With imputabilities 2 to 4 and completed investigations**

<p>In 2002, only 4 incidents with post-transfusion positive serologies with imputabilities of 2-4 and completed investigations were notified. Investigations most often lead to conclude to an excluded or uncertain imputability. Labile blood products such as red blood cell, platelet and plasma products, have a very low residual risk of transmission of viral affections.</p>	Post-transfusion serologies per year of transfusion <b>imputabilities 2 to 4</b>								
		1995	1996	1997	1998	1999	2000	2001	2002
	HCV	14	12	9	14	6	3	5	
	HBC	3	5	2	2	5	1	2	1
	HIV	2			1	1			1
	HTLV								
	CMV	1	2	3	1	4	4	2	1
	Other viruses *	1	3		1	1	1	2	1
	Other					1			
	<p>Note: * The other viruses involved are listed hereafter in the "Other delayed incidents" section.</p>								

Reminder: these figures only represent the incidents notified for a transfusion performed in 2002.

For the record, 84 post-transfusion positive serologies notified for transfusions performed in 2002 lead to conclude to imputability **nil** (imputability 0) after investigations and only 1 doubtful imputability (imputability 1).

- **With imputabilities 3 to 4 and completed investigations**

HCV (imputabilities 3 to 4, completed investigations, 1995-2002):  
 < 2 per year  
 Risk of ≈1 TI for 1,363,000 BCs, CI95% [907,400;2,714,700]  
*mean deviation interval (due to the type of data)*

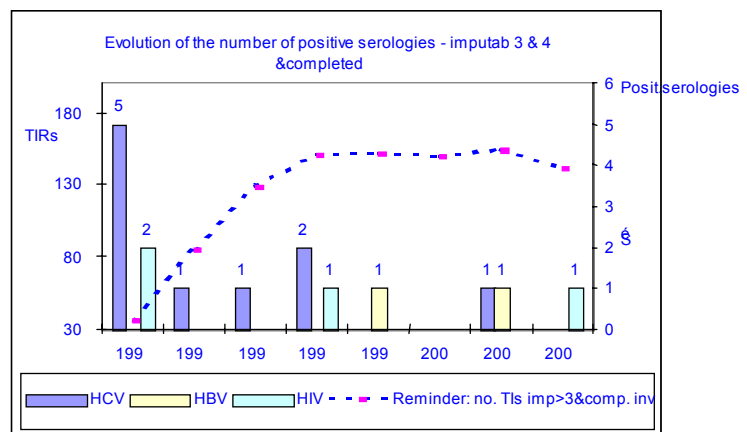
**Post-transfusion serologies per year of transfusion – imputabilities 3-4**

Proved or probable HIV and HCV transmission cases have almost disappeared, with only one HIV case reported in 2002.

**Imputabilities of 3 to 4 and completed investigation**

	1995	1996	1997	1998	1999	2000	2001	2002
HCV	5	1	1	2			1	
HBV					1		1	
HIV	2			1				1

Note: TI = year of occurrence, serologies = years of transfusion, if documented



- **Review of the HCV seroconversions (2001-2002, for all imputabilities)**

The following notes use some elements of the thesis by Cécile Péchaire, a trainee at the Afssaps haemovigilance unit from April to July 2003 ("Review of the TIs associated with HCV seroconversions observed in 2002")

Concerning the cases notified in 2001 and 2002, she observed that:

- In almost 70% of cases, the exclusion of the liability of transfusion is obtained through negative recontrol of all the donors (either with notification issued by the BTC or upon

later blood donation)

- 87% of imputabilities 0 and almost 80% of imputabilities 1 are associated with seroconversions dating from the previous year (2001-2002). Half of the TI cases associated with an HCV seroconversion are detected within the 4 months following the incriminated transfusion (probably to be related to the systematic post-transfusion controls)
- Almost 80% and 100% of imputabilities 2 and 3 respectively are due to old seroconversions (dating from more than 5 years). 12,5% of imputabilities 1 are due to old transfusions (over 10 years).

The author concluded that:

- "The majority of TIRs associated with HCV seroconversions to be notified in the years to come will still be due to old transfusions performed before 1990."
- "Contaminations due to recent transfusions and related to the HCV mute window should now become exceptional due to the introduction of the VGD in the donation biological qualification in July 2001." It seems the implementation of the VGD hasn't had a direct impact yet on TIs with high transfusion imputabilities detected in 2000, 2001, and 2002 but the majority of reported dossiers correspond to old transfusions..."

#### 4.2.7.2. Incident post-transfusion anti-erythrocyte antibodies IAEAb

**IAEAb** (imputabilities 2 to 4, completed investigations, 1995-2002)  
 Mean value: 1,350 IAEAB per year, standard deviation: 110  
 Risk of  $\approx 1$  IAEAB for 2,000 BCs, CI95% [1,100;2,200]  
 • mean deviation interval (due to the evolution of data)

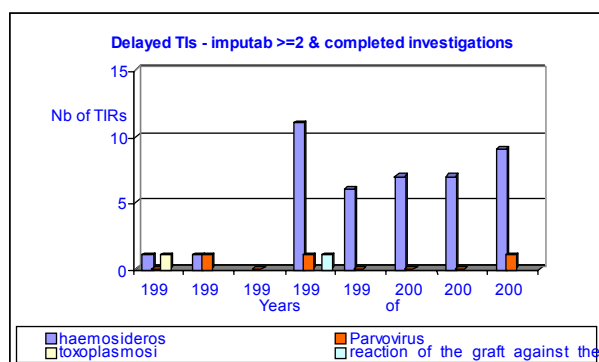
A slight decrease in anti-erythrocyte antibodies reporting was observed in 2002. At present, no use is made of that type of incident due to the absence of accessibility of the antibody specificity criterion. In 2004, it is planned to integrate a thesaurus enabling their identification.

Furthermore, the regional haemovigilance coordinator activity reports showed that there exists a strong regional disparity with regard to both the reporting of these immunization cases and the practical isoimmunization prevention measures, especially with Rh Kell.

IAEAb per year of occurrence								
	1995	1996	1997	1998	1999	2000	2001	2002
TIRs	202	466	1160	1404	1455	1397	1402	1293

#### 4.2.7.3. Other delayed incidents

Parvovirus B19 or the reaction of the graft against the host are complications which are reported exceptionally only, as shown in the histogram opposite. Haemosiderosis is more commonly notified but probably still very much underreported.

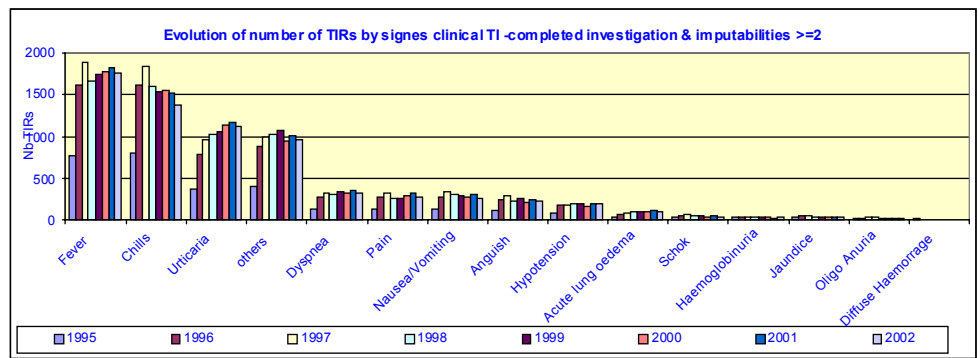


### 4.3. Principal clinical signs

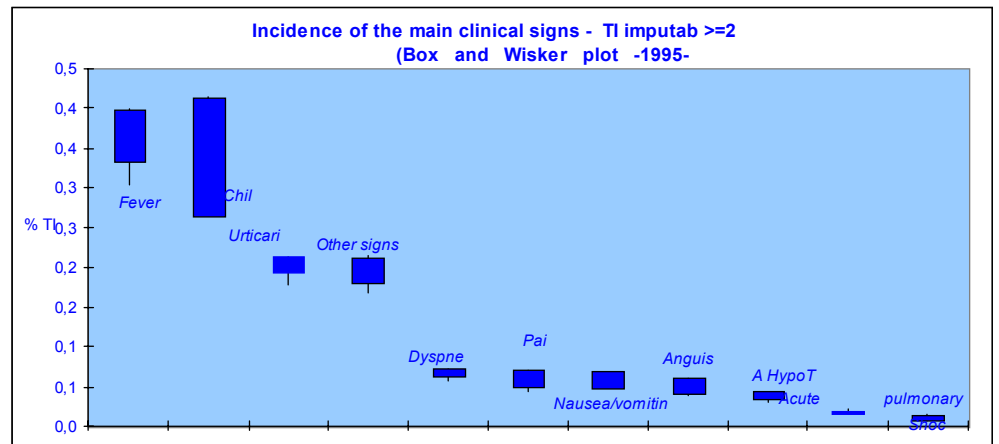
#### 4.3.1. Frequency and evolution of clinical signs

The most frequent symptomatology is:

- fever
- chill (or chill-hyperthermia syndrome)
- urticaria
- dyspnea
- nausea/vomiting
- pain...



Fever and chill are the most common and the most variable clinical signs; conversely, acute pulmonary oedema and shocks - rarer - are relatively stable with a percentage in the order of 1% or lower.

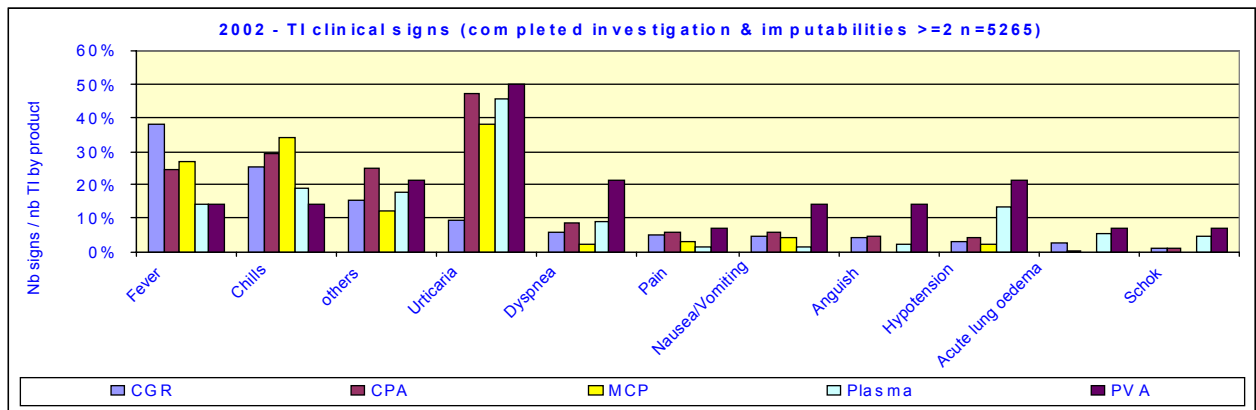
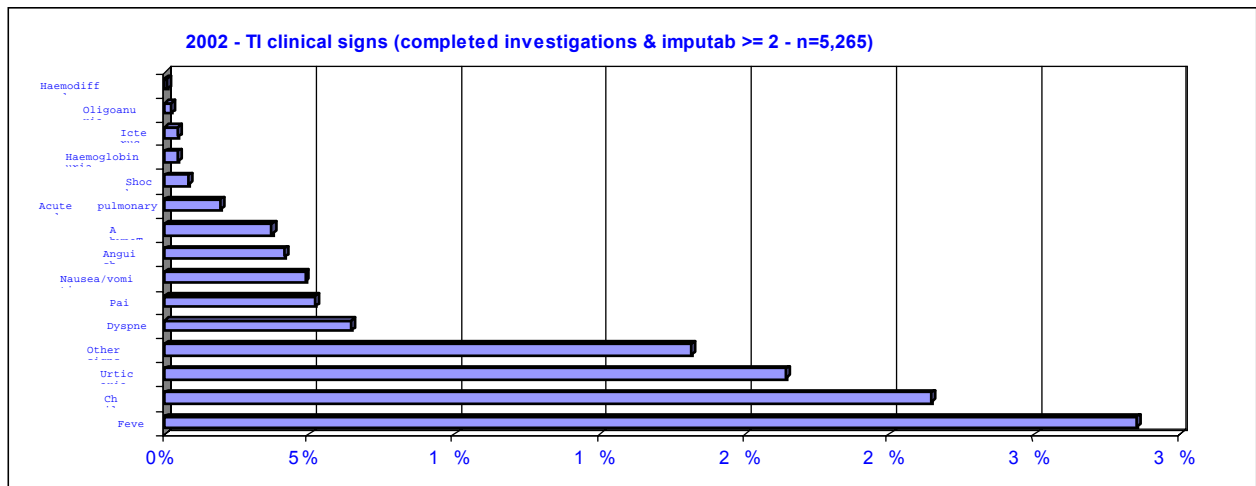


It is to be mentioned that each of these signs might be the first element of a serious clinical scene:

- the chill-hyperthermia syndrome, very often associated with the "non-haemolytic febrile reaction" diagnosis, may also be the first sign of an immunologic shock;
- urticaria, anguish or nausea/vomiting may be the first signs of an anaphylactic shock but also sometimes of bacterial contamination;
- dyspnea may be the first sign of an overload volumes;
- pain may be the first sign of an immunologic shock or an anaphylactic shock.

#### 4.3.2. Clinical signs in 2002

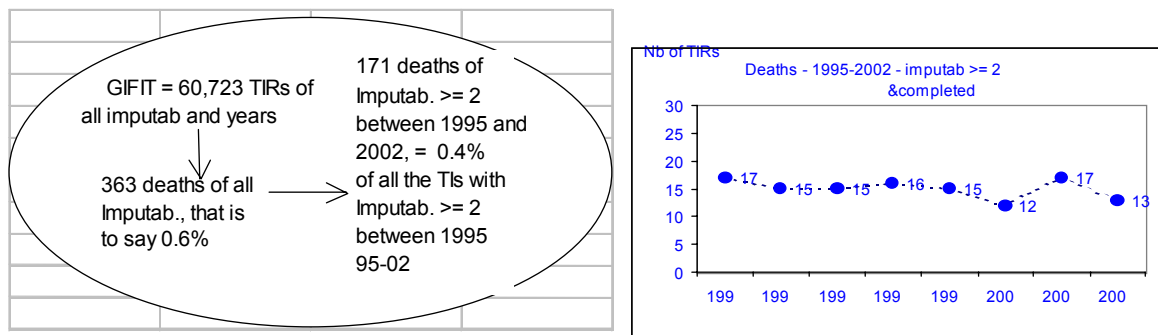
The study of clinical signs also contributes to establishing what is the relation with the type of product used. As a result, fever is observed in almost 38% of incidents after RBCC transfusion, and 46% of the incidents occurring after the transfusion of therapeutic plasma products bear clinical signs of urticaria. On the contrary, chill and fever are little present in these incidents after the transfusion of plasma products. It shall also be pointed out that the highest incidence of haemodynamic signs (hypotension, acute pulmonary oedema and shock) occurred with TIs involving plasma (donor retested) products or SD plasmas.



#### 4.4. Deaths

Grade 4 TIs (imputabilities 2 to 4, completed investigations, 1995-2002):  
 Mean value: 15 TIs per year, CI95% [13.5;16.5]  
 Risk of  $\approx 1$  TI for 183,200 BCs, CI95% [166,692.0;199,708.0]

##### 4.4.1. Number of notifications and evolution – imputabilities >= 2 and completed investigations



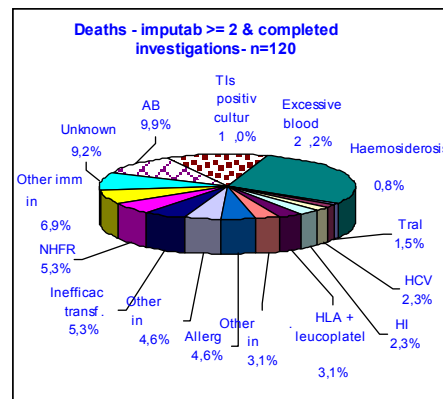
Since 1995, an average of 15 deaths per year with imputabilities >=2 and completed investigations was recorded. In 2002, 13 deaths were notified. However, strong disparities appear from one French region or department to another. Of course, the situation is to be analysed taking into account the geographical dispersal of towns with a high urban concentration (with large hospital structures), which present higher mortality rates.

In this case, the risk of death imputable to transfusion is estimated to be 0.6 per 100,000 BCs (ratio of grade 4 and imputability 2-4 TIs with completed investigations to the number of distributed BCs) It shall be reminded that the comparative study ISBT 2002 on the Quebec, French and United Kingdom data showed that France ranks between these two countries in terms of risk (0.17 and 2.1 in 2001).

#### 4.4.2. Diagnosis of death with imputabilities $\geq 2$ and completed investigations

The GIFIT database enabled us to identify the 5 main causes of death over the past 8 years, or in decreasing order:

- overload volume (37 TIs)
- TIs with BC positive culture (17)
- ABO type TIs (13)
- unknown type incidents (12)
- NHFR (7)



## 5. Conclusion

The French haemovigilance network, which has been existed since the law dated January 4<sup>th</sup>, 1993, has now reached a "mature" stage. It is endowed with a transfusion incident database including more than 62,000 report forms which represent the largest available epidemiological source. After an increasing phase for 4 years, the frequency of transfusion incidents notifications became stabilized at a level of 7,700 TIs per year; however, a slight decrease has been noticed, probably in relation with the decrease of a few percentage points a year in the regular use of labile blood products, except in the year 2002, which shows a stabilization of the distribution for the first time.

One is often inclined to reduce haemovigilance to the notification of transfusion incidents and to the collection of information concerning unexpected or undesirable effects. In fact, haemovigilance shall be conducted further and one will realize that it now provides both material and tools for exploitation and epidemiological evaluation with the benefit of 10 years' hindsight. The network's fields of intervention are also varied. In the first place, the haemovigilance network implemented surveillance procedures and the collection of information concerning unexpected or undesirable effects resulting from the therapeutic use of labile blood products. Then, it extended its field of competence to the whole transfusion process, going back to donor incidents, the haemovigilance network being based on a fundamental principle: traceability of labile blood products from donor to recipient.

Such involvement in the implementation of a total traceability for labile blood products is written in the missions assigned to the haemovigilance network in the decree concerning its functioning (Article R-666-12-1 of the PHC). Besides, the need for perfect traceability is clearly reminded in recent European Directive 2002-98 EC dated January 27<sup>th</sup>, 2003. All the actors of the haemovigilance network will thus be appealed to through the intermediary of the regional haemovigilance coordinators to tend to 100% effective traceability and achieve operational computerization.

Finally, the system is now strengthening its role through actions at the level of both communication - to all the network participants - and prevention especially in terms of occurrence of incidents (recommendations for haemovigilance correspondents and laboratory personnel, ad hoc working groups: traceability, incidents by bacterial contamination...). The great many local and regional training courses (more than 1,500 training actions listed by RHC in 2002), as well as the collaboration with medical and nursing schools demonstrate the haemovigilance network actors' dynamism and commitment. The communication tools shall however be developed and modernized. The access of haemovigilance correspondents to the electronic transfusion incident notification website (e-TIR) will be completed with online documentation and publications in the middle of 2004.

Progress is encouraging but haemovigilance and transfusion safety will always depend on a good knowledge of the risk in relation with the use of labile blood products and the origins of unexpected or undesirable effects. The analysis of these two points has already enabled us to determine problems in relation with daily practices (ABO incidents or bacteriological contamination) and to react if necessary.

It is also for this purpose that two new improvements in the management of the transfusion incident report forms were introduced in 2002: 1) the computerized notification of grade 0 dysfunctions, incidents without clinical or biological sign, and 2) diagnosis of transfusion related acute lung injury (TRALI). Clearly identified in the TIR, these two effects can now be subjected to evaluations and analyses. In the first case, notification analyses showed that some dysfunctions could lead to the transfusion of inappropriate products to the patient without any undesirable effect being noticed at the moment of transfusion. These incidents are often related to identification errors or product management errors. The numbering and the investigations of

these incidents appear to be particularly valuable and likely to improve the BCs delivery safety. In the second case, the data recently received showed that these incidents were often mistaken for overload volume incidents. Consciousness-raising campaigns regarding this type of incident has already led to a better determination of the biological criteria (anti-granule antibodies, anti-HLA I and II), and should result in an identification of the donation factors. A preventive action could result from such work.

Insufficiently controled, the bacterial risk tends to decrease though. Two working groups, namely "Incidents by BCs contamination" and "TIBC validation", composed of bacteriologists and haemovigilance professionals, were able to produce a document on the conduct to adopt in case of bacterial incident related to transfusion and the centralisation of strains of bacteria, while regularly following and analysing the evolution of these incidents and their characteristics.

Although it isn't often mentioned in haemovigilance analyses in the medical literature, overload volume is identified as a major cause of morbidity and mortality during and following transfusion in the French system. It is certain that difficulty in monitoring patients, who are very often in a precarious haemodynamic or general condition when deciding to transfuse them, make it very complex to finely analyse these incidents. However, it seems to us that such difficulty make the active collaboration between health care centers and blood transfusion centers within the haemovigilance network even more evident and necessary for a better identification and prevention of incidents.

ନିର୍ବାହକଙ୍କୁ ଜଣାଇବା

## 6. Annexes

### 6.1. WEB - Afssaps

- 2001 annual report, Haemovigilance unit : <http://afssaps.sante.fr/pdf/5/hmv2001.pdf>
- Results of the reevaluation of the IgG and total anti-CMV antibodies detection reagents (anti-CMV IgG) - biologist information : <http://afssaps.sante.fr/htm/5/reactif/cmv.htm>
- Final control devices at the patient bed - user information - updated version: February 12<sup>th</sup>, 2003: <http://afssaps.sante.fr/htm/5/reactif/culm.htm>
- Good Practice Recommendations (GPR): Platelet transfusion - Granulocyte transfusion: <http://afssaps.sante.fr/htm/5/rbp/tpf.htm>
- National quality control of medical biology analyses: <http://afssaps.sante.fr/htm/10/cnq/data2003/cal2003.htm>
- Good transfusion practice: <http://www.legifrance.gouv.fr/WAspad/Visu?cid=341444&indice=1&table=JORF&ligneDeb=1>

### 6.2. List of abbreviations and formulae

**AFS:** Agence Française du Sang

**Afssaps:** Agence Française de Sécurité Sanitaire des Produits de Santé - French Health Products Safety Agency

**Anti-HCV Ab:** Antibodies to hepatitis C virus

**BC:** Labile blood product

**BTCo:** Blood Transfusion Correspondant

**BTCe:** Blood Transfusion Center

**CDC:** Centers for Disease Control and Prevention

**DGS:** Direction Générale de la Santé

**DHOS:** Direction de l'Hospitalisation et de l'Organisation des Soins

**DNA:** Deoxyribonucleic acid

**EFG:** Etablissement français des greffes

**EFS:** Etablissement français du Sang

**EMA:** European Agency for the Evaluation of Medicinal products

**FDA:** Food and Drug Administration (USA)

**HBV:** Hepatitis B virus

**HCC:** Health care center

**HCV:** Hepatitis C virus

**HCV Ag:** Hepatitis C virus antigen

**HIV:** Human Immunodeficiency Virus

**IAEAb: Anti-erythrocyte antibodies**

**INTS:** Institut National de la Transfusion Sanguine

**InVS:** Institut National de Veille Sanitaire

**LFB:** Laboratoire français du Fractionnement et des Biotechnologies

**ND:** Not documented

**POAT:** peri-operative autologous transfusion POAT

**RHC:** Regional haemovigilance coordinator

**RNA:** Ribonucleic acid

**SFTS:** Société française de Transfusion Sanguine

**TI:** Transfusion incident

**TIR:** Transfusion incident report

**TIBC:** Transfusion incident with positive bacteriological culture

**UHC:** University Hospital Complex

**VGD:** Viral Genomic Detection

**Mean deviation:** a measure of dispersion in a set of values; = the mean of the absolute deviations of the observed values from their arithmetical mean.

standard deviation: a measure of dispersion of the observed values from their mean

**95% IC:** 95% confidence interval

**Box and Wisker plot:** chart summarising the data and displaying the suspicious and abnormal points for one or several



variables.