Agence nationale de sécurité du médicament et des produits de santé

REPORT

FRENCH HAEMOVIGILANCE ANNUAL REPORT – YEAR 2023 – EXECUTIVE SUMMARY

NOVEMBER 2024

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
BC	Blood Component
BEs	Blood establishments
CHV-ST	Haemovigilance and transfusion safety correspondents of hospitals, clinics and blood establishments
CRH-ST	*Coordonnateurs régionaux d'hémovigilance et de sécurité transfusionnelle* : Haemovigilance coordinators for the regional Public health agencies
CTSA	*Centre de Transfusion Sanguine des Armées*: French Army blood service
DMU	Single-use medical device (ex: blood bag set)
DHTR	Delayed Hemolytic Transfusion Reaction
DSAR	Donor serious adverse reaction
DSR	Delayed serologic reactions
EFS	*Etablissement Français du Sang*: French National blood Service
FEIGD	*Fiche d'effet indésirable grave donneur:* Blood donor serious adverse reaction form
FEIR	*Fiche d'effet indésirable receveur*: Recipient adverse reaction form
FIG	*Fiche d'incident grave,* Serious incident form
FIPD	*Fiche d'information post don:* 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 2023. This report corresponds to the 21st 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 facilities (hospitals and clinics) and blood establishments (CHV-ST).

This Executive Summary provides information on blood and blood components (B&BC) 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 receveur 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, 2024 and concerning reactions and events which occurred during the fiscal year 2023 (FEIR, FEIGD, FIG) or post-donation information that was discovered during the fiscal year 2023 (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, 2024 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 2023 are analysed in this report.

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

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)

2,799,548 labile blood products (LBP) were issued in 2023 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 2023.

Among 2,625,470 blood donations (of which 2,608,655 were completed), 85% were whole blood donations and 15% were apheresis donations. Nationwide 1,547,679 donors donated blood, regardless of the blood collection type.

LBP were transfused to 524,196 recipients (51% female, 49% male), representing an average of 5.0 LBP transfused per recipient. The transfusion rate in France represents 7.7 recipients per 1,000 inhabitants in 2023.

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 4.6% in events is observed, compared with 2022:

- +1.5% for recipient ARs (FEIR),
- +15.1% for donor SARs (FEIGD),
- +11.7% for SAEs,
- -13.4% for PDIs (FIPD).

Overall, 22,184 events or reactions were reported in 2023, regardless of the investigation status and their date of occurrence (or discovery), of which:

- 9,647 recipient ARs ;
- 7,991 blood donor SARs ;
- 1,149 SAEs ;
- 1,933 PDIs.

Recipient Adverse Reactions

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

Among the 9,647 recipient ARs reported, 9,065 occurred in 2023 (94%), i.e. an incidence rate of 343 reactions per 100,000 LBP transfused and 173 reactions per 10,000 recipients. Among all 9,065 adverse reactions occurred and reported in 2023, the investigation status of 8,884 was completed, as of 5 February 2024, and 90% of these were of grade 1 severity. Among them, 5,412 adverse reactions of imputability level probable (2) or certain (3) were analysed and summarised as follows (except Transfusion-related Acute Lung Injury (TRALI) and delayed hemolytic transfusion reaction (DHTR), for which the reactions summarised below were of imputability possible (1), probable or certain). Concerning grade 4 adverse reactions, two deaths with strong causality were reported in 2023, involving RBCC: 2 Transfusion-related circulatory overload (TACO) (of imputability probable).

Delayed serologic reactions (DSR) (Alloimmunization (AI)) represented the most frequent adverse reaction (65%), of which the overwhelming majority (99.5%) of grade 1 severity, mostly transfusion-related RBC (92%).

Febrile non hemolytic transfusion reaction (FNHTR) was the second most frequently reported adverse reaction (11%), almost all of which of grade 1 severity (97%). This adverse reaction is specific for transfusion, RBCC and platelets being the most frequently involved.

Allergic reactions were the third most frequently reported adverse reaction (10%), most of which of grade 1 severity. In 2023, allergic reactions (all levels of severity) were reported mainly transfusion-related of platelets.

Transfusion-related circulatory overload (TACO) represented 5% of adverse reactions of imputability 2 or 3, i.e. an incidence rate of 9.4 TACO per 100,000 LBP issued. The overwhelming majority (94%) were adverse reactions of grade 1 or 2 severity, but two deaths were reported in 2023 for this adverse reaction. TACO is mostly RBCC transfusion-related. It is mainly reported in elderly recipients, especially over 70 old-years.

Almost 4% of all adverse reactions, of imputability 2 and 3, consisted of Acute Hemolytic Transfusion Reactions (AHTR), of which 22 were related to ABO incompatibility. Three ABO accidents were reported following RBCC transfusion. 70% were platelets transfusion-related of which 78% were related to the HLA system.

Delayed Hemolytic Transfusion Reaction (DHTR) in Sickle cell Disease (SCD) represented 0.6% of adverse reactions of imputability 1 to 3; i.e. an incidence rate of 1.3 per 100,000 LBP issued. Among the reported DHTR, 13 were of grade 3, and two death have been reported.

Transfusion-related Acute Lung Injury (TRALI) represented 0.1% of adverse reactions of imputability possible, probable or certain, i.e. an incidence rate of 0.4 TRALI per 100,000 LBP issued. Among the reported TRALI, only one was defined as immunological TRALI (of imputability certain): one grade 3 involving MCG-ST,

Transfusion-transmitted bacterial infections (TTBI) remain very rare. Three TTBIs (G1, n=2; G2, n=1) were reported in 2023, involving 2 RBCCs (*Yersinia enterocolitica* and *Serratia marcescens*) and one PRP-PR (Bacillus cereus).

For Transfusion-transmitted viral infections (TTVI), all the reactions reported in 2023 were considered in this Executive Summary. Two Hepatitis E virus (HEV) infections of imputability 2 or 3 were reported: 1 of grade 1 (RBCC) and 1 of grade 2 (fresh frozen plasma). The estimated incidence rate is 0.07 HEV per 100,000 LBP issued, and 0.04 HEV per 10,000 recipients.

Serious Adverse Reactions in Donors

According to the French legislation for 2023 fiscal year, 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 7,991 reactions reported in 2023, the investigation of 7,767 reactions had been completed on February 5, 2024, with imputability 1 to 3 and not assessable, i.e. an incidence of 296 DSARs per 100,000 blood collections and 50 DSARs per 10,000 blood donors.

The **incidence of DSARs was higher after an apheresis donation** compared to whole blood, i.e. 404 versus 277 serious reactions per 100,000 blood collections respectively.

Serious adverse reactions were mostly reported in female blood donors, with an estimated rate of 357 serious adverse reactions per 100,000 blood collections compared to an estimated rate of 241 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: 87 versus 43 per 10,000 blood donors, while first-time blood donors represented almost a third (30%) of blood donors who presented a DSAR.

Approximately 76% of DSARs were classed as grade 2 severity (n=5,933), 1,834 as grade 3 severity. **No death was reported in 2023.** An overwhelming majority (96%) of serious adverse reactions were found to have no medical consequence for the blood donor.

Immediate vasovagal reaction is the most frequently reported diagnosis (87%), i.e. an estimated rate of 256 serious reactions per 100,000 blood collections. The incidence rate appears higher after apheresis donation (316 per 100,000 collections) than after whole blood donation (246 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 11%).

In 2023, 31,905 grade 2 of “anaemia” (according to the WHO definition) or “aggravation of anaemia” type were notified and 11 of grade 3 were reported.

Venous and/or arterial thromboembolic-type DSAR are more serious but rarer and were reported in 15 blood donors in 2023.

Five major cardiovascular events (MCE): cardiac, pulmonary and neurological-type were grade 3 adverse events (no deaths reported in 2023), mainly after whole blood donation. These are one myocardial infarction and stroke (n=4). 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.

1,149 SAEs were reported in 2023. Among them, 1,043 occurred in 2023, including 996 SAE reports having a “completed investigation” as of February 5, 2024 which have been analysed in detail, represent an estimated rate of 37 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 (73%) while 22 % 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 (49%) 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 (81%) grounds for reporting of SAEs, of which 45% 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 300 SAEs (19%), of which transfusion represents the main ground for reporting (88%).

Recipient re-sampling for biological analysis is the most frequently reported consequence (26%), before impact on LBP traceability (13%) and LBP wastage (12%).

Approximately 99.2% of all SAEs led to preventive measures.

Wrong patient transfused reported in 2023

In 2023, 65 wrong patients transfused were reported, including 54 errors of RBCC transfused (82%) of which 3 were associated with ABO incompatibilities (2 SARs of grade 2 and 1 of grade 1).

These wrong patients transfused resulted in 28 consequences for transfused patients (42.4% of wrong patient transfused). They are due to a succession of reported failures (224 in total: 2 to 7 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 patient identity checking at the bedside, patient identity checking at the time of reception of blood components in the clinical area, blood component issue step and the pre-transfusion performance and/or interpretation of the pre-transfusion ABO compatibility test at the patient's bedside.

Issuance of blood components to the wrong patient reported in 2023

In 2023, 109 SAE of “issuance of blood component to the wrong patient” type were reported.

All of them 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 (170 in total: 1 to 7 failures per SAE, i.e. on average around 1.6 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 1,933 PDIs reported, 1,882 have been detected and reported in 2023, regardless of the investigation status, i.e. an incidence rate of 71.7 PDIs per 100,000 blood collections, 72.1 PDIs per 100,000 donations and 12.2 PDIs per 10,000 blood donors. 1,805 PDIs having a “completed investigation” as of February 5, 2024 (96% 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 one PDI. A total of 4,461 LBPs (data from reporting forms) were reported among all PDIs, of which 40% were plasma, 37% were RBCC and 23% were platelets. 91.5% of PDIs mention at least one RBCC, 99.8% at least one plasma and 55.5% at least one platelet.

Following the PDI, 42% of the LBP were already transfused (a majority of platelets, 83%) and 21% were destroyed (the majority of RBCC, 63%).

90% of PDIs involved an infectious disease risk (confirmed infection in the donor or donor exposure to an infectious risk). The most reported PDIs were:

- Syphilis (n=98) with an incidence rate of 3.7 PDI per 100,000 blood collections;
- Infections by SARS-CoV-2 (n=91) with an incidence rate of 3.5 PDI per 100,000 blood collections;
- Infection by HEV (n=44) with an incidence rate of 1.7 PDI per 100,000 blood collections.

Among risks other than infectious risks, a medication (estimated rate 7.0 PDI per 100,000 blood collections) was the most frequently reported information. The most frequently reported medications were raloxifene, topiramate and valproic acid and derivatives, together accounting for almost 42% of medicine-related PDIs. They were often reported during the pre-donation interview to the subsequent donation (96%) and most blood donors (51%) 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 2023

TABLE 1: DATA OF COLLECTION AND TRANSFUSION ACTIVITY, 2023 (DENOMINATORS)

Blood recipients	
Total number of patients transfused regardless the type of component	524,196
Number of patients transfused per 1,000 inhabitants	7.7
Blood donors	
Total number of blood donors	1,547,679
% of blood donors in the general population in category of age 18-69 years	3.5%
% First time donors in the general population in category of age 18-69 years	0.6%
Blood donations	
Total number of blood collection	2,625,470
Total number of completed donations	2,608,655
Average number of blood donation per blood donor	1.70
Blood components issued	
Total number of units issued regardless the type of component	2,799,548
Average number of units issued per 1,000 inhabitants	40.9
Average number of RBC issued per 1,000 inhabitants	32.9
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	3.1
Total number of units transfused regardless the type of component	2,640,367
Average number of blood components transfused per patient	5.0
Average number of units transfused per 1,000 inhabitants	38.6
Average number of RBC transfused per 1,000 inhabitants	30.8
Average number of platelets (apheresis platelets+recovered pooled platelets) transfused per 1,000 inhabitants	4.9
Average number of plasma transfused per 1,000 inhabitants	3.0
Number of blood component returned appropriately to the stock of blood establishment	112,918
Rate of blood component returned appropriately to the stock of blood establishments (BEs)	4.03 %
Number of blood component wastage	20,551
Blood component wastage's rate	0.73 %
Number of blood components not traced	25,712
LBPs traceability's rate	99.1 %
Medical facilities	
Number of transfusion facilities	1,342
Number of recipient ARs reporting establishments	748
Number of SAEs reporting establishments	289
Hospital blood banks activity	
Total number of hospital blood banks (HBBs)	622
Number of blood component distributed by BEs to HBBs	807,928
Rate of blood component distributed by BEs to HBBs	28.9 %
Number of blood component issued by BEs to HBBs	276,575
Rate of blood component issued by BEs to HBBs	9.9 %
Number of blood component issued by HBBs (emergency situations and routine issuing)	429,112
Rate of blood component issued by HBBs (emergency situations and routine issuing)	15.3 %
Number of blood component issued by HBBs to their hospitals	410,657
Rate of blood component issued by HBBs to their hospitals	14.7 %
Number of blood component issued by HBBs to another hospital (emergency situations)	8,529
Rate of blood component issued by HBBs to another hospital (emergency situations)	0.3 %

TABLE 2: DATA OF REPORTING ACTIVITY OCCURRED IN 2023, REACTIONS AND EVENTS REPORTED IN 2023, REGARDLESS OF THE INVESTIGATION STATUS (NUMERATORS)

Category of reporting	Number	Rate
Recipient adverse reactions (all severity grades and all imputability levels)	9,647	365.4 per 100 000 blood components transfused 184.0 per 10 000 recipients transfused
Serious adverse events (SAEs)	1,149	41.0 per 100 000 blood components issued 279 SAEs with transfusion 43.5 per 100 000 blood components transfused
Donor Serious adverse reactions (SARs all imputability levels)	7,991	304.4 per 100 000 blood collections 51.6 per 10 000 blood donors
Post-donations informations (PDIs)	1,933	74.1 per 100 000 blood collection 12.5 per 10 000 blood donors

TABLE 3: DISTRIBUTION OF HOSPITAL BLOOD BANKS BY TYPE OF ACTIVITY EN 2023

	Activated in 2023	Inactivated in 2023	Active in 2023
Issuing Hospital blood bank (HBB) *	3	0	165
Relay HBB **	1	0	21
Vital Emergency HBB ***	10	5	215
Vital emergency and relay HBB	1	3	227
Total	**15**	**8**	**628**

*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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