2015

ANNUAL REPORT

EFS
ÉTABLISSEMENT FRANÇAIS DU SANG
Du donneur aux patients

Introduction

Committed Teams

To Find Out More

Introduction

“In 2015, EFS proved to be well organised and capable of providing a rapid response”

A MESSAGE
FROM FRANÇOIS TOUJAS,
PRESIDENT OF EFS

In more ways than one, 2015 was a historic year for the French Blood Establishment (Établissement Français du Sang - EFS). **It also left its mark on our country's history as a result of the terrorist attacks committed in January and November. In the midst of these crises, EFS proved to be well organised, capable of providing a rapid response, and fully integrated into the healthcare chain.** During these emergencies, healthcare teams never faced a shortage of blood products. In addition, in the wake of these events, we were able to effectively manage the influx of donors at our collection centres.

All EFS teams, from collection and testing to processing and distribution, worked diligently, illustrating the value of our public service in an exemplary manner. These tragic and exceptional attacks were not the only events that stood out in 2015. We also signed our Objectives and Performance Contract (COP *contrat d'objectifs et de performance*) with our administrators and adopted our establishment project. The COP functions as a road map for the 2015–2018 period and lays out six major strategic directions.

It will allow EFS to continue to efficiently fulfil its public service mission in accordance with exacting standards despite its limited budget. To help all employees embrace these objectives, an establishment project was put in place for the very first time. It contains a detailed action plan for achieving our goals.

A milestone decision was also made in 2015. French Health and Social Affairs Minister Marisol Touraine announced in early November that men who have or have had sexual relations with men can now donate blood under specific conditions. This group had previously been banned from giving blood since 1984. The decision, which required a revision of the decree concerning selection criteria for blood donors, went into effect on 10 July 2016.

Another event that had a profound impact on EFS was ANSM's (French National Agency for Medicines and Health Products Safety) decision to no longer automatically withdraw batches of plasma-derived medicines in cases where blood donors have a suspected case of sporadic Creutzfeldt-Jakob disease. This policy, which neighbouring countries do not follow, placed a definite handicap on the reputation of French plasma and posed an economic risk for the entire sector.

EFS also completed a major IT project. Our organisation now has a single database for all blood donors in metropolitan France. This increases the safety of blood transfusions and facilitates EFS' modernisation.

Finally, since April 2015, EFS has been experimenting with having nursing staff conduct the pre-donation interview on a national level. Previously, only doctors were authorised to meet with candidates to determine their eligibility for blood donation. This eighteen-month programme, which we hope to make standard practice, allows nurses to learn new skills and enables doctors to showcase their medical and managerial expertise.

"Regardless of the challenges we face, EFS will continue to provide a blood transfusion public service and deliver blood products to patients"

Since it was created fifteen years ago, EFS has had to face a number of significant events...
Over the years, these events have shaped the organization's history and caused it to rethink its strategy, organisation, and governance. However, in spite of uncertainties and setbacks, EFS, which I am proud to lead, has continued to provide transfusion public service and deliver blood products to patients all while guaranteeing an exceptionally high level of safety and quality.

This accomplishment is, of course, the result of a team effort. We owe this success to the work of 9,800 EFS employees who demonstrate their commitment and professionalism on a daily basis. Our work is also made possible as a result of the involvement of blood donors' associations and their volunteers, patient associations, companies, and all of our partners who, through their actions, help promote blood donation. I would like to thank them and reiterate just how invaluable their work is to us.

Many challenges await us in 2016, especially when it comes to ensuring a self-sufficient supply of blood products in France. We must also continue to improve our efficiency. Driven by its essential values, which include public service, respect, excellence, and efficiency, EFS will do everything in its power to continue to fulfil its key role in public health.

Highlights in 2015

July 2015/ SIGNING OF THE COP AND THE ESTABLISHMENT PROJECT

On 10 July 2015, EFS signed its second Objectives and Performance Contract (COP) for 2015–2018 with its two supervising ministers, France's Health and Social Affairs Minister Marisol Touraine and Finance and Public Accounts Minister Michel Sapin. This strategic document establishes six strategic directions : strengthening links with healthcare organisations to benefit patients; adapting the future challenges of self-sufficiency; maintaining an extremely high level of health safety; improving the efficiency of EFS's associated activities; continuing to refocus research on core business; and improving overall efficiency while ensuring the health and balance of EFS's finances. For the first time, the COP also includes an establishment project, the goal of which is to present all EFS employees with an action plan that will enable the organisation to reach these goals.

November 2015/ 13 NOVEMBER TERRORIST ATTACKS

Following the terrorist attacks in Paris and Saint-Denis, an adequate supply of blood products made it possible to effectively contend with exceptional circumstances. Beginning on the morning of 14 November, a large number of volunteer blood donors came to EFS centres. That day, 9,474 people volunteered to give blood, i.e. two times the expected number of people on a typical Saturday. This major turnout continued the following week. EFS created a special advertising campaign to thank donors for their support and its teams for their hard work.

February 2015/

MANAGERS' MEETING IN MARSEILLE

On 2 and 3 February 2015, 580 EFS managers met at the Palais du Pharo in Marseille for the sixth Managers' Meeting. During round table discussions, debates, and question and answer sessions, attendees spoke about the major issues affecting EFS in the future, including the COP and the 2015–2018 establishment project.

November 2015/

REVISION OF THE DECREE ON THE SELECTION OF BLOOD DONORS

On 4 November 2015, French Minister of Health and Social Affairs Marisol Touraine announced that men who have or have had sexual relationswith men can now donate blood under certain conditions. This decision was reached through a broad consultation process involving all stakeholders (patient associations, donor associations, LGBTQ rights groups, HIV organisations, EFS, CTSA, INVS, ANSM, NAEC, and many more) reflecting the desire for a collective public decision-making process, as part of a "participatory health democracy". This decision led to the revision of the 2009 decree stipulating the selection criteria for blood donors. A new decree was published on 10 April 2016 in the *Official Gazette of the French Republic.* It came into effect on 10 July 2016.

December 2015/

MERGER OF REGIONAL BLOOD ESTABLISHMENTS

EFS has had fifteen regional establishments since 1 January 2016. EFS Rhône-Alpes-Auvergne, which was created from the merger of EFS Rhône-Alpes and EFS Auvergne-Loire, and EFS Alsace-Lorraine-Champagne-Ardenne, the product of a merger between EFS Alsace and EFS Lorraine-Champagne, as well as the Marne and Ardennes departments, were officially created. The ministerial decrees that created the blood transfusion master plan (SOTS) for both of these establishments were published in the *Official Gazette of the French Republic* in November. In December, the French National Agency for Medicines and Health Products Safety (ANSM) certified these two new establishments for a ten-year period, thereby authorising them to provide blood transfusion services.

2015/

APPOINTMENT OF A BLOOD TRANSFUSION PUBLIC SERVICE MEDIATOR

Like many other public agencies, EFS has chosen to appoint a mediator. The role of this office is to offer blood transfusion stakeholders an alternative method for resolving conflicts and disagreements. Against a backdrop of significant transformation, a neutral and impartial third party is needed to help reestablish communication and social ties by preventing or helping to settle legal disputes.

June 2015/

WORLD BLOOD DONOR DAY

EFS's tenth annual World Blood Donor Day event was once again a success thanks to the involvement of its teams and support from volunteer associations. Between 8 June to 14 June, 69,505 blood donations were collected; 12,937 people (16.9%) who had never given blood before also came to donate during the week. The event also received significant press coverage, including segments during the 8:00 evening news on TF1, the 12 to 1 pm news on France 3, and the 7.45 pm news on M6.

November 2015/

COMPLETION OF THE "U" PROJECT IN METROPOLITAN FRANCE

At the end of November, Aquitaine-Limousin and Lorraine-Champagne (the last two regional establishments still using a regional configuration to manage their blood donor database) completed their switch to the national database. This was the final step in the "U" project (short for "unification") in metropolitan France, where twelve regional establishments now use a single blood donor database.
This major IT project began over five years ago. It will help modernise EFS and make blood transfusions safer.

September 2015/

CONSOLIDATION OF BIOBANKS

EFS finished consolidating its blood transfusion biobanks in September 2015. Instead of having a single biobank for each regional establishment in metropolitan France (14), EFS chose to concentrate this activity in four locations, namely Lille, Montpellier, Bordeaux, and Dijon. As part of this process, the procedure for producing and storing samples was changed. Previously, plasma vials were stored in liquid nitrogen for five years. Now, samples, called aliquots, are produced at the four sites using automatic pooling machines that deposit a sample from each blood donation into a microtube. The samples are then placed in electrical cold storage, where they are maintained at -30 °C in a centralised storage centre in Bordeaux. By consolidating its blood transfusion biobanks, EFS was able to cut its operating costs in half while also improving working conditions for its teams.

2015/ INAUGURATION OF NEW PLATFORMS FOR MANUFACTURING ADVANCED THERAPY MEDICINAL PRODUCTS

In 2015, EFS opened platforms authorised to produce Advanced Therapy Medicinal Products (ATMP) in Saint-Ismier, Toulouse, and Besançon, thereby complying with the highest standards of quality and safety. These innovative, new-generation medicines rely on EFS's expertise in tissue and cellular engineering *(see p. 48, ATMP Sidebar)*.

December 2015/ ENDING THE SYSTEMATIC WITHDRAWAL OF PLASMA-DERIVED MEDICINE BATCHES DUE TO SUSPECTED SPORADIC CREUTZFELDT-JAKOB DISEASE

In mid-December, the French National Agency for Medicines and Health Products Safety (ANSM) announced that it had discontinued its policy of systematically withdrawing batches of plasma-derived medicines due to suspected cases of sporadic Creutzfeldt-Jakob disease (CJD) in a blood donor whose blood was used to manufacture the batch in question. Several analyses have concluded there is no risk of transmitting the sporadic form of the disease. ANSM specified it would uphold its policy of withdrawing plasma-derived medicine batched in the event of a suspected case of variant CJD.

April 2015/ PILOT PROJECT FOR NURSE-LED PRE-DONATION INTERVIEWS

Since April 2015, six months after the decree was issued, EFS has been piloting nurse-led pre-donation interviews under specific conditions. Previously, France had stood out as one of the few countries in Europe to entrust only physicians with the pre-donation interview. One hundred and six nurses were trained to participate in this national pilot project. Following theoretical and practical training, they were authorised to conduct pre-donation interviews. The goal is to make this eighteen-month pilot programme standard practice. By training nurses to conduct pre-donation interviews, EFS aims to help nurses develop new skills and assist doctors with showcasing their medical and managerial expertise, all while maintaining a very high level of safety in the blood transfusion system. Between April and December 2015, 112,000 pre-donation interviews were conducted by state-certified nurses.

EFS In Brief

Created on 1 January 2000 by the law of 1 July 1998 and placed under the authority of the French Ministry of Health, the French Blood Establishment is the only public blood transfusion service in France. As such, its role is to ensure that France is self-sufficient for labile blood products and that it continues to meet quality and safety standards.

A Major Stakeholder in the Public Health Sector

Made up of fifteen regional establishments as of 1 January 2016 (and previously seventeen), EFS oversees the collection, processing, screening, and distribution of labile blood products (LBPs) and supplies over 1,500 health facilities (hospitals and clinics) throughout France. It is present throughout the country (including in France's overseas departments), with 132 collection sites and 40,000 mobile collection sessions organised every year. Its main activity concerns blood donation, plasma donation, and platelet donation. Thanks to the generosity of blood donors, the professionalism of its personnel, and the commitment of a vast network of volunteers, it meets the needs of one million patients every year. EFS also supplies plasma to the French Fractionation and Biotechnologies Laboratory (LFB), a French biopharmaceutical group that manufactures plasma-derived medicines.

The First BAL in France

EFS is also the largest biomedical analysis laboratory (BAL) in France. In 2015, it conducted 520 million "B" testing value units and is renowned for its expertise in recipient immunohaemotology and immunogenetics (the verification of the recipient's compatibility with those of the product he or she will be given).

Optimal Quality and Security

Quality and security are two requirements that govern every EFS action. EFS has invested in monitoring and vigilance activities and the continuous assessment of medical practice. It is also a key player in the provision of locally based healthcare. With its 89 health centres located in thirteen regional establishments *(see p. 13),* it provides healthcare services such as plasma and cellular exchanges, bloodletting, and stem cell collection.

EFS: At the Cutting Edge of Innovative Therapies...

In addition to fulfilling its core purpose, EFS also provides treatments and conducts research in innovative fields such as cell and tissue therapy. It also has two cord blood banks and eighteen cell and/or tissue product processing sites.

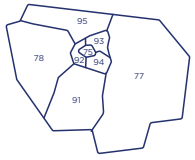
...and Research

Research is also a major focus at EFS. Nineteen teams spread out among ten regional establishments are staffed by researchers, engineers, and technicians, representing 155 full-time equivalent positions and coordinating with universities, INSERM, and CNRS. This research helps set the future course for the blood transfusion sector, both in terms of the procedures it follows to obtain blood products and the safety and quality of transfusions. EFS protects and directly uses a portion of its research findings.

Self-Sufficiency: A Crucial Goal

In accordance with the founding principles of blood transfusion in France, namely anonymity, charity, free-will, and non-remuneration, EFS has expanded its business and ensured that France has had a continuously self-sufficient blood product supply for the past fifteen years.

The Fifteen EFS Regional Establishments



EFS Île-de-France

75 Paris
93 Seine-Saint-Denis
94 Val-de-Marne
92 Hauts-de-Seine
78 Yvelines
95 Val-d'Oise
77 Seine-et-Marne
91 Essonne

EFS Nord de France

59 Nord
02 Aisne
60 Oise
80 Somme
62 Pas-de-Calais

EFS Alsace-Lorraine-Champagne-Ardenne

54 Meurthe-et-Moselle
57 Moselle
67 Bas-Rhin
68 Haut-Rhin
88 Vosges
52 Haute-Marne
10 Aube
51 Marne
08 Ardennes
55 Meuse

EFS Normandie

14 Calvados
76 Seine-Maritime
27 Eure
61 Orne
50 Manche

EFS Bretagne

22 Côtes-d'Armor
35 Ille-et-Vilaine
56 Morbihan
29 Finistère

ETS Pays de la Loire

53 Mayenne
72 Sarthe
49 Maine-et-Loire
85 Vendée
44 Loire-Atlantique

EFS Bourgogne-Franche-Comté

21 Côte-d'Or
70 Haute-Saône
25 Doubs
39 Jura
71 Saône-et-Loire
58 Nièvre
89 Yonne
90 Territoire-de-Belfort

EFS Centre-Atlantique

28 Eure-et-Loir
45 Loiret
41 Loir-et-Cher
18 Cher
36 Indre
37 Indre-et-Loire
86 Vienne
79 Deux-Sèvres
16 Charente
17 Charente-Maritime

EFS Rhône-Alpes-Auvergne

74 Haute-Savoie
73 Savoie
01 Ain
38 Isère
69 Rhône
26 Drôme
07 Ardèche
03 Allier
42 Loire
43 Haute-Loire
15 Cantal
63 Puy-de-Dôme

EFS Aquitaine-Limousin

87 Haute-Vienne
23 Creuse
19 Corrèze
24 Dordogne
33 Gironde
47 Lot-et-Garonne
40 Landes
64 Pyrénées-Atlantiques

EFS Pyrénées-Méditerranée

46 Lot
12 Aveyron
48 Lozère
30 Gard
34 Hérault
11 Aude
66 Pyrénées-Orientales
09 Ariège
31 Haute-Garonne
65 Hautes-Pyrénées
32 Gers
82 Tarn-et-Garonne
81 Tarn

EFS Alpes-Méditerranée

05 Hautes-Alpes
04 Alpes-de-Haute-Provence
06 Alpes-Maritimes
83 Var
13 Bouches-du-Rhône
84 Vaucluse
2B Haute-Corse
2A Corse-du-Sud

EFS Martinique

971 Guadeloupe

EFS Guadeloupe-Guyane

EFS La Réunion

EFS in the French Healthcare System

Ministry of Health, Ministry of Finance and the Economy
Directorate General of Health - Social Security Directorate
Budget Directorate - Directorate General for Healthcare Services
- Sets the prices of labile blood products (LBP)
- Approves regional organisation for blood transfusion services

European Union
Council of Europe

Healthcare Institutions
- Purchase LBPs from EFS
- Attribute laboratory activities to EFS
- Establish research partnerships with EFS

French National Agency for Medicines and Health Products Safety
- Certifies and inspects regional EFS regional establishments
- Controls LBPs
- Oversees the haemovigilance network

EFS
ÉTABLISSEMENT FRANÇAIS DU SANG
Du donneur aux patients

Blood Donors' Associations
Help promote blood donation and collection

French Laboratory for Fractionation and Biotechnologies
Fractionates plasma collected by EFS to manufacture plasma-derived medicinal products

Patients' Associations
Help promote blood donation and track issues related to the safety of the blood donation system

French Biomedicine Agency
Coordinates the development of cellular therapy and tissue banks as well as activities related to voluntary bone marrow and cord blood donation

French National Agency of Public Health
Analyses epidemiological data sent by EFS

French National Institute for Health and Medical Research
Made up of research units present in certain regional establishments

National Alliance for Health and Life Sciences
- Coordinates French research in health and life sciences
- EFS is an associate member of Aviesan

Education
Carried out by universities, EFS teams, and the National Blood Transfusion Institute (INTS)

EFS in Figures

Institution
The only civilian
blood transfusion operator

15 blood transfusion establishments (including three in overseas departments)

132 collection sites

40,000 mobile collection sessions

4 steps in the journey of a blood bag: collection, processing, screening, and distribution

1,500 hospitals and clinics
supplied with blood products

1 million patients treated

Human Resources
9,833 employees

73% women

13 years of seniority
on average

44 years old on average

More than 1 out of 2 employees
has undergone **training** throughout the course of the year.

Collections
2,980,327 collections, including **399,743** collections by apheresis

Blood Donors
1,852,422 prospective donors

1,645,325 donors

324,330 new donors

Voluntary Bone Marrow Donors (VBMD)
18,848 new donors registered

EFS recruitment share:
17,400 (92.6%)

Biomedical Analysis Services
520 million "B" testing value units

Volunteer Associations
2,850 associations

750,000 members
of the French Federation for Voluntary Blood Donation

Cord Blood
715 units of cordblood
registered by EFS into the French blood marrow transplantation registry, i.e. 79% of total registered units

2 banks
(Bordeaux and Besançon)

Healthcare Services
89 healthcare centres

Research
19 teams

155 full-time equivalent positions
filled by researchers, engineers, and technicians

A budget of €21.7 million, €14.9 million of which is directly funded by EFS

Economic Data
Net income:
2.8 million euros

Turnover:
871.7 million euros

Investments:
31.9 million euros

Operating Expenses
948.2 million euros

Organisation Chart as of 1 May 2016

RESPONSIBLE PERSON FOR LABILE BLOOD PRODUCTS & TISSUES AND CELLS
Prof. Pierre TIBERGHIEN

RESPONSIBLE PHARMACIST FOR ATMP, RESPONSIBLE PERSON FOR HOSPITAL EXEMPTION ATMP
Dr. Anne FIALAIRE-LEGENDRE

CENTRAL ACCOUNTING OFFICE
Bernard SABY

GENERAL ECONOMIC AND FINANCIAL CONTROL
Alain BOURDELAT

CHIEF SECURITY AND DEFENCE OFFICER
Thierry BAUDONET

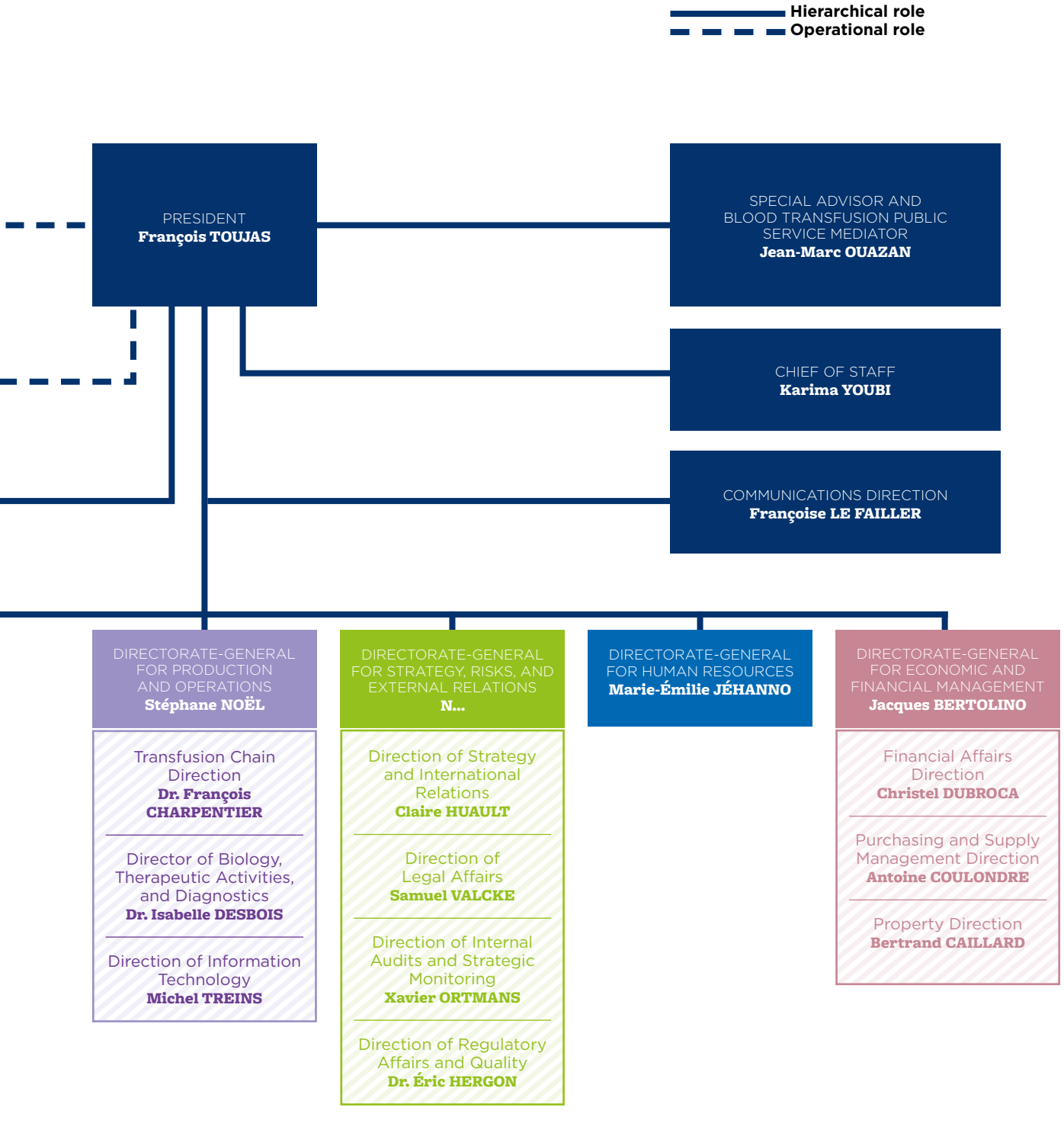
REGIONAL ESTABLISHMENT (ETS) DIRECTORS

ETS Alpes - Méditerranée **Prof. Jacques CHIARONI**	ETS Alsace - Lorraine - Champagne-Ardenne **Dr. Christian GACHET**	ETS Aquitaine - Limousin **Dr. Azzedine ASSAL**	ETS Bourgogne - Franche-Comté **Dr.Pascal MOREL**
ETS Bretagne **Prof. Gilbert SEMANA**	ETS Centre - Atlantique **Dr. Frédéric DEHAUT**	EFS Guadeloupe - French Guyana **Dr. Françoise MAIRE**	ETS Île-de-France **Dr. Rachid DJOUDI**
EFS La Réunion **Dr. Hervé RENARD**	ETS Martinique **Dr. Pascale RICHARD**	EFS Nord de France **Dr. Rémi COURBIL**	ETS Normandie **Dr. Patrice RASONGLES**
ETS Pays de la Loire **Dr. Frédéric DEHAUT**	ETS Pyrénées - Méditerranée **Dr. Francis ROUBINET**	ETS Rhône-Alpes - Auvergne **Dr. Dominique LEGRAND**	

DIRECTORATE-GENERAL FOR MEDECINE, RESEARCH, AND INNOVATION
Prof. Pierre TIBERGHIEN

Medical Direction
Dr. Sylvie GROSS

Direction of Research and Technology Transfer
Prof. Jean-Christophe PAGES


Hierarchical role
Operational role
PRESIDENT
François TOUJAS
SPECIAL ADVISOR AND BLOOD TRANSFUSION PUBLIC SERVICE MEDIATOR
Jean-Marc OUAZAN
CHIEF OF STAFF
Karima YOUBI
COMMUNICATIONS DIRECTION
Françoise LE FAILLER
DIRECTORATE-GENERAL FOR PRODUCTION AND OPERATIONS
Stéphane NOËL
Transfusion Chain Direction
Dr. François CHARPENTIER
Director of Biology, Therapeutic Activities, and Diagnostics
Dr. Isabelle DESBOIS
Direction of Information Technology
Michel TREINS
DIRECTORATE-GENERAL FOR STRATEGY, RISKS, AND EXTERNAL RELATIONS
N...
Direction of Strategy and International Relations
Claire HUAULT
Direction of Legal Affairs
Samuel VALCKE
Direction of Internal Audits and Strategic Monitoring
Xavier ORTMANS
Direction of Regulatory Affairs and Quality
Dr. Éric HERGON
DIRECTORATE-GENERAL FOR HUMAN RESOURCES
Marie-Émilie JÉHANNO
DIRECTORATE-GENERAL FOR ECONOMIC AND FINANCIAL MANAGEMENT
Jacques BERTOLINO
Financial Affairs Direction
Christel DUBROCA
Purchasing and Supply Management Direction
Antoine COULONDRE
Property Direction
Bertrand CAILLARD

Governance

Executive Board (EB)

The role of the EB, as defined by the French code of public health, is to set EFS's general policies and debate the major actions involved in their implementation.

Executive Committee

The Executive Committee is EFS's managing authority; it is in charge of overseeing its activities and making the organisation's strategic decisions. To consolidate the directors' arbitrage and decision-making capabilities and to ensure they remain harmonious with the reality of the field, President François Toujas appointed a new member to the Executive Committee in 2015. Dr. Azzedine Assal, Director of EFS Aquitaine-Limousin, was chosen to represent the regional establishments within this authority, which includes the president, the five deputy managing directors, and the president's chief of staff. The Executive committee meets twice a month.

Directors' Committee (DC)

The DC reports to the president and includes the deputy managing directors, the head office directors, and the regional establishment directors. The Directors' Committee helps draft the organisation's policies and strategic decisions; it also assesses and corrects them as needed.

Head Office Directors' Committee

The Head Office Directors' committee includes the president, five deputy managing directors, the president's chief of staff, head office directors, the chief accounting officer, the responsible pharmacist, the international affairs advisor, the blood transfusion public service mediator, the medical software project manager, and the head office human resources director. The Head Office Directors' Committee is a governing body for information sharing and discussion. It also examines topic-specific issues.

Auditing Committee

The Auditing Committee is made up of five administrators (Budget Directorate, General Directorate of Health, Social Security Directorate, French National Health Insurance Agency for Wage Earners, and the Secretariat-General of the Ministries of Social Affairs). A representative from the General Economic and Financial Control also attends these meetings. The chief accounting officer, EFS directors, and external auditors are invited to participate depending on the themes discussed at the meetings. The role of the Auditing Committee is to inform the Executive Board about financial and accounting issues, EFS's internal and external auditing programmes, and the effectiveness of the risk management systems. It met five times in 2015.

Scientific Advisory Board

The Scientific Advisory Board is made up of members and a president appointed by the Health Minister in accordance with article R 1222-10 of the French code of Public Health. The Scientific Advisory Board is made up of members and a president appointed by the Health Minister in accordance with article R 1222-10 of the French code of Public Health. It meets three times per year.

Ethics and Professional Conduct Committee

EFS has had an Ethics and Professional Conduct Committee since January 2014. Its role is to provide assistance to the president, responsible person, and the Executive Board with respect to ethical issues involving EFS's activities. This committee includes nine members who come from outside of EFS and serve for three years.

Fifteen Blood Transfusion Establishments

The directors of the fifteen regional establishments report directly to the president of EFS. Within their respective regions, they are in charge of managing medical services related to blood transfusions (collection, processing, screening, and distribution). Depending on the region in question, they also oversee health centres, biomedical analysis laboratories, and cell and tissue engineering activities associated with research projects. Each establishment includes a board, a processing platform, and several facilities which perform blood collection, patient immunohaematology testing and blood products distribution and delivery to health facilities (hospitals and clinics).

Activity-Specific Networks

These networks cover various fields of expertise, including collection, haemovigilance, IT systems, communications, and human resources, among others. This structure helps EFS promote the collaborations, exchanges, and dialogue necessary to pool experience and standardise practises.

Employee Representative Bodies

These groups make up the legal framework for consulting and exchanging information with employees regarding issues related to EFS's organisation and working conditions. The group that serves this purpose on the national level is called the Central Corporate Committee. On a regional level, the Establishment Committees, Staff Delegates, and the Health, Safety, and Working Conditions Committees fulfil this role.

The Executive Board

Composition as of 31 December 2015
Chaired by EFS President François Toujas, the Executive Board includes representatives from the French government, health organisations, donor and patient associations, and EFS personnel.

President
François Toujas

Eleven Representatives from the French Government

GENERAL DIRECTORATE OF HEALTH
Ex-officio member
Benoît Vallet
Representatives
Catherine Choma and Raphaël Capian

GENERAL DIRECTORATE FOR HEALTHCARE SERVICES
Ex-officio member
Jean Debeaupuis
Representative
Christian Thuillez

SECRETARIAT-GENERAL OF THE MINISTRIES OF SOCIAL AFFAIRS
Ex-officio member
Pierre Ricordeau
Representative
Agnès Quiot

SOCIAL SECURITY DIRECTORATE
Ex-officio member
Thomas Fatome
Representatives
Damien Vergé and Édouard Hatton

CENTRAL DIRECTORATE OF THE ARMED SERVICES HEALTHCARE SERVICE
Ex-officio member
Jean Debonne
Representative
Anne Sailliol

BUDGET DIRECTORATE
Ex-officio member
Denis Morin
Representatives
Claire Vincenti and Timothée Mantz

COMPETITION, CONSUMPTION, AND ANTI-FRAUD GENERAL DIRECTORATE
Ex-officio member
Nathalie Homobono
Representative
Catherine Argoyti

GENERAL DIRECTORATE OF CORPORATIONS
Ex-officio member
Pascal Faure
Representative
Alain-Yves Brégent

GENERAL DIRECTORATE FOR RESEARCH AND INNOVATION
Ex-officio member
Roger Genet
Representative
Brigitte Bouchard

GENERAL DIRECTORATE FOR HIGHER EDUCATION AND PROFESSIONAL DEVELOPMENT
Ex-officio member
Simone Bonnafous
Representative
Richard Audebrand

GENERAL DIRECTORATE OF OVERSEAS TERRITORIES
Ex-officio member
Alain Rousseau
Representatives
Hervé Creusvaux and Thérèse Clément

Six representatives from organisations and associations

HEALTH INSURANCE (CNAMTS)
Jean-Claude Fichet
and Élisabeth Lemaure

FRENCH HOSPITAL FEDERATION (FHF)
Prof. Jean-Luc Wautier

PATIENT ASSOCIATION REPRESENTATIVE—FRENCH ASSOCIATION FOR HAEMOPHILIACS
Thomas Sannié

BLOOD DONORS' ASSOCIATION REPRESENTATIVE
Roger Praile and Bernard Dalion

Representative of Private Hospital Organisations
Emmanuel Daydou

Two EFS Employee Representatives
Élodie Thibaudeau
(deputy: Frédéric Didelot)
Serge Dominique
(deputy: Daniel Bloom)

Two Qualified Experts
Prof. Sylvie Castaigne
Prof. Yves Ozier

Consulting Experts

GENERAL ECONOMIC AND FINANCIAL CONTROL "SOCIAL RISK COVERAGE, SOCIAL COHESION, AND HEALTH SAFETY" MISSION
Alain Bourdelat

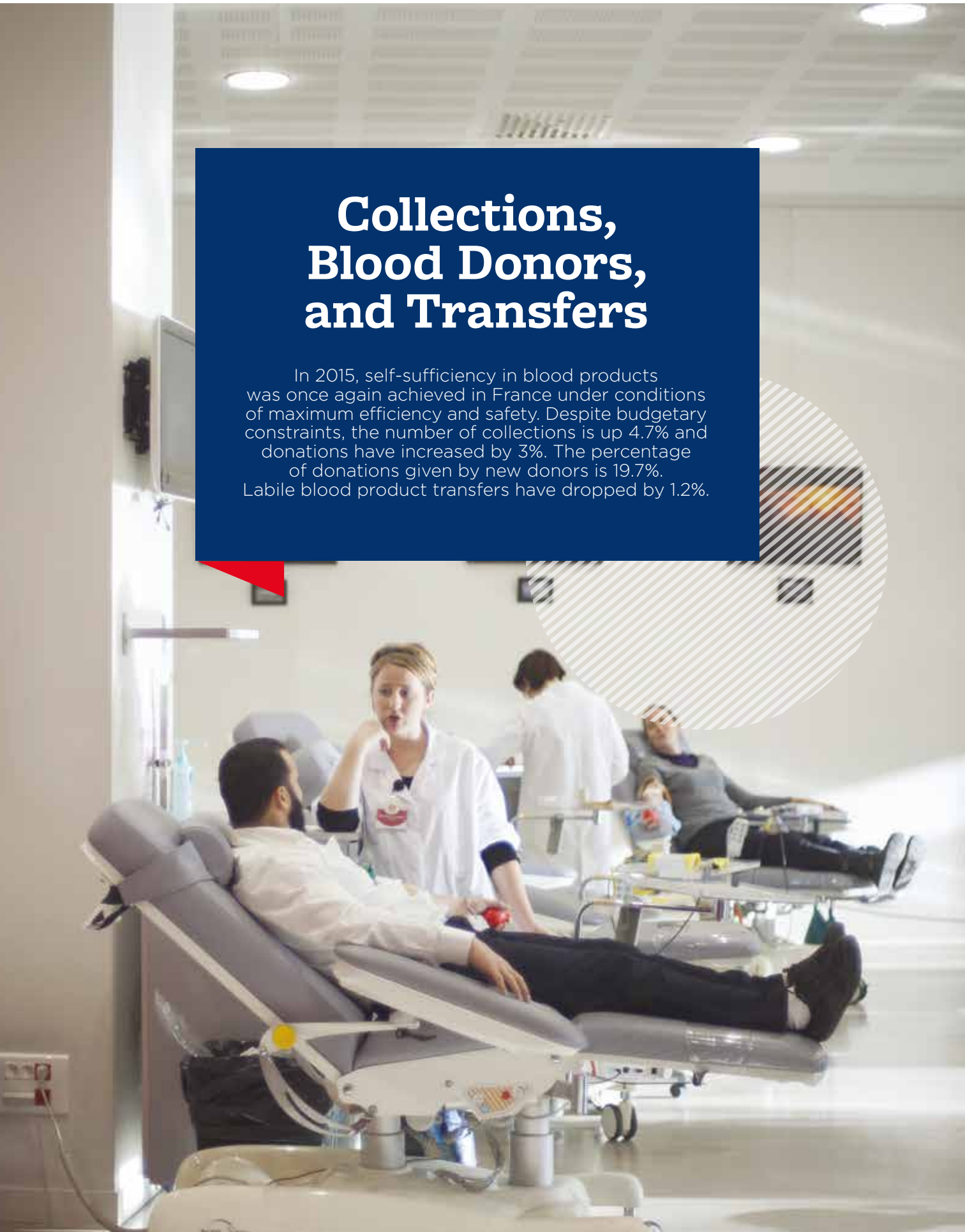
EFS CHIEF ACCOUNTING OFFICER
Bernard Saby

Two Guest external auditors

ERNST & YOUNG
Dominique Pageaud

PRICE WATERHOUSE COOPERS
Florence Pestie

Committed Teams



Collections, Blood Donors, and Transfers

In 2015, self-sufficiency in blood products was once again achieved in France under conditions of maximum efficiency and safety. Despite budgetary constraints, the number of collections is up 4.7% and donations have increased by 3%. The percentage of donations given by new donors is 19.7%. Labile blood product transfers have dropped by 1.2%.

A Significant Rise in Collections

In 2015, the number of collections continued to rise for the second year in a row following a drop in 2013, during which 270,944 fewer units were collected. There are 1,645,325 donors (3% increase over 2014), including 1,320,995 returning donors and 324,330 new donors, for a total number of 2,980,327 collections, i.e. 134,705 more collections than in 2014 (4.7% rise).

The increase in the number of collections and donors is the result of two main factors:

• The influx of donors in the weeks following the 13 November attacks in Paris and Saint-Denis. This show of solidarity resulted in of 40,000 extra whole blood donations. The increased stock of donated red blood cells (RBCs) lasted until early January 2016. Through careful management based on the pooling of blood products between and within regions according to their collection date, EFS was able to minimise the risk of product outdating, and the expiry rate remained at a usual low level.

• The increase in plasma apheresis activities (65.1% increase) to meet the demand from the French Fractionation and Biotechnologies Laboratory (LFB), which produces plasma-derived medicinal products.

	2015
Blood donors	1,645,325
New donors	324,330
Returning donors	1,320,995
Collections	2,980,327

Whole blood Collections

The number of whole blood collections rose to 2,580,584 in 2015, i.e. a 1.3% increase over 2014 (33,437 more donations).

	2015	2014	Changes between 2014/2015
Whole blood	2,580,584	2,547,147	up 1.3%
Plasma	278,750	168,820	up 65.1%
Platelets*	121,118	129,657	down 6.6%
TOTAL	**2,980,452**	**2,845,624**	**4.7%**

**From single-product and combined apheresis.*

Though the number of whole blood collections slightly increased in 2015 over 2014, the proportion of blood collections decreased compared to the proportion of plasma collections (65.5% increase). This type of collection accounted for 81.6% of collections in 2014 with 2,547,147 collections. In 2015, it was 75.5% (2,580,584 collections).

Collections by Apheresis

Collections by apheresis have increased by 33.9% (101,268 donations) compared to 2014. Depending on the method of collection, this type of collection is either up or down:

- Collections by simple apheresis increased by 63.2% (109,970 donations) over 2014. Collections by plasma apheresis increased by 65.1% due to the increase in demand from LFB. Apheresis platelet collections decreased by 1.9% due to a strategy of focusing on whole blood platelets.
- Combined apheresis collections decreased by 7% (8,702 fewer donations) over 2014.

(Number of procedures performed)	2015	2014	Difference between 2014/2015	
			Quantity	%
Total number of collections started	2,980,452	2,845,622	+ 134,705	+ 4.7%
Homologous and autologous whole blood collections	2,580,584	2,547,147	+ 33,437	+ 1.3%
Homologous whole blood collections	2,580,456	2,546,858	+ 33,598	+ 1.3 %
Autologous whole blood collections	128	289	- 161	- 55.7%
Collections by apheresis	399,743	298,475	+ 101,268	+ 33.9%
Single-product apheresis	283,904	173,934	+ 109,970	+ 63.2%
Plasma apheresis	278,750	168,819	+ 109,931	+ 65.1%
Platelet apheresis	4,922	5,016	- 94	- 1.9%
Granulocytes	232	99	+ 133	+ 134.3%
Combined apheresis	115,839	124,541	- 8,702	- 7%
Apheresis platelet concentrate/Plasma	110,773	114,258	- 3,485	- 3.1%
Apheresis platelet concentrate/Red blood cell concentrate	397	713	- 316	- 44.3%
Red blood cell concentrate/Apheresis platelet concentrate/ Plasma	4,669	9,570	- 4,901	- 51.2%

Candidates and Deferrals

The number of potential donors evolved at the same rate as the number of collections, with a slight increase in the number of deferred candidates and attendances. The rate of deferred donor attendances (273,137) increased by 0.3%, rising from 8.1% in 2014 to 8.4% in 2015. The rate of deferred candidates (262,754) increased by 0.6% in a year, rising from 13.6% to 14.2%.

Pending confirmation, this trend is in part due to more stringent health safety measures put in place to respond to epidemiological issues such as the West Nile virus outbreak that occurred in south-eastern France during the third quarter of 2015.

	2015	2014	%
ATTENDANCES	3,253,101	3,085,899	+ 5%
Deferred attendances	273,137	250,294	
Percentage of deferred attendances	8.4%	8.1%	
CANDIDATES	1,852,422	1,779,580	+ 4%
Deferred candidates	262,754	241,307	
Percentage of deferred candidates	14.2%	13.6%	

Donation type and locations

In 2015, collection was conducted at both fixed sites and mobile sessions. Thirty percent of collections (900,083) took place at fixed sites, while 70% (2,080,244) were performed at mobile sessions.

	Fixed sites	Mobile Collection Sessions
Whole blood	509,717	2,070,739
Plasma	269,248	9,502
Platelets	121,118	-
TOTAL	**900,083**	**2,080,241**

In 2015, 19.75% of whole blood donations occurred at the 132 fixed collection sites. This is an improvement compared to 2014 and 2013 (18.6%) and is due to a campaign to increase donations in cities. These sites conducted 96.6% of plasma collections (269,248 collections) and all platelet collections (121,118).

French National Blood Bank of Rare Blood Units (BNSPR)

A rare blood type or rare erythrocyte phenotype occurs in less than 4/1,000 people from a reference population.
On an individual level, a person with a rare blood type might have difficulty finding a compatible donor or getting a blood transfusion, due to the development of antibodies.
To prevent and treat this type of situation, and to safely provide these patients with blood transfusions, it is essential to have a frozen stock of red blood cell concentrates with specific phenotypes.

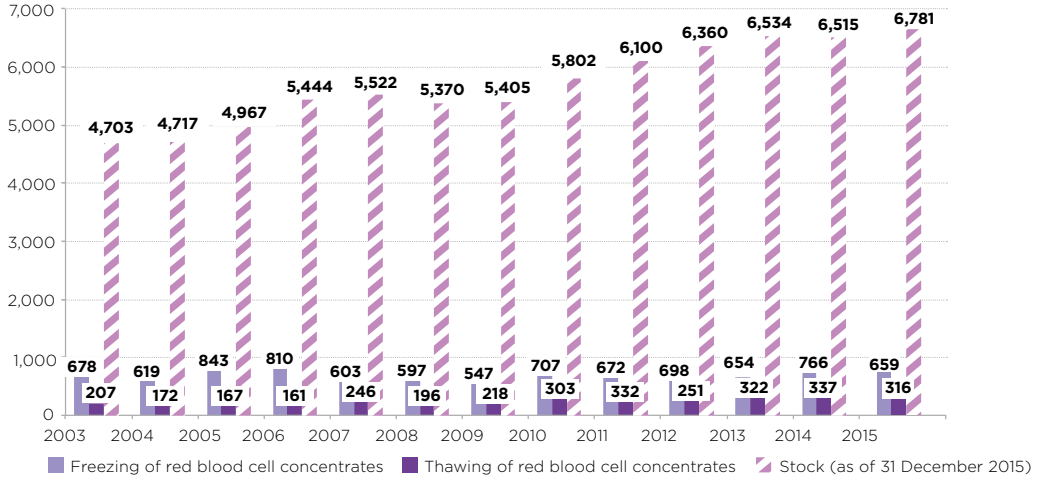
There are currently 6,781 red blood cell concentrates being stored at -80 °C in approximately twenty cryogenic storage units. The special characteristics of these concentrates cover nearly 30% of the specific rare blood types found in populations of African and Caribbean descent.

These red blood concentrate transfusions are mostly given to patients with sickle cell disease.

In 2015, the BNSPR added 659 red blood cell concentrates. It should be noted that 252 red blood cell concentrates came from donors of Afro-Caribbean descent, and that a majority of donors live in the Île-de-France region (122 red blood cell concentrates). BNSPR-related issuing and distribution activities involved 316 red blood cell concentrates in 2015. Out of the total number of concentrates taken from cryogenic storage, 124 units had characteristics specific to donors of Afro-Caribbean descent: these units were used to transfuse patients with sickle cell disease. Seventy-seven units were used to treat patients with sickle cell disease in the Île-de-France region.

BNSPR's activity has increased significantly in the past ten years on both a qualitative and quantitative level. This rise is due to an increase in the demand for rare phenotype red blood cell concentrates to be used in patients with sickle cell disease.

CHANGE IN BNSPR'S ACTIVITIES



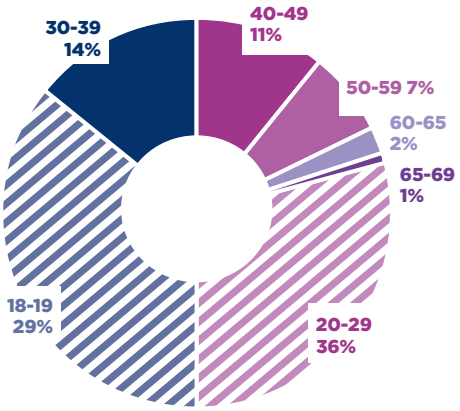
Who Donated Blood in 2015?

n 2015, more women than men donated blood: 851,145 compared to 794,180. They represent 51.7% of total donors and 55% of new donors.

The share of male donors decreased in 2015 (49.1% in 2013/2014 compared to 48.3% in 2015). In the coming years, new efforts will be necessary to increase the number of male donors.
Taking into account both men and women, 49.5% of donors were under 40 years old in 2015, and 50.5% of donors were older than 40. More women give before the age of 40 (53.8%), while more men give after the age of 40 (55.1%). The largest number of collections was donated by people in the 20-29 age group (25.8%), followed by the 40-49 age group (20.1%).

Slight decrease in the number of new donors*
The number of first-time donors is slightly down compared to 2014. There were 324,330 new donors in 2015 (compared to 334,967 in 2014), i.e. 19.7% of total donors. They made up 20.9% of total donors in 2014.
New donors from the 20-29 age group provided the largest proportion of collections (36.5%). Women represent 55% (181,095) of the total number of new donors.

BREAKDOWN OF NEW DONORS ACCORDING TO AGE GROUP



Increase in the number of returning donors
The number of returning donors, i.e. people who have already donated blood, is up (1,320,995 in 2015 compared to 1,267,236 in 2014), which indicates increased loyalty among donors.

Larger Number of Donations per Donor

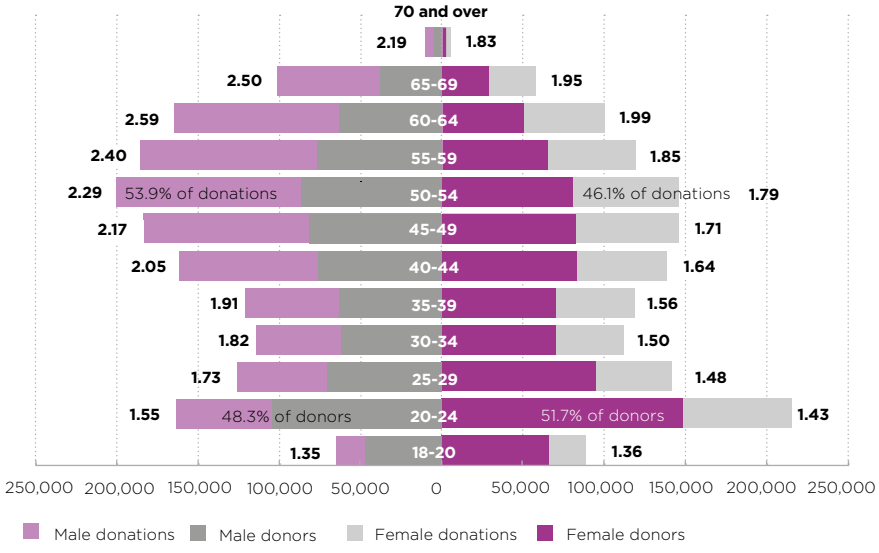
After two consecutive years of decline, the average number of donations per donor increased again in 2015 to reach 1.81 compared to 1.78 in 2014. Though fewer men than women donate (48%), men give more donations. In 2015, 53.9% of all collections were given by men. This figure is slightly down from 2014 (55%), however. In its effort to guarantee self-sufficiency, EFS continues to rely on male donors.

**Before 2015, a donor was statistically counted as a first-time donor whenever he or she donated in a given region for the first time, even if he or she had previously donated elsewhere. Since 2015, the year when the single national donor database was completed in metropolitan France, only first-time donations are considered as such. This change in perspective partially explains the declining percentage of new donors in 2015. In reality, this decrease was only 0.11% in 2014 and 0.39% since 2013.*

CHANGE IN THE NUMBER OF DONATIONS PER DONOR SINCE 2005

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Number of collections	2,571,992	2,617,452	2,774,567	2,858,151	3,053,010	3,044,924	3,190,226	3,104,295	2,833,351	2,845,622	2,980,327
Number of donors	1,506,082	1,527,209	1,617,478	1,649,172	1,689,495	1,643,947	1,725,495	1,708,541	1,625,735	1,602,203	1,645,325
Average number of donations per donor	1.67	1.69	1.72	1.73	1.81	1.85	1.85	1.82	1.74	1.78	1.81

DONATION AND DONOR AGE PYRAMID IN 2015



In studying the age pyramid for donations and donors of all kinds, it is clear that the average number of donations per year increases regularly with the donor's age. The age group that gives the most is 60-65 years old with an average number of donations per donor of 2.59 for men and 1.99 for women. In other words, donors, and men especially, tend to visit collection centres more often the older they become (between 2.05 and 2.19 donations per year among men aged 40 to 70 compared to 1.64 to 1.83 donations for women of the same age group). LBP transfers decreased in 2015 compared to 2014 by 1.2%.

Promoting Bone Marrow Donation

In 2015, EFS continued to raise awareness among blood donors about bone marrow donation. A significant proportion of volunteer bone marrow donors is recruited from this group. This action made it possible to add 17,400 new volunteer bone marrow donors (92.6% of registered individuals) to the French bone marrow transplantation registry, thereby furthering the Biomedicine Agency's 2010-2015 transplant agenda (*Plan greffe*). The goal of this agenda was to reach 240,000 registered bone marrow donors in 2015. In 2016, EFS set an internal goal of recruiting 18,000 new bone marrow donors.

17,400

NEW VOLUNTEER BONE MARROW DONORS (I.E. 92.6% OF THOSE REGISTERED) ADDED TO THE FRENCH BONE MARROW TRANSPLANTATION REGISTRY

VOLUNTARY BONE MARROW DONATION

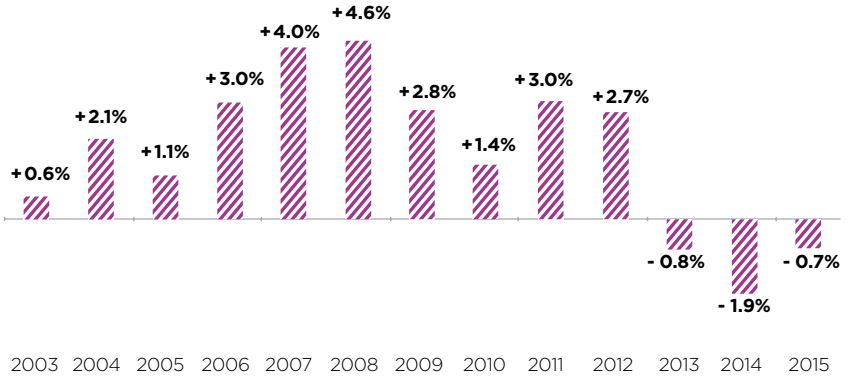
	2008	2009	2010	2011	2012	2013	2014	2015
Total number of registered donors	13,824	18,041	16,207	14,587	15,391	20,368	19,423	18,848
EFS's contribution to recruitment	12,583 (92.6%)	16,156 (89%)	14,477 (89%)	13,191 (90%)	13,666 (89%)	17,681 (87%)	17,355 (89%)	17,400 (92%)
EFS's contribution to HLA typing	10,560 (76%)	13,584 (75%)	11,952 (73%)	11,006 (75%)	11,361 (74%)	15,912 (78%)	14,429 (74%)	14,060 (75%)

Labile Blood Product (LBP) Transfers

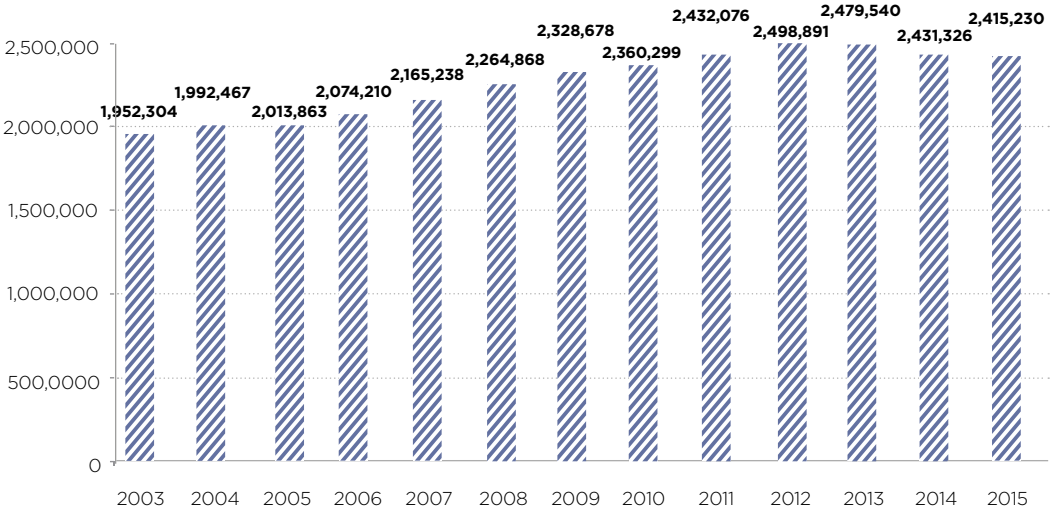
Red Blood Cell Concentrate Transfers

For the third year in a row, red blood cell concentrate transfers have dropped in 2015 compared to 2014 (a 0.7% decrease, or 16,096 fewer units).

CHANGE IN RED BLOOD CELL CONCENTRATE TRANSFERS SINCE 2003 IN %



CHANGE IN RED BLOOD CELL CONCENTRATE TRANSFERS SINCE 2003 IN FIGURES



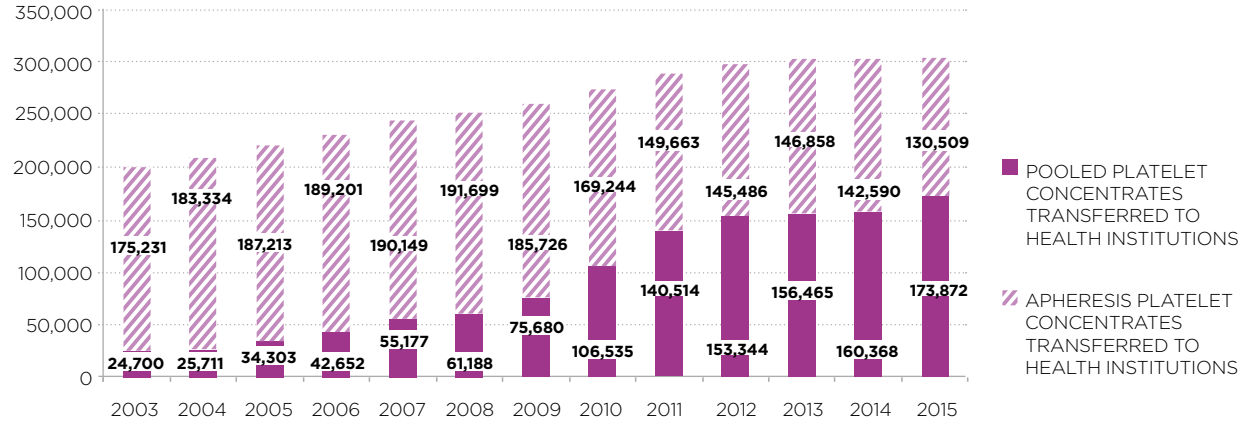
Platelet Transfers

Platelet transfers have increased slightly over 2014 (0.5% increase). Pooled platelet concentrates from whole blood donations increased by 8.4% compared to 2014, while apheresis platelet concentrates decreased by 8.5%. Pooled platelet concentrates accounted for 57.1% of all platelet transfers, compared to 52.9% in 2014.

	2003	2004	2005	2006	2007	2008
Pooled platelet concentrates transferred to health institutions	24,700	25,711	34,303	42,652	55,177	61,188
Apheresis platelet concentrates transferred to health institutions	175,231	183,334	187,213	189,201	190,149	191,699
TOTAL	**199,931**	**209,045**	**221,516**	**231,853**	**245,326**	**252,887**

	2009	2010	2011	2012	2013	2014	2015
Pooled platelet concentrates transferred to health institutions	75,680	106,535	140,514	153,344	156,465	160,368	173,872
Apheresis platelet concentrates transferred to health institutions	185,726	169,244	149,663	145,486	146,858	142,590	130,509
TOTAL	**261,406**	**275,779**	**290,177**	**298,830**	**303,323**	**302,958**	**304,381**

CHANGE IN PLATELET TRANSFERS SINCE 2003



Plasma Transfers

EFS no longer has a monopoly in this sector as of 1 February 2015. Nevertheless, EFS has decided to maintain its market presence. The establishment reorganised its production chain to offer therapeutic plasma products to healthcare establishments which meet high quality and safety standards In 2015, there were 794,702 litres of plasma from whole blood donations transferred to LFB for the production of plasma-derived medicinal products (PDMPs) compared to 769,615 litres in 2014. This represents an increase of 3.3%, or 25,088 litres.

Biomedical and pre-transfusion patient testing

The drop in LBP transfers in 2015 has affected EFS's laboratory services. There were 520.7 million "B" testing value units performed in 2015, i.e. a 0.3% decrease from 2014. This was partially made up for by an increase in the scope of business in EFS Nord de France region.

Around 70% of analyses concerned erythrocyte immunohaematology.

**All biomedical analyses are identified by a code number corresponding to a coefficient paired with the "B" testing value unit.*

EIH DOWN 0.8% BETWEEN 2014 AND 2015

(in thousands of "B" testing value units)	2015	2014	Difference between 2014/2015	
			Quantities	%
Laboratory tests	520,662	522,370	- 1,709	- 0.3%
Including immunohaematology	363,913	366,869	- 2,956	- 0.8%
Other	156,749	155,501	+ 1,248	+ 0.8%

Blood Products: Safety and Quality

EFS's Quality Policy

Activities related to labile blood products (LBPs) must comply with standards and regulatory requirements that guarantee their safety and quality throughout the transfusion chain. EFS implements a continuous improvement approach for its quality management system, in order to maintain a very high level of compliance with health regulation.

EFS's safety policy stipulates the safety and quality rules regarding the collection and management of LBPs as well as the application of these requirements. This is made possible by a risk and quality management system that is currently in place in every EFS establishment. The EFS safety policy also covers the monitoring of haemovigilance and quality control data with respect to LBPs. EFS is constantly working to improve its organisation and practices to meet the constant health safety challenges inherent to the transfusion sector.

Switching from a Quality Management System to a Risk and Quality Management Approach

In 2015, EFS continued to improve its quality management governance in its establishments. It incorporated the requirements mandated by the Decree of 12 September 2014 regarding human blood (the "Blood Decree II"), which stipulated that EFS's quality management system be expanded to account for risk management as well.

The formal introduction of a risk-based approach in the management system aims to strengthen preliminary risk analysis processes and *subsequent* risk management practices as well as the methods for identifying emerging risks that may affect the achievement of objectives regarding quality and safety. The Swan single database for managing non-compliances is currently being finalised.

EFS also strengthened the composition and intervention methods of its Safety Risk Committee, which oversees the management of major and critical non-compliances and monitors the implementation of corrective and preventative actions.

A Single IT System for all Sites

For the past several years, EFS has been standardising certain procedures on a national level. In 2015, it completed the implementation of two IT programmes with the aim of improving the efficiency of its organisation: Gedeon, an electronic document management system that allows users to share standards and texts issued by EFS and its administrative supervisors more efficiently, and Swan, which makes it easier to report problems and non-compliances and allows headquarters to conduct analyses and manage issues more simply.

Rigorous Quality Control

The regional quality control laboratories certify the quality and safety of the LBPs as well as the conformity of the procedures implemented during their collection and processing. All EFS sites are regularly audited by internal auditors and externally audited by the French National Agency for Medicines and Health Products Safety, known by its French acronym ANSM, which regularly inspects all EFS activities. Finally, EFS developed an active monitoring approach towards medical, technical, scientific, and vigilance topics.

In 2015, EFS's efforts to standardise its quality management system, which it had been working on for the past few years, culminated in Afnor ISO 9001 multi-site certification. Previously, each regional establishment was certified separately.

Vigilance Systems: Prioritising Safety

Haemovigilance Highlights in 2015

- Stabilisation in the number of reported cases of serious donor adverse reactions.
- Increase in reports related to excessive volume of blood collections (serious adverse events—SAE).
- Absence of new cases of hepatitis E virus (HEV) among therapeutic plasma recipients (recipient adverse reactions).
- Decrease in the number of cases of sporadic CJD reported among blood donors.

The safety of blood product recipients and blood donors is EFS' daily priority. Dedicated vigilance systems aim to collect every adverse event report related to donations and transfusions. The analysis of these health reports enables EFS to implement preventative measures and improve transfusion safety.

Severe Donor Adverse Reactions (SDAR): Vasovagal Reactions Continue to make up the Vast Majority of the Reports

In 2015, there was a slight drop in the ratio of severe donor adverse reactions per every 100,000 donations. This figure went from 182 in 2014 to 178 in 2015. Vasovagal reactions still account for the vast majority of these reports (84.3%). The stabilisation is probably due to the preliminary results of the Évasion study, which led to reinforced awareness about the importance of donor hydration and the gradual implementation of muscle tensing exercises during the donation process. The number of vasovagal reactions had increased in the two previous years.

Other events occur more rarely and include haematomas at the venepuncture site (8.91%), arterial punctures (2.58%), and reactions to citrate (1.01%). Very rarely, cardiovascular or cerebrovascular accidents are reported (10). The causal link with the blood donation in these cases is always debatable. The number of thrombo-embolic adverse reactions remains stable (16 in 2015 compared to 14 in 2014).

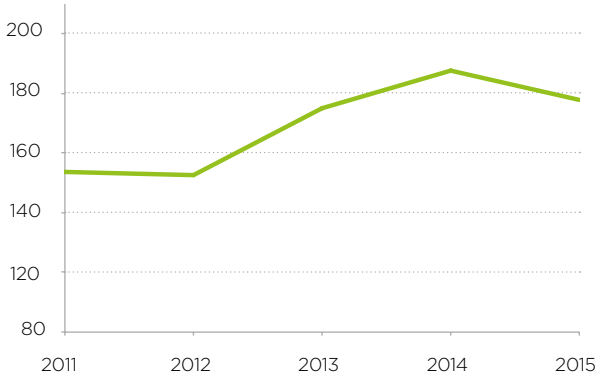
Variations in the reporting of these events among regional blood establishments in metropolitan France are stabilising.

The ratio between the regional establishment that reports the most events and the regional establishment that reports the least has dropped from 2.94 to 2.88. The ratio widens to 5.43 when the French overseas departments are included. The goal of 4, set by the Objective and Performance Contract (COP), has yet to be reached.

Serious Adverse Events (SAE) in the Transfusion Chain: An Increase in Reports at the Time of Collection

The 38% increase (compared to 158% between 2013 and 2014) in the number of SEs occurred at the time of collection only. This rise, which is due to excessive blood volume collections, seemed to plateau in 2015 once all EFS regional establishments switched to a new medical-technical software known as "U". However, there has been a sharp drop in the number of reports related to optional serologic tests (malaria and Chagas disease) and a significant increase in those related to non-compliance with eligibility criteria (interval between donations and annual number of donations). Once again, it was easier to detect these anomalies once all donors were added to the national database.

INCIDENCE OF SEVERE DONOR ADVERSE REACTIONS* OUT OF 100,000 COLLECTIONS BETWEEN 2011 AND 2015



*SERIOUS DONOR ADVERSE REACTIONS of severity level 2, 3, and 4 and imputability level 1, 2, and 3 and non-assessable.

Change in Serious Adverse Events (SAE) between 2010 and 2015

The number of reports related to distribution and issuing processes and recipient immunohaematology activity shows little variance. However, the proportion of SAEs for "non-compliance with respect to prescription/instructions/protocols" and "inconsistency between issuing file/LBP" as well as that for "typographical error/result transmission error" is increasing, which seems to indicate a lack of vigilance on the part of teams with respect to these two processes. The number of SAEs within other parts of the chain is low and remains stable. There are always very few reports related to processing and donations screening, reflecting the teams' skill with respect to these steps. Screening and processing seem to be more affected by malfunctions related to transport and storage than issues with the procedures themselves.

Arbovirus: Transfusion Risk and Precautionary Measures

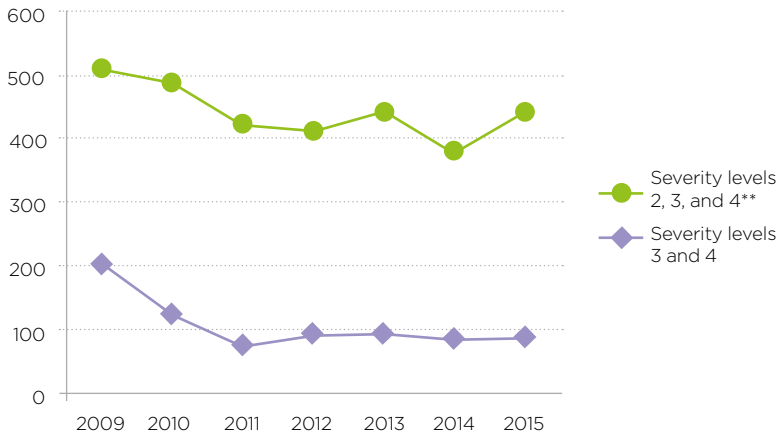
For the past several years, arboviruses such as the West Nile Virus (WNV), dengue fever, and, more recently, Chikungunya and Zika have become a constant concern, even in metropolitan France due to the presence and distribution of vectors capable of spreading the virus (Culex, Aedes). In 2015, EFS implemented NAT testing for WNV in certain EFS regional establishments in metropolitan France just as it did in 2014 for Chikungunya in Martinique and Guadeloupe-Guyana regional establishments. This same measure will be put in place for the Zika virus in 2016.

Adverse Reaction in Recipients: Fewer cases

The total number of adverse reactions in recipients remains stable at 7,880, including 6,289 closed cases.
No cases of HIV, HBV, or HCV seroconversion in recipients with a strong causal link were reported for transfusions that took place in 2015. However, three cases of HEV with a strong causal link (two pooled platelet concentrates and one apheresis platelet concentrate) were reported. In terms of bacterial risks, two transfusion-transmitted bacterial infections with a strong causal link and with a severity level 3 and 4 were reported in 2015 (three adverse reactions of severity level 3 in 2014). The two apheresis platelet concentrates in question were contaminated by *Klebsiella pneumoniæ* and *Citrobacter koseri.* The improved prevention of bacterial risk during platelet transfusions, for which bacterial testing (BactAlert®, BacTx®) and pathogen reduction (Intercept®) evaluation studies were conducted, remains one of EFS's main objectives.

Allergic and immunologic risks persist. One case of immunological TRALI of severity level 4 definitely related to transfusion occurred after the transfusion of red cell concentrates from a poly-immunised female donor (class I and II anti-HLA antibodies). Once again, no cases of immunological TRALI were declared this year following an apheresis platelet or FFP transfusion. Despite the safety and regulatory measures put in place, four cases of ABO incompatibility reaction related to transfusion of red blood cell concentrates were reported, but none of these cases was due to an error on the part of EFS. In terms of allergic reactions, seventeen cases of serious allergies related to transfusion occurred following a platelet transfusion in 2015 (compared to nineteen in 2014) and eighteen occurred following a transfusion containing plasma (twelve in 2014 with a statistically insignificant difference of p = 0.2).
Finally, the six deaths due to transfusions in 2015 (twelve in 2014) were caused by one transfusion-transmitted bacterial infection and one TRALI (mentioned above), one case of haemolysis in a patient with sickle cell disease, and three cases of TACO after a transfusion of red blood cell concentrates.

NUMBER OF ADVERSE REACTIONS IN RECIPIENTS WITH STRONG IMPUTABILITY LEVEL* CATEGORISED BY LEVEL OF SEVERITY FOR 100,000 LBPS TRANSFERRED BETWEEN 2009 AND 2015.



*Imputability level 2 (likely) and 3 (certain).
**Severity level 2 (severe), 3 (immediate threat to survival), and 4 (death).

Post-Donation Notifications: Risk of Infection Is Most Common

In 2015, 1,724 post-donation notifications (+ 11.3%) were reported to ANSM. The majority of post-donation notifications, i.e. 69.08% of reports, were related to a risk of infection (fever, flu-like illnesses, gastroenteritis, bacterial infections, exposure to a parasitic infection, etc.).
Theoretical risks (transfusion history, stay in Ireland or the United Kingdom, etc.)

Creutzfeldt-Jakob disease (CJD): Zero Batch Withdrawals

In 2015, seven cases of sporadic CJD were identified in blood donors. Top-down transfusion studies did not result in the withdrawal of any batches of plasma-derived medicinal products. No case of sporadic CJD transmission by plasma-derived medicinal products has ever been reported to date throughout the world. On 17 December 2015, ANSM announced the end of automatic withdrawals of batches in the event of sporadic CJD. The batch withdrawal policy remains in place in the event of variant CJD (vCJD) in a donor, and if the form of the disease is undetermined. This shift should lead to a marked decrease in the withdrawal of plasma-derived medicinal products. The last time plasma-derived medicinal products were withdrawn from the market due to a case of vCJD in a blood donor was in 2005.

are the second-most common cause of post-donation notifications (23.73%). A range of other causes (vaccinations, medication, etc.) account for 7.18% of reports. This distribution is stable compared to 2014 (70.24%, 23.76%, and 6% respectively).

Medical device vigilance

Medical device vigilance relies on top-down and bottom-up alerts as well as our internal circuit of non-compliance reporting, which led to 56 reports being transmitted to ANSM in 2015 (same number as in 2014): forty-eight percent involved breakage, 27% involved device defects (arrangement, assembly, clamp, needle, valve, etc.) and 25% involved an anomaly that prevented the device and/or machine from working. These anomalies are most often reported at collection (63%) and processing (16%) facilities.

Clinical Studies and Monitoring of Medical Literature

The use of data collected in haemovigilance databases made it possible to conduct several case-control studies including one on immediate and delayed vasovagal reactions in blood donors. The results were presented at national and international conferences. The nationwide survey entitled "Un jour donné" (On any given day) describing our population of blood components recipients has shown that transfusion practices, except for therapeutic plasma transfusions, comply with the guidelines of the French High Authority of Health. Up-to-date monitoring of medical literature offers a weekly review of contents of the latest issue of each journal, and general and specialised press reviews, on topics such as immuno-haematology and online access to books.

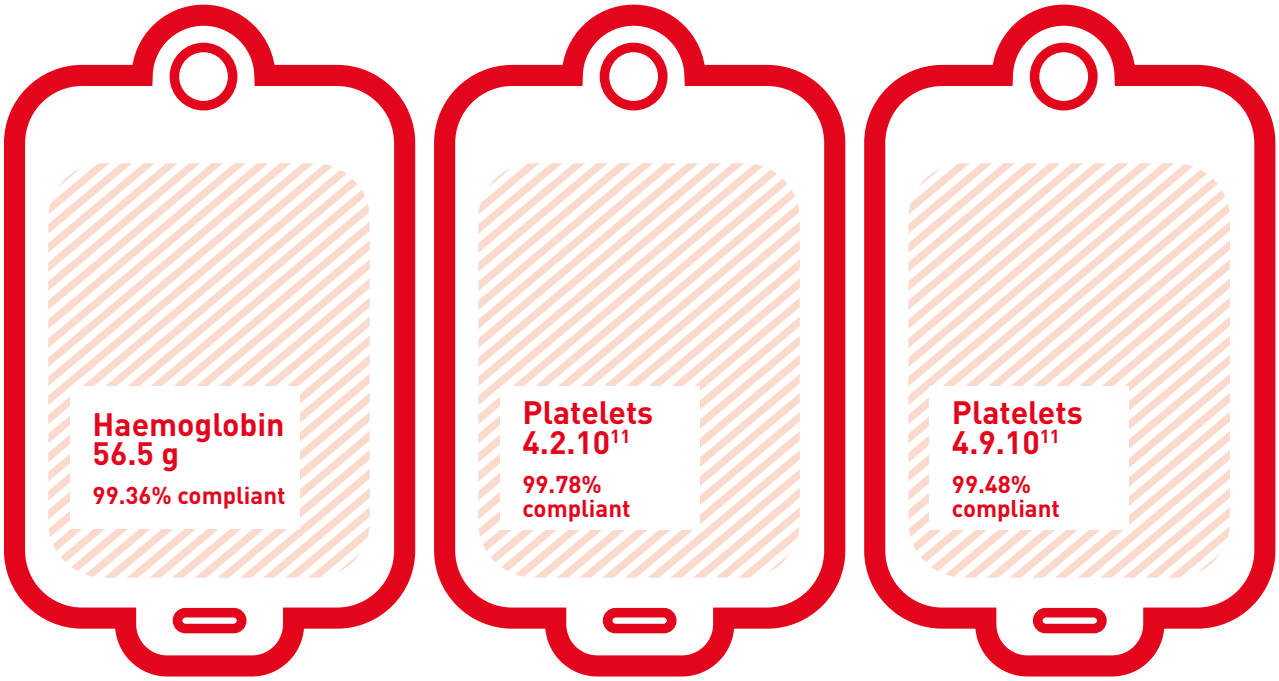
Adverse Reactions in Recipients—Strong imputability out of 100,000 transferred LBPs

		Indicators						
		2009	2010	2011	2012	2013	2014	2015
Platelet allergy	Severity levels 3 and 4	13.77	3.63	1.38	3.68	4.29	6.27	5.58
	Severity levels 2, 3, and 4	14.15	18.13	18.95	15.06	17.47	17.49	22.67
Plasma allergy	Severity levels 3 and 4	4.05	5.48	4.76	3.36	4.78	3.34	5.33
	Severity levels 2, 3, and 4	*4.05*	*9.14*	*9.25*	*8.80*	*9.56*	*8.08*	*13.63*

Analysis of LBP Quality Control Data

Labile blood products (LBPs) are prepared from blood, plasma, and platelet donations collection by EFS. LBP quality control monitoring is achieved by regional laboratories sampling programs. The results are then aggregated on a national level.

In 2015, the main cellular LBPs feature the following characteristics*:



Leucocyte-Depleted Red Blood Cell Concentrates

Pooled Leucocyte-Depleted Platelet Concentrate

Leucocyte-Depleted Apheresis Platelet Concentrates

**The results are expressed in averages ± a standard deviation, except for leucocyte reduction, for which the median is used. The percentage of non-compliant values for all production is given by the value of the pSup, or the upper limit of the confidence interval (degree of confidence of 95%) of the estimate.*

Leucocyte-Depleted Red Blood Cell Concentrates

Leucocyte-depleted red blood cell concentrates are prepared using whole blood donations or collections done by apheresis and are systematically leucodepleted. The active component in this product is haemoglobin. Leucocyte-depleted red blood cell concentrates must contain at least 40 grams of haemoglobin (Hb).

In 2015, the average haemoglobin content of these types of concentrates prepared by EFS was 56.5 g. This figure is particularly stable from one year to another.

Leucocyte-Depleted Apheresis Platelet Concentrates

Leucocyte-depleted apheresis platelet concentrates are obtained from single donors via apheresis. The leucocytes are then removed.

The active ingredient in this product is the total quantity of platelets. This type of concentrate must contain at least 2.0×10^{11} platelets.

In 2015, the average platelet content of leucocyte-depleted apheresis platelet concentrates was 4.9×10^{11} platelets/unit. This figure has not changed over the years.

Pooled Leucocyte-Depleted Platelet Concentrates

Pooled leucocyte-depleted platelet concentrates are prepared from whole blood by mixing an average of five buffy-coats from the same blood type.

The active component in this product is the total quantity of platelets. This type of concentrate must contain at least 1.0×10^{11} platelets. In 2015, the average platelet concentrate stayed above 4.0×10^{11}/ Pooled leucocyte-depleted platelet concentrate.

Residual Leucocyte Content in Cellular LBPs

In terms of leucocyte reduction, regulatory requirement stipulate that a minimum of 97% of units must be compliant (decision of 20 October 2010). All of the aforementioned concentrates prepared by EFS are compliant with this requirement.

A Healthcare Establishment

Biomedical Analysis Laboratory Activity

Whereas the immunohaematology laboratories of EFS conduct serology tests and blood typing, the twelve histocompatibility and immuno-genetics laboratories practise biological tests related to the HLA system*. The first type of laboratory helps ensure health and transfusion safety, while the second contributes to the success of organ and stem cell transplants.

Immunohaematology

EFS's immunohaematology (IH) laboratories developed a biomedical activity focused on patient transfusion safety and the immunological monitoring of pregnant women. This activity is carried out in integrated multi-site laboratories located in EFS's fifteen regional establishments (metropolitan France and French overseas departments). These laboratories, which are all certified under the NF EN ISO 15189 standard with the exception of the Guadeloupe-Guyana lab(certification pending), made it possible to streamline the organisation and standardise practises. Some 520 million "B" testing value units have been completed in these labs, including 364 million B units related to immuno-haematology.

The EFS laboratory network is related to the coverage of issuing sites (EFS own issuing sites or hospital blood banks). Indeed, IH and issuing are overseen by a single provider, EFS. This arrangement plays a critical role in ensuring transfusion safety and was reaffirmed by the French General Directorate of Healthcare Services (DGOS) in its recommendation to the French Regional Health agencies (ARS) in 2010. This link between IH, transfusion consulting, and the issuing of LBPs is one of the pillars of the French blood transfusion model and is essential to health safety.

IH laboratories' expertise is focused on two fields:

- Traditional testing as well as more specific serological exams such as:
  - specific direct antiglobulin testing (anti-IgG, -IgM, -IgA, -C3c, -C3d),
  - anti-erythrocyte antibody screening,
  - elution,
  - adsorption testing,
  - anti-erythrocyte antibody titration,
  - cross-match,
  - Rh (RH2, RH3, RH4, RH5) and KEL (KEL1) phenotype,

**HLA (human leucocyte antigen) typing is a sort of biological ID card.*

- Duffy, Kidd, and MNS phenotype and rare phenotypes such as RH46, VEL1, etc.,
- ABO variantsion screening,
- ABO system immune antibody screening and titration,
- rare erythrocyte phenotype confirmation and screening.

• Molecular blood type testing via three specialised laboratories created to genotype the most immunogenic blood types (FY, JK, MNS, DO, KEL, etc.), screen and confirm rare erythrocyte phenotypes/genotypes, and identify new allele variants. The laboratories perform the following tests:

- common erythrocyte genotyping (FY*1, FY*2, JK*1, JK*2, MNS*3, MNS*4),
- genotyping not covered by common erythrocyte genotype testing,
- RH system variant screening (RHD gene),
- RH system variant screening (RHCE gene).

Histocompatibility and Immunogenetics

Histocompatibility and immunogenetics laboratories perform biological testing related to the HLA system, which determines whether or not a transplant will be rejected (screening for anti-HLA alloantibodies and HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB345, HLA-DQA1, HLA-DQB1, HLA-DPA1and HLA-DPB1 typing). These labs also conduct platelet immunology testing (HPA system typing and anti-platelet auto-alloantibodies), granulocyte immunology testing (HNA system typing and anti-granulocyte antibodies), and chimerism testing.

Twelve laboratories in metropolitan France help care for transplant patients; healthcare facilities also help perform this public service. They identify the graft or transplant that is the most compatible with the patient and monitor his or her immune response.

In 2015, over 900 patients monitored by these laboratories received a haematopoietic stem cell graft, and nearly 2,440 patients received an organ transplant.

Most of these laboratories are also voluntary bone marrow donation centres *(see sidebar on p. 27).*

Histocompatibility and immunogenetics laboratories also help perform haemovigilance, pre-transfusion diagnostics for transfusion-related acute lung injury (TRALI), platelet and granulocyte compatibility testing, foetal-maternal platelet incompatibility diagnostics, and care for neonatal thrombocytopenia (over 5,000 cases). They also conduct biological immunological diagnostics (HLA and disease, platelet and granulocyte immunology).

148

EFS SITES DELIVER LABILE BLOOD PRODUCTS (LBP) THROUGHOUT MAINLAND FRANCE

Issuing of blood products

The 148 EFS sites issue labile blood products (LBP) throughout metropolitan France. One hundred and eighteen sites also distribute these products to hospital blood banks. This process requires a close cooperation between establishments to ensure transfusion safety and the continuous provision of healthcare services.

Distribution refers to the supply of LBPs by an establishment to other regional establishments, health institutions that manage blood banks (621 blood banks including 197 emergency blood banks), and manufacturers of healthcare products derived from human blood or its components. Issuing is the provision of LBPs to a specific person with a medical prescription so that they can be administered to a certain patient. Distribution and issuing, which are part of EFS's public service mission, are stipulated in the decision of 6 November 2006, which defines the good practise principles set in article L.1223-3 of the French code of public health and, more specifically, the guidelines on issuing and distribution, which include:

- the management of distribution channels, from LBP reception to their provision for therapeutic use in health establishments;
- the management of information and documents, from prescription to the establishment of traceability;
- transfusion consulting.

In 2015, 2,415,230 red blood cell concentrates, 304,381 platelet concentrates, and 357,454 fresh frozen plasma units were transferred to health establishments.

EFS issuing sites serve approximately 1,500 health institutions, and by extention the patients, 24/7. As a result, orders from prescribers are always fulfilled.

Moreover, transfusion consulting is also available at all times and is given by doctors and biological pharmacists whose qualifications comply with the French Code of Public Health.

Highlights of 2015 Included:

- as of 1 February, a discontinuation in the production, storage, distribution, and issuing of solvent/detergent treated fresh frozen plasma (SD-FFP), which was recategorised as a medicinal product. EFS is now placed in competition with other actors on the therapeutic plasma market. The decision also led to the deregulation of prices;
- the implementation of a "HEV-free" plasma category , to compensate for the end of SD-FFP production as a LBP and to meet the demand from prescribers for certain targeted indications;
- the publication of the good practise recommendations from the High Authority of Health and the French National Agency for Medicines and Health Products regarding the transfusion of platelet concentrates, thereby ensuring consistency across the various types of LBPs in terms of qualification and transformation indications;
- the end of the Effipap study on the haemostatic effectiveness of platelets pathogen-reduced with the Intercept® technology *(see p. 48)*.

Cells, Tissues, and Cord Blood

In 2015, EFS confirmed its place as a leader in the national cell and tissue therapy products market. It is also highly involved in the pre-clinical and clinical development of advanced therapy medicinal products (ATMP).

EFS and Cell Therapy

For over thirty years, EFS has offered health establishments all haematopoietic cell therapy products as well as other innovative therapeutic products (pancreatic islet grafts and dendritic cells, for example). Within eleven regional establishments, eighteen sites perform the following activities:

- freezing/thawing of autologous haematopoietic stem cells;
- transformation of haematopoietic stem cells;
- processing and freezing of donor lymphocyte infusion;
- processing and storage of units of intrafamilial cord blood;
- processing of mononuclear cells for extracorporeal photochemotherapy.

These activities, which represent 60% of the national volume, are strictly regulated and controlled by the establishments themselves and by the processing procedures authorised by the French National Agency for Medicines and Health Products Safety (ANSM). University hospitals benefit from the nearness of the sites and the expertise of EFS personnel, who are well-versed in the implementation of processing best practises.

Finally, EFS also maintains partnerships with industry stakeholders. These partnerships play a key role in developing increasingly innovative collection and product processing devices.

EFS and Tissue Banks

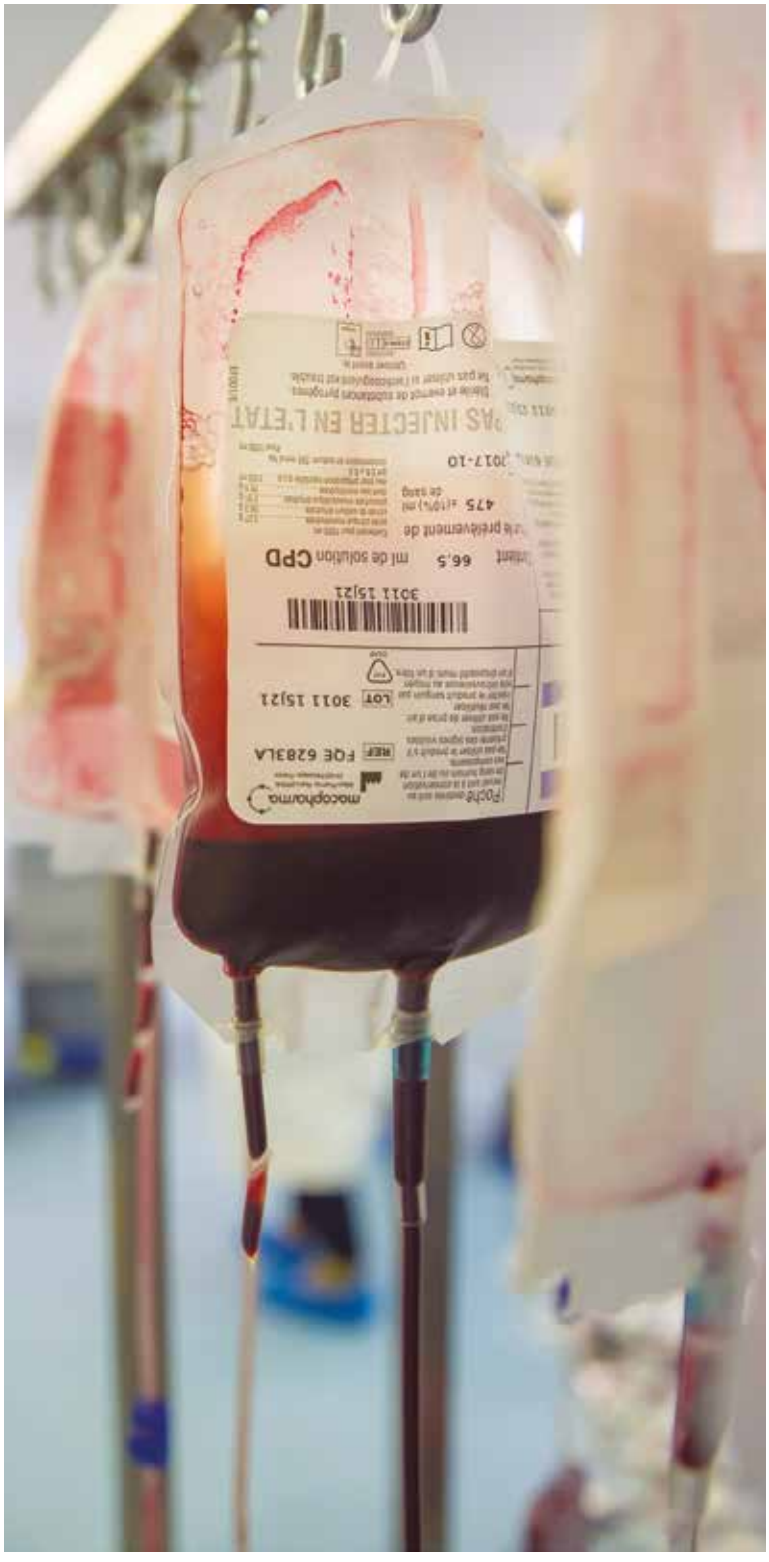
EFS is able to prepare the majority of human tissues that patients need (corneas, vein and arterial tissue, amniotic membrane, and bone with or without viral inactivation). The processing and storage of these tissues have been performed since 2011 in six

multi-tissue banks[1] and two cornea banks, one of which is specialised in trimming corneal grafts.
These banks are also authorised to import tissues that are not available in France.

The role of the partnership and development managers is to inform health establishments about these tissue products, which, due to their high quality and ethical management, help bolster the reputation of EFS in a very specific and highly competitive field.
Furthermore, EFS maintains very close ties to the Biomedicine Agency. This important partner assists EFS in collecting tissues in health establishments.

EFS and Cord Blood Banks

EFS keeps on expanding and enriching its inventory of cord blood units available to national and international patients in accordance with the requirements of the Biomedicine Agency. The target of 30,000 cord blood units registered with the French Network of Cord Blood (FCBN) was reached in November 2013 by the deadline[2] set by the French transplant and graft plan. EFS provides three-quarters of this stock, while French university hospitals provide the final quarter.
A reorganisation of the network of EFS banks was carried out in 2014 to continue the storage of new cord blood units, which have a higher cell content. Evidence shows that the higher the cell content in the transplant or graft, the more these products are likely to be used. Currently, two banks in Bordeaux and Besançon receive and process cord blood units, whereas the other banks (Créteil, Grenoble, Lille, Lyon, Poitiers, and Rennes) distribute their stock where it is needed.



1. EFS has six multi-tissue banks (Besançon, Bordeaux, Marseille, Lyon, Paris, and Tours) and two cornea banks (Saint-Étienne and Brest).

2. Starting in 2009, subsidies granted as part of the French cancer plan made it possible to expand the stock to 30,000 cord blood units (based on production costs of €2,000). Between 2010 and 2013, €29.4 M in funding was provided.

Healthcare Centres

EFS provides healthcare that is regulated and limited to certain, very specific services (bloodlettings, apheresis, etc.) that are performed in its health centres, These centres also take part in clinical studies as part of EFS's research activities.

Therapeutic Activities

EFS's healthcare activity was developed due to the expertise of its staff in collection techniques (whole blood and apheresis). These services are provided in its 89 health centres within thirteen regional establishments and are a part of EFS's public service mission; indeed, the organisation plays an important role as an outpatient care provider.

All EFS health centres have a specific certification, and those that collect haematopoietic stem cells operate under certification issued by the Regional Health Agency following an opinion by the Biomedicine Agency.

In 2015, EFS health centres performed:

- bloodlettings for patients with haemachromatosis and other diseases that cause an iron overload (76,390). Among these, 23.4% were converted into blood donations (17,871);
- collections of autologous (2,915) and allogenic (484) blood haematopoietic stem cells and mononuclear cells (1,375);
- extracorporeal photophoresis (3,151);
- erythrocyte exchanges (1,793);
- transfusions (4,809);
- white blood cell depletions.

The 5,906 other acts of therapeutic apheresis include plasma exchanges, LDL (low density lipoprotein) apheresis, and platelet apheresis.

EFS health centre teams mostly care for patients on an outpatient basis, but they go to health establishments as needed. In 2015, 1,189 apheresis services were performed outside of EFS health centres, particularly for paediatric patients.

The number of transfusions and other services excluding apheresis decreased by 15.6% compared to 2014 (4,809 vs. 5,697).

Participation in Clinical Studies

The health centres take part in clinical studies in collaboration with industry and hospital stakeholders. They contribute by collecting stem cells, which are then reinjected into patients. In 2015, five clinical studies were conducted:

- the Emsai study: a multi-centric study on patients admitted to an EFS iterative bloodletting protocol for which EFS is the sponsor. The scientific aspects regarding haemochromatosis are coordinated by the team of Prof. Claude Ferec (Brest UMR 1078) in partnership with INSERM.

- the study to improve Optia cellular separators and the launch of the CMNC programme (sponsored by Terumo).
- the One Study protocol, a monocentric phase I/II cellular immunotherapy study based on the administration of autologous tolerogenic dendritic cells (ATDCs) to patients with kidney failure who are receiving their first kidney transplant from a living donor (sponsored by the University Hospital of Regensburg, Germany—Prof. Edward K. Geissle).
- the CD LAM (acute myeloid leukaemia dendritic cells) protocol, a multi-centric phase I/II cellular immunotherapy study that administers autologous dentritic cells loaded with apoptotic leukaemia cells to patients with acute myeloid leukaemia in their first or second complete remission or to resistant AML patients in their first complete remission (sponsored by the Nantes University Hospital).
- the Diaphreg II study (the French acronym refers to "early diagnosis of genetic haemochromatosis), which aims to identify and determine the frequency of the early signs of genetic haemochromatosis (sponsored by Université Paris-Diderot-Paris-VII).

Apheresis requires the use of automatic blood component separators. Starting in 2013, updating health centre separators has been a national challenge, both in terms of streamlining the equipment pool and training and certifying health centre staff because the teams must also carry out their daily activities, which include the collection of haematopoietic stem cells (HSC). This product is needed to maintain the HSC transplant activity at the technical hubs within local university hospitals.
Most of the health centres that collect stem cells are part of the Jacie accreditation programme, the goal of which is to promote the quality of medical and laboratory practises in the field of HSC transplants.

A Key Actor in the Medicine of the Future

21.7
MILLION EUROS ALLOCATED TO THE RESEARCH BUDGET

Research and Innovation at EFS

Research is a strategic priority at EFS. It enables us to be a key actor of scientific and medical progress and to prepare for the future. EFS research is supported by dedicated resources, strategic management, and a structure with close ties to universities, scientific and technological public research organisations, hospitals, and the manufacturing sector.

EFS is a leader in one medical discipline —transfusion medicine. In the same way that university hospitals oversee other disciplines, EFS has significant responsibilities in terms of research, training, knowledge dissemination, valuation and technology transfer with help from universities and scientific and technological public research organisations such as INSERM and CNRS.

As a producer of over three million therapeutic products derived from living organisms every year, EFS monitors scientific and technical advances, and performs a proactive and innovative research, in a wide variety of fields such as known and emerging microbiological risks, the quality of blood and cell therapy products and how to tailor these services to meet the needs of patients, the immunological interfaces between products and patients, and donation ethics and medicine.

Equipped with significant resources to fulfil its primary missions, EFS aims at using them efficiently in an effort to advance public health.

Finally, EFS must prepare for and actively anticipate scientific and medical changes in its fields of interest. Regenerative medicine and the advent of stem cells are examples of such changes. If the majority of blood products are produced from stem cells in the future, EFS must be prepared to meet this challenge.

From Tissue Repair to Stem Cells: Multiple Fields of Research

EFS performs research in a wide variety of topics, ranging from fundamental research to clinical research.

Several EFS teams help develop new cell therapy products in the field of tissue repair (Toulouse, Créteil, Grenoble), while others focus on anti-tumour immunity (Grenoble, Besançon) or anti-infection immunity (Nantes).
Genetic transfer tools have been successfully used to develop innovative approaches in gene therapy (Nantes) and to produce secured T-lymphocytes (Besançon et Nantes).
The activation and adhesion of platelets, as well as their role in coagulation, thrombosis, and immunity are the subject of studies on humans and experimental models (Strasbourg, Saint-Étienne).
The therapeutic potential of stem cells in transplants (Bordeaux), regenerative medicine (Toulouse, Rennes), and transfusion (Créteil, Paris Saint-Antoine) is being actively explored.

In microbiology, EFS is involved in characterising and detecting emerging pathogens (Montpellier, Marseille). Prion research is making significant advancements in terms of diagnostics and the assessment of transfusion risk (Montpellier). On a related note, various methods for pathogen reduction in LBPs are also being studied (Strasbourg and Grenoble). The development of new blood testing tools based on micro-nanotechnologies (Montpellier) prepares laboratories for future micro-biological and immunohaematological risks. Moreover, the Brest laboratory's extensive expertise in epidemiological genetics is used to effectively advance the characterisation of iron overload treated by bloodlettings (and bloodletting-donations—Emsai study).

In immunology, the work of several EFS teams focuses on the immune relationship between a recipient and the blood products or graft/transplant he or she receives in order to reduce the risks of side effects and avoid situations of poly-immunization, or grafts/transplants rejection (Créteil, Nantes, Besançon).
In the field of donation, EFS analyses the immunogenetic characteristics of populations from French overseas departments and territories, as well as recent immigrants, and their effect on blood donation and transfusions (Marseille, Créteil).
Clinical research on transfusion is a priority for EFS, and the organisation participates in several multi-centric clinical trials. The results of the international Able study *(see sidebar on p. 49)*, regarding red blood cell concentrate shelf life and its influence on the future outcomes of patients receiving transfusions, were published in 2015.

Another important study investigated the haemostatic effectiveness of platelets that underwent pathogen reduction with the Intercept® technology (Effipap study). This study ended with the inclusion of the last patient in December 2015, and preliminary results should be available in 2016.
Finally, cardiovascular risk factors (Besançon) in donors are being investigated through clinical studies conducted in partnership with health institutions.

Three New ATMP Production Platforms in 2015

EFS's pharmaceutical establishment focuses on manufacturing advanced therapy medicinal products (ATMP). These medicines are used in the early stages (I and II) of clinical research focusing on the treatment of cardiovascular and bone/joint disease, strokes, leukaemia, cancer, and inflammatory diseases. This research is in the continuity of EFS's upstream research, development, and technology transfer efforts in constant collaboration with researchers. The production platforms can also be subcontracted by private industry actors who wish to have access to specialised manufacturing and control resources for clinical applications in France.

EFS satisfies new regulatory requirements for ATMPs by incorporating Good Manufacturing Practices (GMP) into its production and control tools. It was recognised as a pharmaceutical establishment in 2014 by the French National Agency for Medicines and Health Products Safety (ANSM), thanks to its first ATMP platform, Atlantic Bio GMP (ABG), located in Saint-Herblain (44) and created through a partnership with the French Myopathy Association, INSERM, and the Nantes University Hospital.

Three other platforms were established in 2015: Toulouse (31), Saint-Ismier (38) and Besançon (25). This endeavor relied on pre-existing innovative cellular engineering activities. The platforms are funded in part by the ECellFrance project. This programme involves the production of mesenchymatous stem cells and is supported by the European Union, the French government's Investissement d'Avenir programme, and local communities. The Saint-Ismier platform was inaugurated on 25 September 2015 and is part of the cellular engineering and therapy unit.

In November 2015, EFS opened its fourth ATMP production platform in Besançon. Finally, construction work to bring the Créteil site up to standard began at the end of 2015, which will allow the fifth and final production platform to request its opening authorisation at the end of 2016.

Two International Clinical Research Studies: ABLE and Ebola-Tx

The goal of the ABLE study, coordinated by Sainte-Justine University Hospital in Montreal and conducted between March 2009 and May 2014, was to verify if the administration of erythrocyte concentrates less than one week old would improve outcomes for adults receiving transfusions in intensive care ("fresh blood" group with 1,211 patients in the study) compared to outcomes of adults receiving blood distributed in accordance with the current standard policy applied by blood banks ("standard" group with 1,219 patients in the study). The article published in 2015 in the prestigious international medical publication *New England Journal of Medicine*[1] concluded that erythrocyte concentrates stored for less than seven days did not improve outcomes for adults receiving transfusions in intensive care compared to concentrates stored for an average of three weeks. This is the first time EFS participated in a clinical study of this magnitude.

In 2015, EFS also demonstrated its innovative and responsive nature by participating in the European Ebola-Tx project in Guinea.

This effort was supported by an emergency research fund under the European Horizon 2020 programme. The main goal was to assess the effectiveness, safety, and feasibility of an emergency therapy based on the blood or plasma of patients who had recovered from Ebola.

The project, which was headed up by the Anvers Institute of Tropical Medicine, was also supported by the London School of Hygiene and Tropical Medicine, Oxford University, the Flemish Red Cross, Aix-Marseille University, EFS (coordinated by Dr. Pierre Gallian, EFS Alpes-Méditerranée, IHU-MI[2]), the Pasteur Institute, INSERM, Doctors Without Borders, and the Conakry National Blood Transfusion Centre.

Several EFS employees, who are specialised in collection and processing, completed a dozen assignments in Conakry in 2015 to implement, install, and train personnel as well as help them set up a local production chain for apheresis plasma treated with the pathogen reduction technology Intercept®. Plasma was collected from convalescent patients starting in February 2015 and then administered to 84 patients suffering from Ebola until early July 2015 as part of a clinical study that had obtained the necessary regulatory authorisations.

The preliminary results[3] were published in the *New England Journal of Medicine* and show that the transfusion of convalescent plasma to patients infected with Ebola does not cause side effects and that the implementation of such a therapy during a health crisis is possible. However, in terms of patient survival, the study did not indicate that receiving two units of plasma from convalescent donors was beneficial. The results do point to encouraging avenues for future research as regards the treatment of children and pregnant women. The data is still being analysed, especially with respect to the correlation between the titres of neutralising antibodies and the survival rate. These latest results will play a decisive role in determining the value of this type of transfusion immunotherapy in Ebola patients.

1. Lacroix J, Hébert PC, Fergusson DA, Tinmouth A, Cook DJ, Marshall JC, Clayton L, McIntyre L, Callum J, Turgeon AF, Blajchman MA, Walsh TS, Stanworth SJ, Campbell H, Capellier G, Tiberghien P, Bardiaux L, van de Watering L, van der Meer NJ, Sabri E, Vo D; ABLE Investigators; Canadian Critical Care Trials Group. "Age of Transfused Blood in Critically Ill Adults", New England Journal of Medicine. *2015 Apr 9; 372(15): 1410-8.*

Marseille University Hospitals' Mediterranean Institute for Infectious Diseases

3. Van Griensven J, Edwards T, de Lamballerie X, Semple MG, Gallian P, Baize S, Horby PW, Raoul H, Magassouba N, Antierens A, Lomas C, Faye O, Sall AA, Fransen K, Buyze J, Ravinetto R, Tiberghien P, Claeys Y, De Crop M, Lynen L, Bah EI, Smith PG, Delamou A, De Weggheleire A, Haba N; Ebola-Tx Consortium. "Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea", New England Journal of Medicine. *2016 Jan 7; 374(1): 33-42.*

An Internal Call-for-Proposals System to Focus on Topics related to EFS's Core Business

EFS bases its scientific strategy on the implementation of yearly internal calls for proposals, which receive a substantial budget. These calls for proposals make it possible to provide greater financial support to topics chosen thanks to two forms of expertise—independent external expertise regarding scientific quality, and internal expertise in terms of matching research projects to the scientific objectives and priorities of EFS. As a result, the scientific topics related to EFS's core business are the priority when allocating resources.

The 2010, 2011, 2013, and 2014 calls for proposals made it possible to fund 58 projects, i.e. over half of all proposals submitted. Thirty-one additional projects received funding after project evolution following discussions with project leaders. Calls for proposals are regularly evaluated as the results are used to produce publications and patents. They are also assessed through collaborations and partnerships with relevant academic and industry stakeholders. Such evaluation makes it possible to estimate the "return on investment" for EFS research.

Fostering EFS inventions to become innovations

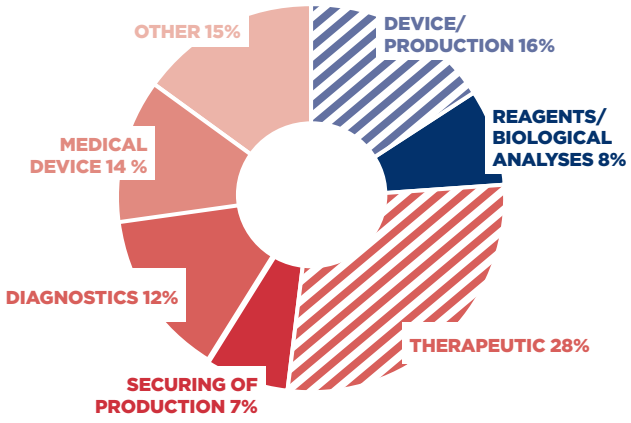
The Intellectual Property and Technology Transfer department continues to protect and promote the results obtained through EFS laboratory research.

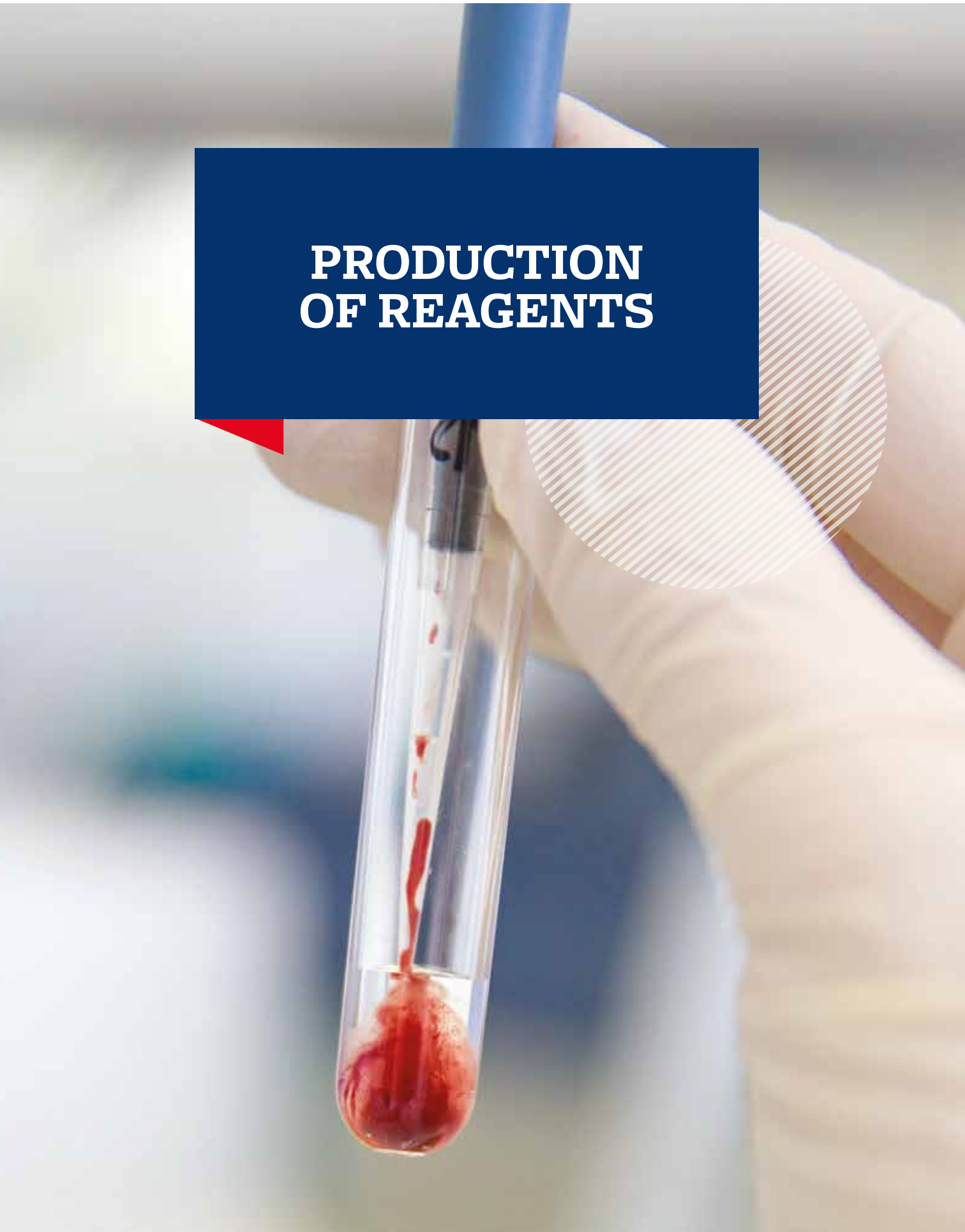
The department processed seven invention disclosure reports, three sealed envelopes (Envelope Soleau), and seven new priority and international patent applications. It also protected a software programme. These results were obtained through a strategy the department has been applying for the past three years to train EFS researchers and developers to intellectual property. As of 31 December 2015, the EFS patent portfolio included 35 patent families and 171 titles, 50 of which were granted.

The patent families are mostly related to therapies, medical devices, and the

improvement of labile blood product manufacturing processes. The patents primarily concern therapies due to EFS's strong focus on researching cell and tissue therapies. Concerning the technology transfer, two new licensing contracts were signed with industry partners in 2015.
The Intellectual Property and Technology Transfer Department is stepping up its efforts to monitor technology changes in strategic fields in order to stay abreast of state of the art inventions and detect new competition. Along with the Legal Affairs Direction, it also helps implement agreements with industry and academic partners.

DISTRIBUTION OF EFS PATENTS





PRODUCTION OF REAGENTS

125
PRODUCT REFERENCES,
INCLUDING 40 WITH CE MARKING

Transfusion Diagnostics

Beside the field of transfusion and as part of its associated activities, EFS is authorised to produce reagents, blood components, and blood products for non-therapeutic use

In 2004, EFS founded its reagent production unit, which is specialised in the manufacture of *in vitro* diagnostic medical devices (IVDMD) in order to comply with European regulations. The unit is run by a staff of approximately forty employees. Its aim is to standardise and certify the production of the reagents it manufactures and distributes. These reagents enable EFS teams to check the compatibility of the donor's blood with that of the recipient and to test and qualify blood products. Blood typing and microbiological testing (HIV, HBV, and HCV serology tests) are run on every blood unit collected by EFS. Reagents are necessary to perform these tests. They are produced with human blood provided by EFS. They are therefore manufactured internally. In addition to lower costs, this ensures a constant supply of compliant products without any risk of a shortage.

Five Manufacturing Sites

Reagents are produced at five sites located in five regional establishments. The EFS Alsace-Lorraine-Champagne-Ardenne (Reims), EFS Alpes-Méditerranée (Marseille), and EFS Pays de la Loire (Nantes) regional establishments specialise in immunohaemotology, and manufacture test cell reagents. The EFS Bretagne (Brest) regional establishment produces molecular biology reagents for nucleic acid testing (NAT). The EFS Nord de France (Lille) regional establishment specialises in microbiological serology (serum or plasma containing hepatitis virus or HIV, etc.). For its part, the EFS head office ensures the global management of the IVDMDs manufacturing process and "CE" marking and registration, regulatory data, IT systems, and quality policy. The reagent production unit is in constant need of "donors", especially for blood with "specific characteristics", i.e. carriers of certain special traits, to produce reagents. In addition, red blood cells have a short shelf life, and reagents can only be stored for four weeks.

In 2015, a new governance system for this activity was put in place. Its purpose is to ensure a greater degree of coordination at the national level to standardise practises and improve efficiency, to manage the activity to guarantee uninterrupted service and scientific developements, to formalise coordination efforts between regional activity and national management, and to involve the EFS regional establishments supplied by the reagent production unit.

A Catalogue of Products

The reagent production unit currently has over 125 product references, including approximately forty that carry the "CE" marking. The unit has a catalogue listing all the IVDMD it manufactures. The reagent production unit continually develops collaborations with external partners (diagnostics laboratories and manufacturers, for example) in order to better adapt its reagents to their equipment.

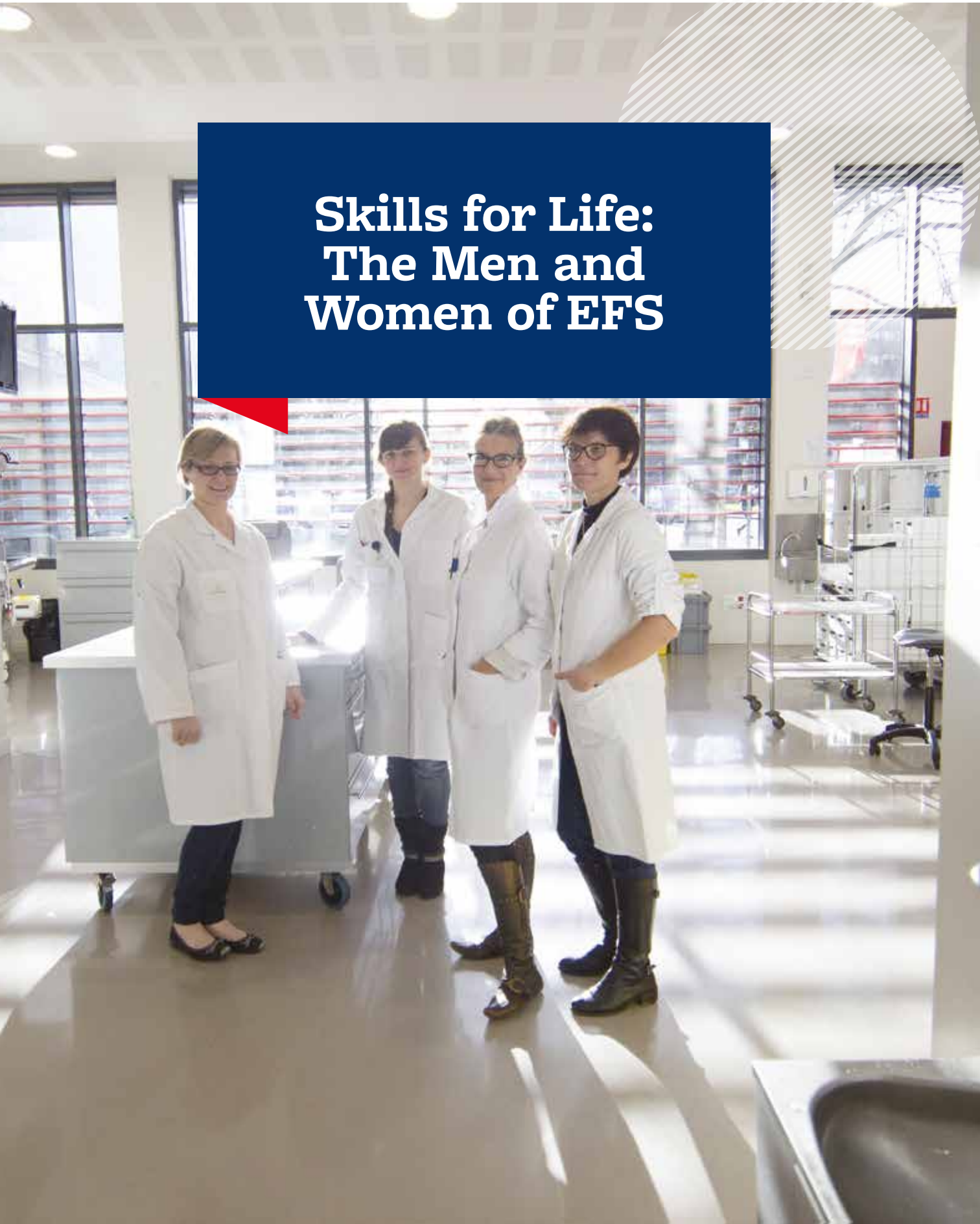
2015 Annual Report

The IVDMDs manufactured by the reagent production unit were distributed to nearly 145 biomedical analysis laboratories, around 25 French and international clients, and four partners in the medical diagnostics sector who then distribute these products to their respective clients. The reagent production unit's turnover exceeded 5.5 million euros in 2015 (a 30% increase over 2014), with the external market representing 34% of total activity. Prospects for 2016 focus on the continued concentrated development of external activities thanks to the structuring of a subcontracting agreement with a leading international diagnostics manufacturer, consolidated synergies with Diagast (EFS's diagnostics subsidiary), and the development of new products based on the recommendations of a committee of internal experts.

Products for Use in Laboratories, Teaching, and Research

When a donor's blood features unusual characteristics or cannot be given to a patient, it can be used for non-therapeutic purposes. EFS is authorised to transfer some of these products, which are then used for teaching and research endeavors. They can also be used to manufacture IVDMDs and conduct medical biology tests and analyses. In 2015, these products generated 6.6 million euros in turnover. Three regional establishments (Nord de France, Normandie and Rhône-Alpes-Auvergne) produced 75% of this turnover.

Skills for Life: The Men and Women of EFS



EFS's HR Policy

More than 9,800 people work at EFS every day to meet patients' needs and liaise with blood donors. From collection to issuing, our teams combine professional rigour with keen personal skills. Their expertise ensures patients receive blood products that meet the highest level of quality and safety standards.

EFS's human resource policy is based on four main areas of focus.

- Employer/employee dialogue: open mindedness, dialogue, and transparency are core values at EFS, and management and labour are considered to be constructive players in the life of the organisation'.
- A participatory approach: the pooling and sharing of experience are essential for EFS. Dialogue and exchanges are carried out using process-specific "networks" (medical affairs, scientific affairs, financial management, etc.).
- Recognition of employees: EFS is committed to developing the careers of its employees by implementing a fair and transparent system.
- Social involvement: EFS has developed an exceptional diversity policy (disability policy, intergenerational policy, etc.). Occupational health is also a major area of focus for EFS.

Human Resources in Figures

Our activities in the "core business", associated activities, research, and support services, employed 9,833 people as of 31 December 2015:
– 8,234 private sector employees,
– 577 seconded civil servants,
– 60 seconded employees,
– 10 public sector contractors,
– 952 temporary workers.
EFS's "core business" activities employ 70.1% of its personnel.

In 2015, EFS personnel can be described as follows:
– 73% women.
– 44 years of age on average.
– 13 years average seniority.
– 28.1% of employees work part time.
– 227 new permanent contract employees:
• 82 technicians and supervisors,
• 94 medical managers,
• 45 non-medical managers,
• 6 employees.
– 246 people on work/study contracts.
– 475 permanent contract employee departures:
• 38% resignations,
• 39% retirements,
• 22% for other reasons (dismissals, deaths, etc.).
– More than one out of two employees has undergone training during the year.
– Proportion of disabled workers: 7%.

EFS's Presence on the Social Networks: Viadeo and LinkedIn

EFS, which is already active on Facebook, Twitter, and YouTube, has recently opened accounts on LinkedIn and Viadeo.

https://www.linkedin.com/company/efs

http://www.viadeo.com/fr/company/efs

The Importance of the Employer/Employee Dialogue at EFS

Since EFS's founding, the labour relations with employee representative bodies has been enriching and constructive. In 2015, this process led to the signing of eleven collective agreements and supplementary clauses. Employer/employee dialogue has always featured sustained exchanges and discussions, especially with union representative bodies. In addition, EFS has often extended social welfare gains to its staff ahead of regulatory deadlines. The programmes established through negotiations most often go beyond what EFS is legally obligated to do. During the yearly round of mandatory negotiations, the topics and schedule of negotiations are set and the salary evolution framework mediated by EFS's administrative supervisors is allocated. The rest of the year, discussions centre around EFS's major strategic projects, including social adaptations related to reorganisations, union demands, and topics proposed by the legislative body.

Among the Eleven Agreements and Supplementary Clauses signed, Four held Particular Significance

Agreement on Employment, Professional Integration, and Continued Employment of Disabled Persons 2015–2018

The second approved agreement for the protection of disabled workers was signed in March by the four representative unions (CFDT, CGT, FO, SNTS-CFE-CGC) and is part of EFS's disability policy. In this field, EFS has made several commitments, including promoting equal opportunities, preventing professional risks, anticipating disabilities, and promoting the continued employment of disabled persons. It has also supported specific actions such as awareness-raising, recruitment, job retention, training, and subcontracting in a sheltered environment.

Profit Sharing Agreement 2015–2017

Signed in May by three representative unions (CFDT, FO, SNTS-CFE-CGC), the goal of this agreement is to recognise the contribution of employees to the economic progress and performance of EFS. The profit sharing bonus is calculated based on three criteria: efficiency (70% for gross operating surplus/turnover), the coverage rate for

blood products (15%), and safety (15% for no formal notices from ANSM). There is also a bonus for low absenteeism: 10% of the available amount if the absenteeism rate in the social data report is less than or equal to that of the previous year.

The Social Project Agreement on Shared Provisions for Assisting Personnel who have been Transferred within the same Geographic Area

Signed in June by three union representative organisations (CFDT, FO, SNTS-CFE-CGC), this amendment specifies the assistance options available to staff in the event of a change of residence or if their commute between home and a new workplace increases travel time.

If personnel are made to transfer to a new job site and move their place of residence, they are entitled to time off to look for housing and to move, help looking for a new home, a moving-in bonus, and reimbursement for their moving fees. If personnel change job sites without having to move their places of residence, they are entitled to temporary assistance due to their increased transportation fees and temporary compensation for their longer commute.

The Vision and Values of EFS

As part of EFS's establishment project *(see Highlights, p. 8)*, President François Toujas wished to establish a vision and four essential values for the organisation. These elements embody EFS and must inform the daily work of each employee.

The vision

- **A more modern and competitive organisation that fulfils its public service mission in a constantly changing environment.**
- **A key actor in the health system that is fully integrated into the healthcare chain.**
- **An agile and high performance organisation that showcases all of its business lines and is renowned for its medical and scientific excellence.**
- **An organisation geared towards serving patients and respectful of donors.**
- **An organisation with highly skilled and diverse personnel.**

The values

- **Public service: using our skills, tools, and business lines to meet patients' needs, donor and partner expectations, and challenges in healthcare. Serving the public interest and guaranteeing the safety of everyone as part of an ethical approach to donation.**
- **Excellence: completing our daily work with excellence, applying our business line, managerial, and technical skills, encouraging the development of knowledge and talent, pursuing our research efforts, and strengthening ties with universities.**
- **Efficiency: respecting the act of giving blood, which is a rare product, by controlling production costs for labile blood products. Maintaining an agile organisation and enabling each individual to be a key player in our mission by using the best tools to accomplish our priorities.**
- **Respect: working together, listening and maintaining a dialogue with our partners, and collaborating with our colleagues throughout the territory to reach the goals set for EFS as the only civilian transfusion operator in France. Respecting the diversity of patients, donors, and our personnel.**

Agreement on the Modification of Article 3.1 of the Collective Convention Incorporating Fixed-Term Specific-Purpose Employment Contracts

Signed in April by three representative unions (CFDT, FO, SNTS-CFE-CGC) and approved by a decree in November, this agreement lets EFS enter into fixed-term specific-purpose contracts, with a duration between 18 and 36 months, in order to carry out a research or consulting assignment. It also allows EFS to call on experts and qualified persons with specific skill sets for a limited time and in exceptional circumstances.

International Relations and Cooperation

EFS: An Actor in the Blood Transfusion Sector in Europe and in the world

In Europe

EFS is part of the impetus to renew French healthcare institutions involvement in Europe and in the world, as advocated by the French General Directorate of Health and the Delegation of European and International Affairs. The Delegation for European and International Affairs operates under the authority of the Secretary General of the Ministries of Social Affairs and is a cross-disciplinary unit working at the centre of the social ministers' international concerns (social policy, health, women's rights, work, employment and the dialogue between employees and labour, urban life). As such, it oversees a network on international affairs in which EFS plays a major role.

In 2015, EFS pursued its international benchmark and information sharing activities with other European and international transfusion organisations. EFS also stayed abreast of the latest developments in Europe and abroad.

A presence within European and Multilateral Institutions

EFS is contributing to the work of European and multilateral institutions in the field of blood transfusion, especially with the European Blood Alliance (EBA) and the Council of Europe's European Committee on Blood Transfusion (CD-P-TS). These institutions share information about changes within the various transfusion systems, problems encountered by each partner, and the strategies they've implemented to resolve these issues.

In 2015, EFS increased its participation in the governing bodies of the EBA with the election of Prof. Pierre Tiberghien, Deputy Managing Director for Medicine, Research, and Innovation at EFS, to the Executive Board, as well as through the efforts of the working group dedicated to drafting common proposals for a future revision of the the European Directives on blood products.

Benchmark and Knowledge Sharing: Essential Tools for EFS

EFS regularly responds to numerous studies and requests from its international partners (EBA, Council of Europe, World Health Organization,

and the European Commission). In 2015, in addition to annual surveys on its transfusion activity, EFS received requests regarding the production of therapeutic plasma and plasma for fractionation, pathogen inactivation and bacterial detection in platelet concentrates, new donors recruitment channels, apheresis granulocyte collection, and donation testing.
This year, EFS focused its benchmarking activities on issues of key importance to the organisation in an effort to help create new internal policies. Studies were conducted on the pre-donation interview processes, the organisation of apheresis plasma collection, pre-transfusion immunohaemotology testing, and the authorisation of blood donations from men who have sexual relations with men in Europe.

In China

An Established Partnership with Jiangsu Province

The agreement between EFS and Jiangsu province was renewed in December. To mark the occasion, the first French-Chinese cornea bank was opened with the Red Cross of Jiangsu. French experts then participated in the second French-Chinese symposium on transfusion safety, which was attended by over 200 people.

In the Middle East

Continued Cooperation with Lebanon

Overseen by the ESA Business School in Beirut, with assistance from EFS and as part of the 2014–2016 action plan, cooperation with Lebanon in 2015 led to the launch of best practises, the strengthening of the existing regulatory framework, the promotion of voluntary blood donation, the development of a national haemovigilance plan, and the standardisation of transfusion IT systems. Moreover, the president of EFS took part in a communications seminar in Beirut in July. In December, the steering committee for this partnership met and proposed a new action plan.

Increased Cooperation with Iran

In May 2015, EFS participated in the scientific and organisation committees of the International Haematology Conference held in Yasuj.
In June, an agreement was signed between the High Institute for Education and Research in Transfusion Medicine (HIER) and Université Paris-Est Créteil (Upec) in collaboration with EFS to create a university degree programme on blood transfusion.
In October, the official visit of Prof. Pourfatholah, president of the Iranian Blood Transfusion Organization (IBTO), provided an opportunity to formalise relations between Upec and HIER with the signature of a memorandum of understanding. The end of the year was marked by the arrival at EFS of three professors in "immunology and transfusion complications and haemovigilance" and "distribution and issuing", as well as the organisation's official partnership with the Third International Congress of Transfusion Medicine on Evidence-Based Use of Blood Components and Plasma Derived Medicines in Tehran.

In South America

Support for Healthcare Professional Training in Chile and Argentina

EFS continued to support transfusion medicine degree programmes, thereby helping to improve the quality and safety of blood transfusion.

EFS provided special support to the Concepción transfusion centre in Chile and the creation of a donor relations programme (analysis of the IT system, segmentation of the "donor" file, and the creation of specific donation schemes). EFS experts also contributed to courses provided through the transfusion medicine degree programme at Isalud University in Buenos Aires, Argentina.

EFS's Long-Standing Cooperation with Brazil Continues: First French-Brazilian Conference on Health

EFS's oldest partnership continued with the arrival of Brazilian delegations and trainees, who focused on topics such as immunohaemotology reagent production and the financial management of blood transfusion organisations. A tour of the biotechnology company Diagast, which has been building up its expertise in the transfusion sector for nearly fifty years, was also organised. Finally, in July, EFS President François Toujas took part in the first French-Brazilian conference together with French Minister of Health and Social Affairs Marisol Touraine and the Brazilian Health Minister.

In Africa

The conference of the French society of blood transfusion, which took place in Montpellier in September 2015, welcomed several representatives from French-speaking Africa to discuss current partnerships and future needs.

A cooperation agreement signed in 2014 with Senegal led to EFS's participation in discussions regarding the construction of a regional blood transfusion centre in the north-west of the country (Louga). This facility is part of a national programme aimed at reducing infant mortality. This partnership is part of a cooperative effort between the French Development Agency, the French Embassy, EFS, and Senegal's National Blood Transfusion Centre.

In Morocco, EFS continued to provide technical assistance to help launch HLA laboratory testing and validate procedures and experimental protocols. In January, EFS renewed its agreement with Tunisia during the Scientific Day event hosted by the National blood transfusion centre.

Cooperation with Cameroon took the form of partnerships with the National Blood Transfusion Programme and technical assistance to help launch the health voucher system with support from the French Development Agency.

Finally, EFS hosted three trainees from Burkina Faso.

To Find Out More

Blood Components and their uses

Blood is a living tissue made up of cells and includes three major components: red blood cells, platelets, and plasma. Each element has its own special characteristics and plays a specific role. Labile blood products (LBPs) come from donated blood and are meant to be administered to patients via a transfusion.

BLOOD PRODUCTS

Red blood cells, platelets, and plasma are some of the blood products prepared by EFS.

Red blood cells

Also referred to as erythrocytes, red blood cells transport oxygen from the lungs to other tissues in the body. These days, whole blood transfusions are replaced by transfusions of red blood cell concentrates. Red blood concentrates are made from whole blood units and obtained through centrifugation. The resulting product is then systematically filtered to remove white blood cells (leucocyte depletion). Red blood cells can last for up to forty-two days and must be stored between 2° C and 6° C by law.

Platelets

Platelets are cell fragments that help prevent or stop bleeding. It is possible to produce platelet concentrates using several blood donations (original procedure). Nowadays, such concentrates can also be made by collecting platelets from a single donor through apheresis. Collection is done using a machine that puts the donor's blood through a centrifuge to remove a portion of the platelets, and then returns the platelet-depleted blood to the donor. This technique, called apheresis, makes it possible to remove enough platelets from a single donor to treat a patient. The donor's platelets regenerate quickly. Platelet concentrates can last for five days with constant agitation and when stored at 20° C to 24 °C.

Plasma

Plasma represents 55% of total blood volume, or around two to three litres (out of the five litres contained in the human body). Plasma is 90% water and contains over a hundred proteins (including 60% albumin) that serve a variety of purposes and are needed for the body to function properly. Nowadays, plasma is mostly collected via apheresis. The process is relatively similar to platelet donation. Once the plasma has been removed, the

remaining blood is then returned to the donor. Plasma can also be obtained by processing whole blood donations in a centrifuge. There are two types of plasma. One is called "therapeutic", which means it will be used in transfusions, while the other is called a "starting material". This type of plasma is used to produce plasma-derived medicinal products.

"Therapeutic" plasma

As of the end of 2014, EFS only produces two types of therapeutic plasma to meet the needs of patients:

- Plasma pathogen-reduced with amotosalen (psoralen S-59) and UVA light. Amotosalen destroys viral DNA and RNA (ribonucleic acid). The pathogen reduction method for plasma includes several successive steps. Residual amotosalen and its degradation products are filtered from the plasma using a filter designed to adsorb them.
- Quarantine plasma. Quarantine involves storing the plasma bag for at least sixty days. After this period, any viruses that might be present in very small quantities in the blood of the donor become detectable through screening. In fact, there is a so-called "window" period following infection during which a virus, even if it is present in the blood, cannot be detected through testing. After the sixty-first day following their initial donation, donors are invited to donate again (whole blood, platelets, or plasma). Depending on the test results, this second donation shows that the first donation is safe to use, after which the bag is released and distributed to health establishments.

"Starting Material" Plasma

Plasma can also be fractionated. Fractionation isolates and purifies specific proteins, including albumin, coagulation factors, and immunoglobulins, that are of major therapeutic value. These blood derivatives are called stable blood products, or plasma-derived medicinal products. They are used to treat hereditary or acquired immune deficiencies or administered in response to certain pathological or surgical conditions.

The number of prescriptions for coagulation factors and albumin have remained stable, while the demand for immunoglobulins has increased sharply. Immunoglobulins are the main treatment for patients suffering from primary or secondary immune deficiency. They allow patients to rebuild the defences they no longer have or to rebalance their immune systems. Immunoglobulins are also used for patients undergoing chemotherapy. The production of plasma-derived medicinal products is carried out by the French Fractionation and Biotechnologies Laboratory (LFB).

USES OF BLOOD PRODUCTS

Blood products are indicated for two major reasons: haemorrhages as well as cancers and blood disorders.

Cancers and Blood Disorders

Cancer (including leukaemia and lymphoma)

Leukaemia is often associated with a lack of blood cells, which are produced in the bone marrow. In addition, chemotherapy, which is used to treat cancer, destroys these same bone marrow cells. To mitigate insufficient production and any resulting toxic effects, patients receive significant amounts of platelet and red blood cell transfusions.

Thalassaemia

Thalassaemia is a hereditary disease that causes anemia. In its severe form, thalassaemia requires patients to receive transfusions throughout their lives.

Sickle-Cell Disease

Sickle-cell disease is a hereditary disease that affects 400 newborns every year in France. The condition is characterised by fragile, sickle-shaped red blood cells that break down quickly, and create blockages in blood vessels causing vaso-occlusive crises.

Haemorrhages

Obstetrics

Haemorrhaging can occur during childbirth and requires significant quantities of blood products to be administered immediately. These blood products must be available within 30 minutes, which is a determining factor in the placement of maternity ward blood banks.

Surgery

Haemorrhaging can occur during a surgery or after a trauma. In such cases, the patient must be treated with a transfusion of red blood cells. The transfusion can either be planned or administered under emergency circumstances. In the latter, if the patient has lost a large amount of blood, a transfusion of plasma and platelets is sometimes necessary to promote coagulation and stop bleeding.

Financial Data

INCOME STATEMENT

€K	2015	2014	2015 vs. 2014	
			€K	%
Operating revenues	941,347	930,841	+ 10,506	+ 1.1%
Operating expenses	948,202	932,809	+ 15,393	+ 1.7%
Operating results	- 6,854	- 1,967	- 4,887	-
Non-operating revenues and expenses	- 176	- 739	+ 563	-
Extraordinary profit or loss	- 1,508	- 8,715	+ 7,207	-
Employee profit sharing	3,140	3,108	+ 32	-
Corporate taxes	- 14,499	- 14,845	+ 346	-
Net accounting results	2,845	442	+ 2,403	-

Operating Results

Operating results are -€6.9 M. They have decreased by €4.9 M over 2014. This change is related to the €10.5 M increase in operating revenues and the €15.4 M increase in operating expenses.

Non-Operating Revenues and Expenses

In 2015, EFS's non-operating revenues and expenses equalled -€0.2 M, which represents a €0.6 M increase compared to 2014.

Extraordinary Profit or Loss

In 2015, EFS's extraordinary profit or loss (- €1.5 M) is up €7.2 M compared to 2014 due to the slowdown in allocations to reserves for transfusion-related litigations.

Analysis of Income Tax and Similar Payments

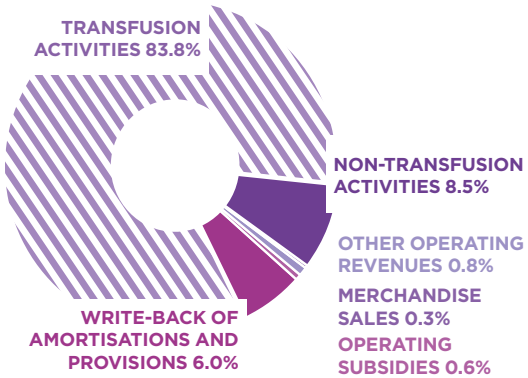
The research tax credit for 2015 equals €4.1 M.
The employment and competitiveness tax credit is €10.2 M.
EFS is not subject to corporate taxes for 2015 due to a negative fiscal result.

Profit Sharing

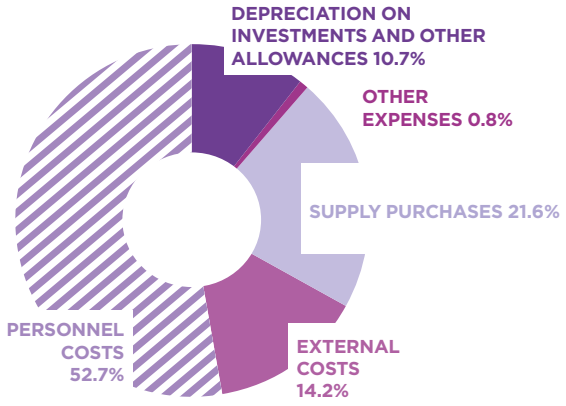
Profit sharing expenses were recorded at €3.1 M in 2015. This figure is stable compared to 2014.

OPERATING REVENUES AND EXPENSES

REVENUES - OPERATING REVENUES EQUAL €941.3 M



EXPENSES - OPERATING EXPENSES EQUAL €948.2 M



EFS Investments

The total amount of tangible and intangible investments from 2015 is €31.9 M, i.e. 3.7% of EFS's turnover. The investments can be broken down by type as follows:
- **intangible assets, €3.6 M,**
- **tangible assets, €28.4 M.**

STATEMENT OF ASSETS AS OF 31 DECEMBER 2015

Assets	Gross value	Amortisations and/or provisions	31/12/2015	31/12/2014
Intangible assets				
Preliminary costs				
Research and development costs				
Licenses, patents, and similar rights	64,065,836	52,556,753	11,509,083	13,498,307
Goodwill	442,120		442,120	442,120
Other intangible assets	867,514	19,361	848,154	265,293
Advance payments and down payments received on assets				
Tangible assets				
Land	14,939,666	1,120,839	13,818,827	12,280,116
Buildings	367,273,876	221,296,026	145,977,849	127,500,945
Mechanical and electrical systems	231,750,095	161,898,327	69,851,768	73,958,386
Other tangible assets	67,336,090	56,588,527	10,747,563	12,465,755
Pending assets	6,540,074		6,540,074	31,790,116
Advance payments and down payments	2,820		2,820	22,423
Financial assets				
Investments evaluated by equity method				
Other investments	5,179,905	520,000	4,659,905	4,789,905
Investment-related receivables				
Other long-term investments	16,200		16,200	16,166
Loans	15,646,828	23,557	15,623,271	14,607,646
Other financial assets	2,400,603	13,755	2,386,848	1,604,461
CAPITAL ASSETS	776,461,627	494,037,146	282,424,481	293,241,643
Inventory and liabilities				
Raw materials and supply	32,587,999	412,486	32,175,512	32,335,722
Work in progress for production of goods	15,492,318	7,860,205	7,632,114	6,911,207
Work in progress for services				
Intermediate and finished products	85,619,649	50,318,208	35,301,440	34,463,866
Merchandise	1,175,950		1,175,950	798,572
Advance payments and down payments on orders	284,260		284,260	317,562
Accounts receivable				
Trade accounts receivable	158,519,265	3,649,904	154,869,361	159,247,666
Other accounts receivable	51,068,814	3,619,916	47,448,899	42,432,114
Subscribed capital called but not paid				
Sundry				
Marketable securities	32,133,515		32,133,515	30,083,852
Cash balances	33,747,403		33,747,403	30,907,942
Accrued income and prepaid expenses				
Prepayments	6,155,237		6,155,237	5,222,171
CURRENT ASSETS	416,784,410	65,860,719	350,923,691	342,720,679
Expenses to be distributed across several fiscal years				
Premiums on redemption of debentures				
Conversion rate adjustment – assets	1,604		1,604	8,578
GRAND TOTAL	**1,193,247,640**	**559,897,865**	**633,349,775**	**635,970,900**

STATEMENT OF LIABILITIES AS OF 31 DECEMBER 2015

Liabilities	31/12/2015	31/12/2014
Share capital	55,751,195	54,787,429
Issue, merger and acquisition premiums		
Revaluation reserves		
Legal reserve		
Statutory reserve		
Regulatory reserve		
Other reserves	154,742,692	154,742,691
Carried forward	78,881,980	78,440,286
Earnings for the fiscal year	2,845,300	441,692
Investment subsidies	30,626,505	33,447,591
Regulated provisions		
OWNERS' EQUITY	322,847,670	321,859,692
Proceeds from non-voting shares		
Conditional advances		
OTHER PRIVATE FUNDS		
Provisions for liabilities	27,336,166	23,883,237
Provisions for expenses	60,142,222	59,055,934
PROVISIONS FOR LIABILITIES AND EXPENSES	87,478,388	82,939,172
Financial debt		
Bond loans		
Other bond loans		
Loans and debt from credit institutions	20,103,177	24,809,498
Sundry loans and financial debts	129,589	129,588
Advance payments and down payments received on orders in progress		
Operating debts		
Supplier debts	110,891,873	108,941,560
Fiscal debts	73,748,951	72,011,033
Sundry debts		
Debts on assets	13,465,296	20,189,919
Other debts	1,881,316	3,007,514
Accrued income and prepaid expenses		
Deferred revenue	2,803,454	2,082,921
DEBTS	223,023,655	231,172,036
Conversion rate adjustment – liabilities	62	
GRAND TOTAL	**633,349,775**	**635,970,900**

Glossary

ABM	French Biomedicines Agency (Agence de la biomédecine)
ABO	Blood type classification system
AFD	French Development Agency
A-FFP	Apheresis Fresh frozen plasma
ANSM	French National Agency for Medicines and Health Products Safety
APC	Apheresis platelet concentrates
ARS	Regional Health Agency (Agence régionale de santé)
ATMP	Advanced Therapy Medicinal Product
Aviesan	French National Alliance for Health and Life Sciences (Alliance nationale pour les sciences de la vie et de la santé)
B	Biomedical analysis value unit, according to the nomenclature of the French Social Security System
BAL	Biomedical analysis laboratory
BHN	Non-listed biomedical analysis service according the nomenclature of the French Social Security System (acte de biologie hors nomenclature)
BPTC	Best practices regarding the processing, storage, transport, distribution and transfer of tissues and cell therapy preparations
BTC	Blood Transfusion Centre
CBU	Cord blood unit
CCC	Central Corporate Committee
CDI	Permanent contract (contrat à durée indéterminée)
CD-P-TS	European Committee on Blood Transfusion
CDS	Healthcare centre (centre de santé)
CE	European conformity marking
CFDT	French Democratic Confederation of Labour (Confédération française démocratique du travail)
CFE-CGC	French Confederation of Management – General Confederation of Executives (Confédération française de l'encadrement – Confédération générale des cadres)
CFTC	French Confederation of Christian Workers (Confédération française des travailleurs chrétiens)
CGEFI	General economic and financial control (Contrôle général économique et financier)
CGT	French General Confederation of Labour (Confédération générale du travail)
CHSCT	Hygiene, Safety, and Working Conditions Committee (Comité d'hygiène, de sécurité et des conditions de travail)
CHU	University Hospital (centre hospitalier universitaire)
CJD	Creutzfeldt-Jakob disease
Cnam	French National Health Insurance Agency (Caisse nationale d'assurance maladie)
CNAMTS	French National Health Insurance Agency for Wage Earners (Caisse nationale d'assurance maladie des travailleurs salariés)
Cofrac	French Accreditation Committee (Comité français d'accréditation)
Comex	Executive Committee (Comité exécutif)
COP	Performance and Objectives Contract (Contrat d'objectifs et de performance)
CRTS	Regional Blood Transfusion Centre
DAR	Donors Adverse Reactions
DARQ	Regulatory Affairs and Quality Direction (Direction des affaires réglementaires et de la qualité)
DB	Budget Directorate (Direction du budget—Ministry of Finances and the Economy)
DC	Directors' Committee
DGCCRF	Competition, consumption, and Anti-Fraud General Directorate (Direction générale de la concurrence, de la consommation et de la répression des fraudes—Ministry of Finances and the Economy)
DGE	General Directorate of Corporations (Direction générale des entreprises—Ministry of the Economy, Industry, and Digital Technology)
DGESIP	General Directorate for Higher Education and Professional Development (Direction générale pour l'enseignement supérieur et l'insertion professionnelle—Ministry of Research and Higher Education)
DGOS	General Directorate for Healthcare Services (Direction générale de l'offre de soins—Ministry of Health and Social Affairs)
DGRI	General Directorate for Research and Innovation (Direction générale de la recherche et de l'innovation—Ministry of Research and Higher Education)
DGS	General Directorate of Health (Direction générale de la santé—Ministry of Health and Social Affairs)
DSS	Social Security Directorate (Direction de la Sécurité sociale—Ministry of Health and Social Affairs)
DLI	Donor lymphocytes infusion
DNA	Deoxyribonucleic acid
DRVI	Direction of Research and Technology Transfer (Direction de la recherche et de la valorisation de l'innovation)
DS	Donation Screening

TO FIND OUT MORE

EB	Executive Board
EBA	European Blood Alliance
EBMT	European Group for Blood and Marrow Transplantation
EC	Establishment Committee
EIH	Erythrocyte immunohaematology
EMA	European Medicines Agency
ETS	EFS Regional Establishment
FBMTR	French bone marrow transplantation registry
FCBN	French Cord Blood Network
FFDSB	French Voluntary Blood Donors' Association (Fédération Française pour le Don de Sang Bénévole)
FFP-IA	Fresh frozen plasma treated with amotosalen
FHF	French hospital federation
FO	Workers Force Trade Union (Force ouvrière)
FTE	Full-time equivalent
GMP	Good Manufacturing Practices
HAS	High Authority of Health (Haute Autorité de santé)
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HEV	Hepatitis E virus
HIV	Human immunodeficiency virus (AIDS virus)
HLA	Human leucocyte antigen
HNA	Human neutrophil antigen
HPA	Human platelet antigen
HSC	Hematopoietic stem cells
IAS	Irregular antibody screening
IFBDO	International Federation of Blood Donor Organizations (Fédération Internationale des Organisations de Donneurs de Sang)
IFRC	International Federation of the Red Cross and Red Crescent (Fédération internationale des sociétés de la Croix-Rouge et du Croissant-Rouge)
IH	Immunohaematology
Inserm	National Institute of Health and Medical Research (Institut national de la santé et de la recherche médicale)
IP	Intellectual property
ISBT	International Society of Blood Transfusion
ISO	International Organization for Standardization
IVDMD	In vitro diagnostic medical device
JACIE	Joint Accreditation Committee ISCT and EBMT
LBP	Labile blood product
LD-APC	Leucocyte-depleted apheresis platelet concentrates
LD-PPC	Leucocyte-depleted pooled platelet concentrate
LD-RBCC	Leucocyte-depleted red blood cell concentrates
LFB	French Fractionation and Biotechnologies Laboratory (Laboratoire français du Fractionnement et des Biotechnologies)
MC	Mononuclear cells
MTI-PP	Hospital exemption - Advanced Therapy Medicinal Product (Médicament de thérapie innovante préparé ponctuellement)
NAEC	National Advisory Ethics Committee (Comité consultatif national d'éthique)
NAT	Nucleic acid testing
NBTP	National Blood Transfusion Programme
NC	Non-compliant
PC	Platelet concentrates
PCE	Extracorporeal photochemotherapy
PCT	Patent Cooperation Treaty
PDMP	Plasma-derived medicinal product
PDN	Post-donation notification
PLTR	Products for use in laboratories, teaching, and research
PPC	Pooled platelet concentrate
pSup	Upper limit of the confidence interval
QC	Quality control
Q-FFP	Quarantined secured fresh frozen plasma
RAR	Recipient adverse reactions
RBCC	Red blood cell concentrates
RNA	Ribonucleic acid
RPU	Reagent production unit
SAE	Serious event in the transfusion chain
SD	Solvent/detergent
SDAR	Serious donor adverse reactions
SD-FFP	Solvent/detergent-treated fresh frozen plasma
SNTS	National Blood Transfusion Union (Syndicat National de la Transfusion Sanguine)
STPO	Scientific and Technological Public Organisation
SUD	Solidaires Unitaires Démocratiques (French group of trade unions)
TACO	Transfusion Associated Circulatory Overload
TnBP	Tri(n-butyl)phosphate
TRALI	Transfusion Related Acute Lung Injury
TTBI	Transfusion-transmitted bacterial infection
Unsa	National Union of Autonomous Trade Unions (Union syndicale des syndicats autonomes)
UTS-UGTG	Regional Solidarity Unit—General union of workers of Guadeloupe (Unité territoriale de solidarité—Union générale des travailleurs de Guadeloupe)
VBMD	Voluntary bone marrow donation
WBC	White blood cell
WBDD	World Blood Donor Day
WHO	World Health Organization
YIC	Young innovative company

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