Agence nationale de sécurité du médicament et des produits de santé

RAPPORT

FRENCH HAEMOVIGILANCE ANNUAL REPORT – YEAR 2022 – EXECUTIVE SUMMARY

DECEMBER 2023

Content

LIST OF ACRONYMS

AHTR	Acute Hemolytic Transfusion Reactions
AI	Alloimmunization
ANSM	National Agency for the safety of Medicines and Health Products
ARs	Adverse reactions
BEs	Blood establishments
CHV-ST	Haemovigilance and transfusion safety correspondents of hospitals, clinics and blood establishments
CRH-ST	Haemovigilance coordinators for the regional Public health agencies
CTSA	French Army blood service
DHTR	Delayed Hemolytic Transfusion Reaction
DSAR	Donor serious adverse reaction
DSR	Delayed serologic reactions
EFS	French National blood Service
FEIGD	Blood donor serious adverse reaction form
FEIR	Recipient adverse reaction form
FIG	Serious incident form
FIPD	Post-donation information form
FNHTR	Febrile non hemolytic transfusion reaction
HBBs	Hospital blood banks
HEV	Hepatitis E virus
LBP	Labile blood products
MCE	Major cardiovascular events
NCA	National competent authority
P	Plasma
PC	Platelet concentrates
PDIs	Post-donation information
PRP-PR	Platelets, recovered, pooled, pathogen reduced
RBC	Red blood cell
RBCC	Red blood cell concentrates
SAE	Serious adverse event
SARs	Serious adverse reactions
SCD	Sickle cell Disease
SPF	French Public Health Agency
TACO	Transfusion-related circulatory overload
TRALI	Transfusion-related Acute Lung Injury
TTBI	Transfusion-transmitted bacterial infections
TTVI	Transfusion-transmitted viral infections

INTRODUCTION

This is the French Haemovigilance Annual Report Executive Summary for the data for fiscal year 2022. This report corresponds to the 20th national haemovigilance report, relating to the entire transfusion chain, from blood collection to recipient (e.g. patient transfused) follow-up, and compiled from the reports of the haemovigilance and transfusion safety correspondents of hospitals, clinics and blood establishments (CHV-ST).

This Executive Summary provides information on blood and blood components issued nationwide, all adverse reactions (ARs) occurring in patients transfused, serious adverse reactions (SARs) occurring in blood donors, post-donation information (PDIs), and any serious adverse event (SAE) occurring along the transfusion chain between blood donation and transfusion and which could jeopardize the quality of the blood components (e.g. labile blood products) or the safety of the blood donor or the recipient (including but not limited to near misses, blood components defects). It is intended to provide an overview of the main results and findings.

BACKGROUND

Created by the Public Health Code law nr. 93-5 (dated January 4, 1993), French haemovigilance is a key pillar to ensure the quality and safety of transfusion and blood donation. The National Agency for the safety of Medicines and Health Products ("Agence Nationale de Sécurité du Médicament et des produits de santé", ANSM) is in charge of haemovigilance at a national level, comprising monitoring the reactions and events related to haemovigilance, updating the legislative framework to ensure a high level of quality for all labile blood products (e.g. blood components intended for transfusion), in accordance with international standards and adapting to new technology processes, and maintaining a robust haemovigilance system which plays a key role in public health and epidemiological surveillance. The haemovigilance system contributes to an increase in scientific knowledge on haemovigilance reactions and events, the provision of tools for early detection of new risks and defects, and the assessment of the efficacy of preventive measures aimed at mitigating the risks and reducing their occurrence.

The French haemovigilance reporting system of reactions and events is mandatory. Depending on their seriousness, reactions and events are reported and analysed through a multi-level framework:

- hospitals and health facilities, both private and public, including army facilities ;
- blood donation sites/locations, at a local and regional level ;
- French National blood Service ("Etablissement français du sang" EFS) and French Army blood service ("Centre de transfusion sanguine des armées" CTSA), in charge of supervising reported events at a sub-national level ;
- French Public Health Agency ("Santé Publique France" SPF), in charge of the infectious disease surveillance in blood donors ;
- haemovigilance coordinators for the regional Public health agencies (Coordonnateurs régionaux d'hémovigilance et de sécurité transfusionnelle, CRH-ST), in charge of implementing the haemovigilance legal framework and good practices at a regional level ;
- ANSM, national competent authority (NCA), in charge, at a national level, of coordinating and implementing haemovigilance.

All reactions and events reported are directly registered in the electronic national reporting system called "e-FIT", which is a secured web-based application dedicated to haemovigilance, created and maintained by the ANSM. e-FIT provides four types questionnaires or forms, for reporting adverse reactions and events, each dedicated to a specific reaction, event or information in compliance with the regulations:

- recipient adverse reaction form ("Fiche d'effet indésirable reçeveur FEIR" as defined in the July 2, 2020 ANSM Decision).
- blood donor serious adverse reaction form ("Fiche d'effet indésirable grave donneur FEIGD" as defined in the June 1, 2010 ANSM Decision) ;
- serious incident form, for all serious adverse events (SAEs) occurring in one or more steps of the transfusion chain (during the transfusion process), such as near-misses and quality defects ("Fiche d'incident grave FIG" as defined in the December 24, 2010 ANSM Decision) ;
- post-donation information form ("Fiche d'information post-don FIPD" for which the ANSM Decision is currently pending).

e-FIT also provides detailed data on blood collection (number of donors and donations) and transfusion (number of blood components issued, transfused, recalled and number of patients transfused, traceability rate etc.), which are the denominators used to calculate the incidence of adverse reactions and events.

METHODS

Data collected via the e-FIT electronic system consist of reports of the 4 above mentioned types, reported before January 1, 2023 and concerning reactions and events which occurred during the fiscal year 2022 (FEIR, FEIGD, FIG) or post-donation information that was discovered during the fiscal year 2022 (FIPD), (from the 1st of January up to and including the 31st of December). Only reactions and events reported as having "completed investigation" as of the February 5, 2023 are analysed in this report.

The number of labile blood products (LBP) issued and transfused, as well as data concerning blood donations and blood donors are also reported in the e-FIT system since 2015. These data are collected at a national level by the EFS and CTSA, and are reported in the e-FIT system by the ANSM after passing the data quality-control tests. They are further updated and supervised by the CRH-ST according to the latest information regarding traceability in the health facilities.

All data regarding LBP, blood donors and blood donations provided for the fiscal year 2022 are analysed in this report.

Adverse reactions (AR) are graded according to their imputability and severity, regardless of the type of ARE.

Imputability is scored as follows:

- imputability 0: excluded/unlikely
- imputability 1: possible
- imputability 2 : likely, probable
- imputability 3: definite, certain
- imputability 9: not assessable (NA)

Severity is scored for recipients as follows:

- grade 1: non-severe
- grade 2: severe
- grade 3: life-threatening
- grade 4: death

Severity is scored for blood donors as follows:

- grade 1: mild
- grade 2: moderate
- grade 3: severe
- grade 4: death

RESULTS

Labile blood products (see Appendix)

2,910,359 labile blood products (LBP) were issued in 2022 of which around 80% were red blood cell concentrates (RBCC), 12% were platelet concentrates (PC) and 8% were plasma (P), and less than 0.1% were autologous blood components.

The traceability rate is 99.1% in 2022.

Among 2,681,889 blood donations (of which 2,665,306 were completed), 88% were whole blood donations and 12% were apheresis donations. Nationwide 1,593,206 donors donated blood, regardless of the blood collection type.

LBP were transfused to 534,226 recipients (51% female, 49% male), representing an average of 5.1 LBP transfused per recipient. The transfusion rate in France represents 7.9 recipients per 1,000 inhabitants in 2022.

Reported Events and Reactions (see Appendix)

Regardless of the investigation status reported and the date of occurrence or discovery of the event, a global increase of 4.7% in events is observed, compared with 2021:

- -0.6% for recipient ARs (FEIR),
- +10.5% for donor SARs (FEIGD),
- +2.0% for SAEs,
- +16.3% for PDIs (FIPD).

Overall, 19,712 events or reactions were reported in 2022, regardless of the investigation status and their date of occurrence (or discovery), of which:

- 9,510 recipient ARs ;
- 6,942 blood donor SARs ;
- 1,029 AEs ;
- and 2,231 PDIs.

Recipient Adverse Reactions

According to the French legislation, all recipient ARs have to be reported.

Among the 9,510 recipient ARs reported, 8,976 occurred in 2022 (94%), i.e. an incidence rate of 326 reactions per 100,000 LBP transfused and 168 reactions per 10,000 recipients. Among all 8,976 adverse reactions occurred and reported in 2022, the investigation status of 7,335 was completed, as of 5 February 2023, and 92% of these were of grade 1 severity. Among them, 5,394 adverse reactions of imputability level probable (2) or certain (3) were analysed and summarised as follows (except Transfusion-related Acute Lung Injury (TRALI), for which the reactions summarised below were of imputability possible (1), probable or certain). Concerning grade 4 adverse reactions, three deaths with strong causality were reported in 2022, involving RBCC: 3 Transfusion-related circulatory overload (TACO) (of imputability certain).

Delayed serologic reactions (DSR) (Alloimmunization (AI)) represented the most frequent adverse reaction (66%), of which the overwhelming majority (99.4%) of grade 1 severity, mostly transfusion-related RBC (91%).

Allergic reactions were the second most frequently reported adverse reaction (10%), most of which of grade 1 severity. In 2022, allergic reactions (all levels of severity) were reported mainly transfusion-related of platelets.

Febrile non hemolytic transfusion reaction (FNHTR) was the third most frequently reported adverse reaction (9%), almost all of which of grade 1 severity (97%). This adverse reaction is specific for transfusion, RBCC and platelets being the most frequently involved.

Transfusion-related circulatory overload (TACO) represented 5% of adverse reactions of imputability 2 or 3, i.e. an incidence rate of 9.0 TACO per 100,000 LBP issued. The overwhelming majority (93%) were adverse reactions of grade 1 or 2 severity, but three deaths were reported in 2022 for this adverse reaction. TACO is mostly RBCC transfusion-related. It is mainly reported in elderly recipients, especially over 70 old-years.

Almost 5% of all adverse reactions, of imputability 2 and 3, consisted of Acute Hemolytic Transfusion Reactions (AHTR), of which 26 were related to ABO incompatibility. Six ABO accidents were reported following RBCC transfusion. 67% were platelets transfusion-related of which 74% were related to the HLA system.

Delayed Hemolytic Transfusion Reaction (DHTR in Sickle cell Disease (SCD) represented 0.3% of adverse reactions of imputability 1 to 3; i.e. an incidence rate of 0.8 per 100,000 LBP issued. Among the reported DHTR, 3 were of grade 3 and no death have been reported.

Transfusion-related Acute Lung Injury (TRALI) represented 0.2% of adverse reactions of imputability possible, probable or certain, i.e. an incidence rate of 0.5 TRALI per 100,000 LBP issued. Among the reported TRALI, only one was defined as immunological TRALI (of imputability certain): one grade 2 involving Platelets, recovered, pooled, pathogen reduced (PRP-PR) transfusion-related and no death have been reported.

Transfusion-transmitted bacterial infections (TTBI) remain very rare and no case was reported in 2022.

For Transfusion-transmitted viral infections (TTVI), all the reactions reported in 2022 were considered in this Executive Summary. Four Hepatitis E virus (HEV) infections of imputability 2 or 3 were reported: 3 of grade 1 (PRP-PR (n = 2 ; 1 RBCC, n=1) and 1 of grade 2 (fresh frozen plasma). The estimated incidence rate is 0.1 HEV per 100,000 LBP issued, and 0.1 HEV per 10,000 recipients.

Serious Adverse Reactions in Donors

According to the French legislation only “donor SARs” including grade 2 (moderate) and grade 3 (severe) and grade 4 (death occurring within seven days after the donation) reactions have to be reported.

Donor SARs (DSAR) reportable to the European Commission on a voluntary basis are limited to grades 3 and 4; grade 2 (moderate) ARs are excluded. In general, SAR in blood donors should be reported if they were definitely or probably caused by the donation (imputability 2 or 3). Concerning reports where SAR in blood donors are confirmed to be fatal, the total number of fatalities where a link with donation cannot be excluded (imputability not assessable, 1, 2 or 3), is reportable.

Among the 6,942 reactions reported in 2022, the investigation of 6,771 reactions had been completed on February 5, 2023, with imputability 1 to 3 and not assessable, i.e. an incidence of 255 DSARs per 100,000 blood collections and 43 DSARs per 10,000 blood donors.

The **incidence of DSARs was higher after an apheresis donation** compared to whole blood, i.e. 334 versus 241 serious reactions per 100,000 blood collections respectively.

Serious adverse reactions were mostly reported in female blood donors, with an estimated rate of 303 serious adverse reactions per 100,000 blood collections compared to an estimated rate of 206 serious adverse reactions for male blood donors, and the highest incidence rates were among the 18-29 years old blood donor group regardless of gender.

The incidence of DSARs in first-time blood donors was twice that observed in regular blood donors: 77 versus 36 per 10,000 blood donors, while first-time blood donors represented almost a third (31%) of blood donors who presented a DSAR.

Approximately 77% of DSARs were classed as grade 2 severity (n=5,182), 1,588 as grade 3 severity. **One death was reported in 2022**, occurring after a plasma donation (around 20 minutes later) due to a motorcycle accident. Its imputability was rated as not assessable. An overwhelming majority (95%) of serious adverse reactions were found to have no medical consequence for the blood donor.

Immediate vasovagal reaction is the most frequently reported diagnosis (84%), i.e. an estimated rate of 213 serious reactions per 100,000 blood collections. The incidence rate appears higher after apheresis donation (250 per 100,000 collections) than after whole blood donation (209 per 100,000 collections).

Local reactions (such as bruise, arterial puncture, nerve injury or local allergic reaction, tendon injury) are the second most frequently reported diagnoses (about 13%).

In 2022, 46,362 grade 2 of “anemia” (according to the WHO definition) or “aggravation of anemia” type were notified and 13 of grade 3 were reported.

Venous and/or arterial thromboembolic-type DSAR are more serious but rarer and were reported in 16 blood donors in 2022.

Nine major cardiovascular events (MCE): cardiac, pulmonary and neurological-type were grade 3 adverse events (no deaths reported in 2022), mainly after whole blood donation. These are **cardiac dysrythmia** (n=2), angina pectoris (n=1), Takotsubo syndrome (n=1) and stroke (n=5). The imputability of the donation was rated as excluded or not assessable.

Serious Adverse Events (SAE)

According to the French legislation only serious adverse events have to be reported in France.

1,029 SAEs were reported in 2022. Among them, 933 occurred in 2022, including 911 valid SAE reports having a “completed investigation” as of February 5, 2023 which have been analysed in detail, represent an estimated rate of 31 SAEs per 100,000 LBP regardless of the investigation status. The incidence of transfusion-related SAEs was estimated as 9 SAEs per 100,000 LBP transfused, transfusion-related SAEs represent 26% of all SAEs, regardless of the investigation status.

Most of SAEs occurred in hospital and healthcare facilities (74%) while 21 % SAEs occurred at blood donation sites/locations of blood establishments and the remaining 5% occurred in a third party (medical biology laboratory, LBP transporter, etc.).

Each SAE reported can be linked to a series of failing steps (1 to 10) in the transfusion chain. However, only one failing step is identified for the majority (61%) of SAEs and in most cases, only one specification (e.g. contributing factor) is responsible for the failing step. The human error and the system failure represent the most frequently (52%) reported contributing factors among all SAEs. This finding results in ample opportunities to improve and apply best practices in order to reduce the occurrence.

Potential risks represent the most reported (73%) grounds for reporting of SAEs, of which 43% are associated with a potential severe event.

Confirmed risks (including: adverse reaction in patient, adverse reaction in blood donor (whatever the severity) and transfusion) are reported in 266 SAEs (29%), of which transfusion represents the main ground for reporting (89%).

Recipient re-sampling for biological analysis is the most frequently reported consequence (25%), before impact on LBP traceability (14%) and LBP loss or destruction (13%).

Approximately 98.6% of all SAEs led to preventive measures.

Wrong patient transfused reported in 2022

In 2022, 86 wrong patients transfused were reported, including 66 errors of RBCC transfused (77%) of which 7 were associated with ABO incompatibilities (3 SARs of grade 3, 2 of grade 2 and 2 of grade 1).

These wrong patients transfused resulted in 25 consequences for transfused patients (29.1% of wrong patient transfused). They are due to a succession of reported failures (291 in total. 2 to 6 failures per SAE, i.e. on average around 3.4 failures per SAE).

The steps involved in these wrong patients transfused are: final pre-transfusion checking at the bedside (reception in the healthcare department) LBP issue.

Issuance of blood components to the wrong patient reported in 2022

In 2022, 122 SAE of “issuance of blood component to the wrong patient” type were reported.

Among which, 75 were stopped before the transfusion; meaning that one or more control steps worked properly in the care service/unit or in the blood establishments.

They are due to a succession of reported failures (212 in total. 1 to 5 failures per SAE, i.e. on average around 1.7 failures per SAE).

Post-donation information (PDI)

Although post-donation informations (PDI) have been reported to the national competent authority since 2002, this reporting has only been mandatory since 2014.

Are reported in e-FIT: PDIs for which at least one blood component issued from a donation at risk is no longer in the Blood Establishment and the receiving facility (hospitals, clinics, etc.) need to be informed of the PDI.

Among the 2,231 PDIs reported, 2,169 have been detected and reported in 2022, regardless of the investigation status, i.e. an incidence rate of 80.9 PDIs per 100,000 blood collections, 81.4 PDIs per 100,000 donations and 13.6 PDIs per 10,000 blood donors. 2,100 PDIs having a “completed investigation” as of February 5, 2023 (94% of reported PDIs) were analysed. The overwhelming majority (87%) were reported by the blood donor himself or a family member.

One or more LBP can be involved in a PDI. A total of 5,181 LBPs (data from reporting forms) were reported among all PDIs, of which 40% were plasma, 38% were RBCC and 21% were platelets. 94% of PDIs mention at least one RBCC, 99% at least one plasma and 52% at least one platelet.

Following the PDI, 41% of the LBP were already transfused (a majority of platelets, 83%) and 20% were destroyed (the majority of RBCC, 69%).

89% of PDIs involved an infectious disease risk (confirmed infection in the donor or donor exposure to an infectious risk). The most reported PDIs were:

- Infections by SARS-CoV-2 (n=425) with an incidence rate of 15.8 PDI per 100,000 blood collections;
- History of blood transfusion (n=291) with an incidence rate of 10.9 per 100,000 blood collections;
- Gastroenteritis infections (n=230) with an incidence rate of 8.6 per 100,000 blood collections;

Among risks other than infectious risks, a medication (estimated rate 7.9 PDI per 100,000 blood collections) was the most frequently reported information. The most frequently reported medications were topiramate, valproic acid and derivatives, raloxifene, together accounting for almost 35% of medicine-related PDIs. They were often reported during the pre-donation interview to the subsequent donation (97%) and most blood donors (52%) reporting a medicine intake were aged 50 years old and over.

Refer to the whole report to put the data into perspective

APPENDIX: DATA NUMERATORS AND DENOMINATORS 2022

TABLE 1: DATA OF COLLECTION AND TRANSFUSION ACTIVITY, 2022 (DENOMINATORS)

Blood recipients	
Total number of patients transfused regardless the type of component	534 226
Number of patients transfused per 1,000 inhabitants	7.9
Blood donors	
Total number of blood donors	1 593 206
% of blood donors in the general population in category of age 20-64 years	3.7%
% First time donors in the general population in category of age 20-64 years	0.6%
Blood donations	
Total number of blood collection	2 681 889
Total number of completed donations	2 665 305
Average number of blood donation per blood donor	1.68
Blood components issued	
Total number of units issued regardless the type of component	2 910 418
Average number of units issued per 1,000 inhabitants	42.8
Average number of RBC issued per 1,000 inhabitants	34.4
Average number of platelets (apheresis platelets+recovered pooled platelets) issued per 1,000 inhabitants	5.0
Average number of plasma issued per 1,000 inhabitants	3.4
Total number of units transfused regardless the type of component	2 750 665
Average number of blood components transfused per patient	5.1
Average number of units transfused per 1,000 inhabitants	40.4
Average number of RBC transfused per 1,000 inhabitants	32.2
Average number of platelets (apheresis platelets+recovered pooled platelets) transfused per 1,000 inhabitants	5.0
Average number of plasma transfused per 1,000 inhabitants	3.2
Number of blood component returned appropriately to the stock of blood establishment	111 827
Rate of blood component returned appropriately to the stock of blood establishments (BEs)	3.84%
Number of blood component wastage	21 707
Blood component wastage's rate	0.75%
Number of blood components not traced	26 219
LBPs traceability's rate	99.1%
Medical facilities	
Number of transfusion facilities	1 316
Number of recipient ARs reporting establishments	765
Number of SAEs reporting establishments	277
Hospital blood banks activity	
Total number of hospital blood banks (HBBs)	621
Number of blood component distributed by BEs to HBBs	833 291
Rate of blood component distributed by BEs to HBBs	28.6%
Number of blood component issued by BEs to HBBs	287 660
Rate of blood component issued by BEs to HBBs	9.9%
Number of blood component issued by HBBs (emergency situations and routine issuing)	443 128
Rate of blood component issued by HBBs (emergency situations and routine issuing)	15.2%
Number of blood component issued by HBBs to their hospitals	479 808
Rate of blood component issued by HBBs to their hospitals	16.5%
Number of blood component issued by HBBs to another hospital (emergency situations)	9 256
Rate of blood component issued by HBBs to another hospital (emergency situations)	0.3%

TABLE 2: DATA OF REPORTING ACTIVITY OCCURRED IN 2022, REACTIONS AND EVENTS REPORTED IN 2022, REGARDLESS OF THE INVESTIGATION STATUS (NUMERATORS)

Category of reporting	Number	Rate
Recipient adverse reactions (all severity grades and all imputability levels)	9,510	345.7 per 100 000 blood components transfused 178.0 per 10 000 recipients transfused
Serious adverse events (SAEs)	1,029	35.4 per 100 000 blood components issued 269 SAEs with transfusion 37.4 per 100 000 blood components transfused
Donor Serious adverse reactions (SARs all imputability levels)	6,942	258.8 per 100 000 blood collections 43.6 per 10 000 blood donors
Post-donations informations (PDIs)	2,231	83.2 per 100 000 blood collection 14.0 per 10 000 blood donors

TABLE 3: DISTRIBUTION OF HOSPITAL BLOOD BANKS BY TYPE OF ACTIVITY EN 2022

	Activated in 2022	Inactivated in 2022	Active in 2022
Issuing Hospital blood bank (HBB) *	3	1	163
Relay HBB **	1	2	21
Vital Emergency HBB ***	2	10	208
Vital emergency and relay HBB	2	3	229
Total	**8**	**16**	**621**

*Blood bank localised in facility (hospital or clinic), approved by regional health competent authority, who stores and selects blood components compatible with the patient and issues them to him.
**Blood bank localised in facility (hospital or clinic), approved by regional health competent authority, who stores and transfers to the patient blood components previously issued by the blood establishment specifically for this patient
***Blood bank localised in facility (hospital or clinic), approved by regional health competent authority, who stores a limited stock of blood components and can issues, in vital emergency situations mainly to the patients of their hospitals, only RBCC of group O and/or plasma of group AB.

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