CHAPTER 6
Donor vigilance and hemovigilance

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Introduction

Reporting and learning systems in general

The ability to learn from adverse events and near misses is a cornerstone for improving safety in different high-risk areas such as the aviation and oil industries. Commercial passenger aviation has become extremely safe partly due to extensive use of reporting and learning systems (RLS).1

A system for reporting adverse events and learning from these events is a general requirement in all quality work today, and a written procedure (standard operating procedure [SOP]) for reporting deviations is one of six required SOPs in ISO 9001 standards.

In healthcare, it has been more difficult to prove that RLS have improved safety.2 A World Health Organization (WHO) guideline on adverse event reporting and learning systems3 emphasized that the effectiveness of an adverse event reporting system is measured not only by accurate collection and analysis of data, but also by its use for making recommendations that improve patient safety. The guideline outlined the following core concepts:

- The fundamental role of patient safety reporting systems is to enhance patient safety by learning from failures of the healthcare system.
- Reporting must be safe. Individuals who report incidents must not be punished or suffer other ill effects from reporting.
- Reporting is of value only if it leads to a constructive response. At a minimum, this entails feedback of findings from data analysis. Ideally, it also includes recommendations for changes in healthcare procedures and systems.
- Meaningful analysis, learning, and dissemination of lessons learned require expertise and other human and financial resources. The agency that receives reports must be capable of disseminating information, making recommendations for changes, and informing the development of solutions.

When Canada prepared for a reporting and learning system in Canadian healthcare, the Canadian Patient Safety Institute (CPSI) performed a review of RLS to better understand such systems.4 The review found that for RLS to be successful, healthcare workers need incentives to use the systems and these incentives must be stronger than the disadvantages. The systems should be voluntary and confidential. They should be transparent, but at the same time protect the reporter. The users should be invited to take part in the development and maintenance of the system. The system should prove to be able to prevent, detect, and reduce the effect of adverse events due to bad planning, bad practice, or other unfavorable circumstances.

In well-functioning RLS, one commonly found that:

- Adverse events and near misses were analyzed by an independent organization with enough competence;
- Feedback to the reporter was given in a timely manner;
- Suggestions on how to improve the system were given;
- The healthcare system is open for suggestions for system improvement; and
- The system is nonpunitive.

Reporting and learning systems in blood transfusion

The term hemovigilance has become widely used over the past decade to describe the systematic surveillance of adverse transfusion reactions and events, encompassing the whole transfusion chain and aimed at improving the safety of the transfusion process, from donor to recipient, or “vein to vein.”5,6 The term was coined in France in the early 1990s, has been developed and adopted internationally, and is now an integral part of transfusion practice. Today it is unthinkable not to have a system for reporting deviations in transfusion medicine and to use such reports in the ongoing quality improvement work. The hemovigilance system should be an integral part of the risk management or clinical governance framework of the institution.

The concepts mentioned above for RLS are directly relevant to hemovigilance systems and are applicable both at the hospital level and nationally. The scope of the system must be clear to reporters. The system should be robust, easily understood, and user friendly. Collection of complete data on adverse reactions and events requires local awareness and vigilance. There must be a “reporting and learning culture” within which events are viewed as learning opportunities. Such a culture takes time to develop, and it should be developed within a framework of professional competence and accountability.

At the regional or national level, the hemovigilance scheme must be seen as impartial, independent, supportive, and professionally credible. Data should be validated, analyzed, and reported within a predictable time frame, and published in a format that can be used to support education and training. Active involvement and “ownership” by professional bodies will help to ensure that recommendations are incorporated into clinical practice.
**History and development**

Pharmacovigilance was the first surveillance system in the arena of health care, covering medicinal products of all kinds. Hemovigilance, as a separate surveillance system, was implemented in France in 1994, as required by the updated French regulation on blood in a response to a “blood scandal.” Hemovigilance has been defined as “a set of surveillance procedures covering the whole transfusion chain from the collection of blood and its components to the follow-up of its recipients, intended to collect and assess information on unexpected or undesirable effects resulting from the therapeutic use of labile blood products, and to prevent their occurrence and recurrence.”

In the United Kingdom, anticipation of forthcoming European legislation, together with concerns regarding transfusion safety, led to the establishment of the SHOT (Serious Hazards of Transfusion) scheme in 1996. Hemovigilance systems at the regional or national level were seen in numerous countries both within Europe and elsewhere by the end of the 1990s (Table 6.1) and have continued to develop thereafter. According to data reported to WHO, in 2008 a national hemovigilance system existed in 57 of 164 countries that supplied data, and 24 were preparing a system. As might be expected, the percentage is highest in developed countries: a national hemovigilance system had been implemented in 13% of low-income countries, 30% of middle-income countries, and 78% of high-income countries providing data. At the other end of the spectrum, the same survey showed that in 39 countries donated blood is not routinely tested for transfusion-transmissible infections.

The initiative to start hemovigilance as well as the governance of systems varies considerably. Several well-known systems were initiated by professional societies and were subsequently modified to meet new legislative requirements (see under the “Legal Framework” section). Thus, in Norway, a voluntary, anonymous reporting system for complications related to blood donation or blood transfusion was started in 2004 by the Norwegian Society for Immunology and Transfusion Medicine. It received reports on mild, moderate, and severe complications. From 2007, when the EU directive was implemented in Norwegian law, this system has continued, but it has to report serious transfusion reactions, serious donor reactions and serious near misses to the Directorate of Health (receives hundreds of reports yearly, only approximately 10 reports are serious enough to be sent on to the Directorate of Health.

Within hemovigilance systems, the importance of national definitions has been recognized, but inevitably there was a lack of commonality of definitions, terminology, structure, and scope of reporting. In the course of development, variable strategies were followed to address organizational difficulties, need for funding, mandates, training, and so on.

The development of hemovigilance systems was primarily driven by a desire for early detection of harm to patients and for transparency about safety of the blood components. The Danish system was early to emphasize the importance of reporting donor adverse reactions.

Descriptions of several more national hemovigilance systems can be found on the International Haemovigilance Network (IHN) website (www.ihn-org.com).

**Hemovigilance working methods**

**Investigations and assessment**

As part of clinical care, transfusion adverse reactions should be investigated to establish the diagnosis and guide future treatment of the patient. Where there may be implications for other components (e.g., from the same donor), the producer must be informed. Reporting to the hemovigilance system should be accompanied by sufficient information to allow the assessors to verify the type of reported reaction. Commonly also, reports are rated for severity as well as for “imputability,” the likelihood with which a reaction can be attributed to the transfused component.

For donor complications, such as a hematoma or a vasovagal reaction, this is usually no problem. For transfusion reactions, it may be obvious as in a hemolytic transfusion reaction due to the transfusion of incorrect blood. It may, however, be difficult when a severely ill patient on antibiotics and fluid treatment experiences fever, a rash, or fluid overload. Similarly, if a blood donor suffers a cerebrovascular accident less than 24 hours after an uncomplicated blood donation, the possibility of a causal relation is difficult to prove or to exclude.

**Root cause analysis**

As discussed in the introduction, the objective of reporting to a centralized system is to derive recommendations for the

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**Table 6.1 Examples of Hemovigilance Systems**

<table>
<thead>
<tr>
<th>Country</th>
<th>Date of Initiation, Scope of Reporting (Voluntary at inception Unless Otherwise Mentioned)</th>
<th>Governance</th>
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</thead>
<tbody>
<tr>
<td>Japan</td>
<td>1993: Transfusion-associated adverse reactions and infectious diseases</td>
<td>Japanese Red Cross Society</td>
</tr>
<tr>
<td>France</td>
<td>1994: Mandatory system created by national legislation; all severity levels</td>
<td>Inspectorate for Healthcare Products (currently: Agence Nationale de Sécurité du Médicament et des Produits de Santé)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1996: Serious Hazards of Transfusion (SHOT); serious reports</td>
<td>Professional societies</td>
</tr>
<tr>
<td>Denmark</td>
<td>1999: Danish Registration of Transfusion Accidents (DART): modeled on SHOT</td>
<td>Society for Clinical Immunology</td>
</tr>
<tr>
<td>South Africa</td>
<td>2000: All severity levels; donor reactions included from 2010</td>
<td>South African National Blood Service</td>
</tr>
<tr>
<td>Netherlands</td>
<td>2002: Transfusion and transplantation reactions in patients (TRIP); “all”</td>
<td>Professional societies</td>
</tr>
<tr>
<td>New Zealand</td>
<td>2005: All severity levels</td>
<td>New Zealand Blood Service</td>
</tr>
<tr>
<td>United States</td>
<td>2006: National Healthcare Safety Network, Biovigilance reporting system. Gradual increase of participation; incorporated donor vigilance from inception</td>
<td>US Biovigilance Network (public-private collaboration between the US Department of Health and Human Services, including the Centers for Disease Control and Prevention, and organizations involved in blood collection, transfusion, tissue and organ transplantation, and cellular therapies)</td>
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improvement of practice and prevention of future errors and incidents. Underlying a mistake at the moment of transfusion may be several latent causes, such as lack of training, badly designed IT processes, or understaffing. Facilities should assess such causes and supply sufficient information to the hemovigilance system to allow analysis of recurrent problems and weak ”links” in the transfusion chain.12,13 A number of methods for analyzing and classifying contributing causes have been developed;12 a practical toolkit based on techniques recommended by the (former) UK National Patient Safety Agency is available on the SHOT website (www.shotuk.org).14

Risk assessment
An in-depth root cause analysis takes considerable time and effort,13,15 so this is usually performed for selected reports of errors or incidents in the transfusion chain. When an event has occurred, assessment of the potential for harm (even if the worst did not happen) and the likelihood of recurrence can be combined to support prioritization of a particular problem for detailed analysis and preventive measures. A risk matrix based on this principle has been developed, following similar examples that are in use in aviation and high-risk industries, for use in the vigilance of tissues and cells.16 In hemovigilance, such a tool has not been widely implemented.

A prospective risk assessment of the transfusion chain can indicate possible improvement measures, even if no error has been reported (yet). For instance, analysis of the process of blood transfusion in pediatric emergency using the Healthcare Failure Mode and Effect Analysis (HFMEA) indicated that training and audit could be the main tools for improvement.17,18 Another method for prospective analysis is the Bowtie method developed by the UK Civil Aviation Authority.19,20

Hemovigilance report
In order for learning and improvement to take place, the collected information must be made available to the professionals of the transfusion chain. Recommendations for improvement can be made, and ideally these will be incorporated in practice through changes in blood donor care, the production of blood components, recommended practices laid down in transfusion guidelines, or other mechanisms. Through the ongoing reporting, the effects of measures can be evaluated and trends can be tracked. Where possible and relevant, peer-reviewed publication should also be pursued to strengthen rigor and ensure international accessibility of the results for incorporation in meta-analyses.

Rapid alerts
Rapid spread of information about new risks is difficult to manage but potentially very useful. Examples can be problems with disposables or reagents that are discovered in one blood bank and where it may take some time before it is detected in other blood banks. Before an alert is circulated, the finding must be verified; the manufacturer must be informed, and relevant advice or actions in response to the notification included in the alert.

Things to consider when establishing a hemovigilance system
In practice, a reporting and learning system like a hemovigilance system may be organized in several ways. It may be local, regional, or national. It may be voluntary or compulsory. It may be sanction-free or have the possibility of sanctions. It may be anonymous. It may report only serious complications or include mild or moderate complications. It may include near misses. It may be passive or active (see the ”Passive or Active Systems” subsection). It is important to identify the goals of the system before deciding how it should be organized. The available resources should be taken into account.

National, regional, or local systems
Transfusion reactions vary in frequency. Because some are rare, such as transfusion-associated acute lung injury (TRALI), graft-versus-host disease (GvHD), and posttransfusion purpura (PTP), a national system is most often required to get big enough numbers to monitor the incidence and to measure improvements after action has been taken to reduce the incidence further. Other transfusion reactions like FNHTR and mild allergic reactions can be monitored on a regional or local level.

Voluntary or compulsory systems
The Canadian Patient Safety Institute (CPSI) found that voluntary systems were best, and some established hemovigilance systems, like SHOT and the Danish Registration of Transfusion Accidents (DART), are voluntary. When establishing a system on a voluntary basis, some enthusiasts will start using the system and the less enthusiastic will follow. Voluntary systems are often started by the professions or by scientific bodies, and participants may therefore feel more ownership and, hence, more willingness to participate. Compulsory systems are more often initiated by governments and supported by laws or directives.

Anonymous, confidential, and nonpunitive systems
Both WHO and CPSI recommend nonpunitive systems. Many adverse events and near misses involves human error to some extent.21 To encourage reporting and maximize learning from such cases, the hemovigilance system should be nonpunitive. This should not mean that if you make a mistake and then report it in an RLS, you are guaranteed not to suffer any sanctions. The adverse event or near miss will most probably also be detected in other ways, by other staff or by the patient, and complaints from patients and the like will have to be acted on. Staff are always accountable for their actions, and professional competence is of the highest importance, but competence should be assessed in other ways than by reports in an RLS.

Anonymous reporting may be a way to ensure potential reporters that the reporting is nonpunitive. At the local level anonymous reporting is often an illusion, and at the regional or national level it may be irrelevant, but anonymous reporting sends a signal that the person involved is not important. We know that people make mistakes, and it is the system in which they work that is our focus for improvement.21

Confidentiality is always important. When reports are used for learning purposes, it is important that details that could be used to identify people or places are removed or changed.

What should be reported?
Legislation often only requires reporting of serious adverse events. In theory, one may have several less serious adverse events, or near misses, before one serious adverse event, and it is better to analyze these and ideally prevent the more serious event. The number of reports the hemovigilance system will receive will, however, increase dramatically if all adverse events and near misses are reported. The resources available must therefore be taken into consideration. In an ideal system, all adverse reactions and adverse events will be reported, including near misses. The number of reports increases as the benefits of reporting are seen, whereas the
number of serious adverse reactions decreases due to quality improvement because of learning from the reports.

In pharmacovigilance, the focus is on reporting only new or very serious complications, and in reporting systems for cells and tissues the focus is on product-related problems. Hemovigilence usually has a wider scope and in this respect may be more similar to a quality registry than a traditional RLS.

**Background data**

For understanding and analysis of the hemovigilence data from a country or region, it is useful or necessary to have some background data, such as the age group and sex of a patient, and whether universal leukodepletion of blood components is in place. Background data should be limited to parameters that can be analyzed across organizations, regions, or countries because all registration takes time and effort. A frequent problem is that the numerator (e.g., the number of reactions in a particular category) is known, but the denominator (the total number of patients or donors in that group) is not. An example may be that vasovagal reactions are reported more frequently in young women, but if we do not know what proportion of donors are young females, this information has limited value.

Typical background data that are registered for reporting donor complications are the donors’ age and sex, the donation type (whole blood or apheresis), the date and time of donation, and if it was a first-time donation or not. Typical background data for transfusion reactions are patient age and sex, the indication for transfusion, department and/or ward, time from transfusion to reaction, and so on.

In certain cases, more background information may be useful, such as a female donor’s parity in cases of TRALI and the patient’s coronary status when transfusion-associated cardiac overload (TACO) or transfusion-associated dyspnea (TAD) is suspected. Usually, it is better to collect such data only when relevant. A rule of thumb may be “Record what you need to know, not what is nice to know.”

**Passive or active systems**

A passive system is a system where only the adverse events or near misses are reported to the system. In an active system, the fact that a transfusion (or blood donation) was uncomplicated is also reported. On a local level, active systems are preferable because underreporting is less likely. On a regional or national level, passive systems are sufficient. Active systems may also have drawbacks as the findings depend on when the active reporting takes place. If it takes place shortly after the transfusion, the reactions that come later may not be reported. This may include reactions occurring hours, days, or even weeks later. An example is delayed hemolytic transfusion reactions, which typically are detected some 10 days after the transfusion. Conversely, if active reporting takes place a long time after transfusion, the immediate but mild reactions that occurred may be forgotten. In donors, adverse reactions that occur while the blood donor still is present in the blood bank are fairly easy to capture, whereas some serious complications, like faints that occur after leaving the blood bank, may not be reported till the time of the next donation, if ever.

**Contact persons**

At the hospital level, there is a need for a point of contact for clinical staff to report reactions and adverse events. This may be a transfusion practitioner or safety officer, hematologist, transfusion medicine specialist, the blood transfusion laboratory, or a hospital blood bank manager. A national system will also benefit from having a designated contact person in the blood establishment(s) (a blood establishment, blood service, or blood operator is the organization responsible for collecting, processing, and testing blood and can be located in a hospital or outside the hospital). Depending on the situation in a country, these may be the same person. Responsibilities vary but may include teaching, assisting in investigation of adverse reactions and adverse events, and sending reports to the regional or national hemovigilence system.

**Cooperation with other reporting and learning systems, quality registers, and indicators**

When running a hemovigilence system, it is useful to be aware of other sources of information on transfusion safety. Reporting and learning systems in general use in health care may have relevant information. An example from Norway is that the hemovigilence system rarely receives reports of blood transfusion laboratories (hospital blood banks) issuing blood too late, whereas the general RLS has several reports from clinicians about this. Other useful information can be found by looking at patient safety indicators. Frequent ordering of blood during surgery, instead of before surgery, may be an indicator of poor ordering routines. This will probably not be picked up in a hemovigilence system, but it is useful information in quality improvement work. Large administrative databases and electronic health records are often the source for quality indicators and can also be used to study transfusion reactions.22

Cooperation with reporting and learning systems for cells and tissues and for organ transplantation may be useful as many problems are similar. Systems for vigilance relating to devices may have relevant information, and there is a need to ensure communication between these two areas.

**Plasma derivatives**

Plasma derivatives are covered by pharmacovigilance. Both blood banks and pharmacies may issue these products, and in some cases it may be useful to include these products in the hemovigilence system. An example is solvent detergent plasma that is blood group specific and may have similar complications to blood components; in many countries, it has been decided that it should be issued by the blood bank. If plasma derivatives are included in the hemovigilence system, an agreement between the different parties is strongly recommended.

**Approvals and registrations**

In some countries, approval for data registration is required, under data protection legislation, by ethical committees and the like. There may be specific requirements for electronic reporting. Different types of data may have different requirements just as different countries may have different requirements. Relevant laws and regulations should be identified before establishing a hemovigilence system.

**New or not previously recognized side effects of blood donation or transfusion**

Sometimes, donors or patients report complications that are not one of the known complications. This may be difficult to handle, and often the conclusion will be that it was not related to the donation or the transfusion. It may, however, be useful to collect the data because it can lead to the detection of complications that we hitherto were not aware of.
Other considerations

Patient blood management is an important topic. Monitoring over- and undertransfusion may be considered a relevant domain of hemovigilance. It is important to decide if this falls within the scope of your system.

Similarly, it is necessary to consider if complications caused by blood from cell savers, re-infusion drains, and so on should be reported in the hemovigilance system.

International reporting and collaboration

The system should be able to report its results internationally to further analysis and learning on an international level. Currently, the EU, WHO, the Council of Europe, and the IHN (see the “International Hemovigilance Network” subsection) collect data yearly.

Variation in organization, working methods, and definitions is a problem when comparing data from different countries. A number of international organizations are relevant in this respect and play a role in promoting international collaboration and harmonization of hemovigilance activity.

International Hemovigilance Network (www.ihn-org.com)

Founded in 1998 (at first under the name of European Hemovigilance Network) as a nonprofit foundation, the objectives of the IHN are to promote and engage in:
- the exchange of information that is of importance among the members of the network;
- a swiftly functioning alarm system or warning system among members of the network;
- joint activities among the members of the network; and
- educational activities relating to hemovigilance.

The members of the network are the national or, in some cases where there is no national system, regional hemovigilance systems. From 2004, the IHN has worked on development of definitions for transfusion reactions as well as for complications of blood donation. As of 2015, the network has over 30 member systems.

The IHN hosts a database for the capture of aggregate data on transfusion adverse reactions, errors, and failures as well as donor adverse reactions: the International Surveillance Database for Transfusion Adverse Reactions and Events (ISTARE). Despite the limitations of comparisons owing to variations in definitions and working methods, the database allows national systems to anonymously compare their data to those of other member organizations.

International Society for Blood Transfusion (ISBT; www.isbtweb.org)

This international voluntary society has individual professionals as its members. Its first objective is to promote and to maintain a high level of ethical, medical, and scientific practice in blood transfusion medicine, science, and related therapies throughout the world. The hemovigilance working party, in which over 50 members participate, formally collaborates with the IHN in the process of developing tools and definitions (publicly available on the website under Working Parties → Hemovigilance → Definitions).

The present state of the IHN–ISBT hemovigilance definitions is as follows:
- Complications of blood donation: At the end of 2014, revised definitions for the surveillance of complications of blood donation were published, for the first time also in collaboration with the biovigilance working group of the AABB (formerly: American Association of Blood Banks). Further organizations have formally endorsed these definitions. This represents an important step forward in international hemovigilance collaboration.

- Infectious transfusion complications: Definitions and criteria for transfusion-transmitted infectious diseases are challenging to standardize—factors include the differences between the diseases and their epidemiology as well as different standards and methods of testing between countries. Work is being pursued by the ISBT transfusion-transmitted infectious diseases (TTID) working party in collaboration with the hemovigilance working party. To date, no international definitions have been adopted by the IHN or ISBT.
- Errors, failures, and incidents: A number of types of sentinel event have been defined by the ISBT and IHN. Nevertheless, the very term adverse event is used differently in different organizations, and notably the EU legislation defines serious adverse event differently from international pharmacovigilance legislation.
- Severity and imputability of transfusion reactions: Incorporated in the list of noninfectious transfusion reactions.
- Imputability of adverse reactions: Incorporated in the list of noninfectious transfusion reactions.

World Health Organization

WHO, which is in formal relations with ISBT on the subject of safe blood transfusion, has a department of blood safety that recently published an Aide-Memoire on implementing hemovigilance; a longer guidance document is in preparation. A strength of WHO is its direct links with governments and ministries of health. This can provide a strong impetus to initiate activities to implement hemovigilance and improve the safety of blood transfusion.

Within WHO, the cluster on patient safety has produced a taxonomy of terminology. At present, there are some discrepancies with other definitions (including the term adverse event). Collaboration of clusters at WHO level could potentially contribute to reconciling the terminology.

Council of Europe

The Council of Europe has 47 member states, of which 27 are also members of the European Union. It produces a guide with recommended standards for the preparation, testing, and transfusion of blood components. In this guide, both principles and standards for hemovigilance are described.

Legal framework

European hemovigilance and the EU Blood Directives

The key role of hemovigilance in blood transfusion safety is reflected in the EU Blood Directive 2002/98/EC.

This Directive of the European Parliament and of the Council sets standards of quality and safety for the collection, testing, processing, storage, and distribution of human blood and blood components. An entire section is dedicated to hemovigilance, and it encompasses traceability and notification of serious adverse events and reactions. The technical details are further laid down in the so-called daughter directives:
- 2004/33/EC (Directive on donations, donors, and blood components);
- 2005/61/EC (Directive on traceability and notification—hemovigilance); and
According to the Directives on blood, *hemovigilance* is defined as “a set of organized surveillance procedures relating to serious adverse or unexpected events or reactions in donors or recipients, and the epidemiologic follow-up of donors.” It is stated that it is important to introduce a set of organized surveillance procedures to collect and evaluate information on the adverse or unexpected events or reactions resulting from the collection of blood or blood components in order to prevent similar or equivalent events or reactions from occurring thereby improving the security of transfusion by adequate measures. To this end a common system of notification of serious adverse events and reactions . . . should be established in member states.

See Table 6.2 for definitions for serious adverse reactions and events.

The focus of these directives is ensuring a high standard of quality and safety of human blood and of blood components for the protection of human health. They lay down standards in the context of blood matters, including hemovigilance. It is important to understand that the European Treaty (the Treaty of Amsterdam, establishing the European Community) sets limits in Article 152 under the idea that the European Treaty (the Treaty of Amsterdam, establishing the European Community) sets limits in Article 152 that restrict the scope of European legislation to the products: the

<table>
<thead>
<tr>
<th>Table 6.2 Definitions (European Union) for Serious Adverse Reactions and Events</th>
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<tr>
<td>A serious adverse reaction is defined in the Directive as an unintended response in a donor or patient associated with the collection or transfusion of blood or blood components that is fatal, life-threatening, disabling, or incapacitating, or that results in, or prolongs, hospitalization or morbidity.</td>
</tr>
<tr>
<td>A serious adverse event is defined in the Directive as any untoward occurrence associated with the collection, testing, processing, storage, and distribution of blood and blood components that might lead to death or life-threatening, disabling, or incapacitating conditions for patients or that results in, or prolongs, hospitalization or morbidity.</td>
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</table>

Directives on blood apply to collection and testing of human blood and blood components, whatever their intended purpose, and their processing, storage, and distribution when intended for transfusion. The principle of subsidiarity allows other issues to be determined by individual EU member states, which may adopt regulations in addition to the provisions in the Blood Directives.

The current European legislation can therefore cover only the producers (the blood establishments) and to some extent the hospital blood banks (blood transfusion laboratories). However, the Directives do not apply to clinical activities, which are the exclusive responsibility of the individual member states. This obviously creates a complex situation in Europe with regard to hemovigilance systems. From the outset, it had been recognized that hemovigilance (including rapid alert) should encompass the whole blood chain from donor to recipient and vice versa, including both production and clinical use.

The SHOT reports had shown that harm to patients, although sometimes caused by an unsafe (chiefly, infected) blood component, is more often a consequence of physiological reactions or of errors—for instance, in the 2000–2001 annual report, 71.8% of submitted reports were of incorrect blood component transfused (IBCT) and 1% were of transfusion-transmitted infections.

When the mandatory submission of annual hemovigilance reports to the European Commission commenced (2007 data), the nonbinding guidance for member states allowed for the reporting of all types of serious adverse reactions and did not restrict it to cases where the blood component was unsafe.

Because the EU directive includes minimum requirements for reporting to the health authorities, all countries in the European Union have set up hemovigilance systems. These may be comprehensive, well-staffed, and well-funded, like in France, or just the bare minimum to fulfill the requirements of the directives. In some countries, voluntary hemovigilance systems had already been put in place.

**Figure 6.1** Summary of main findings and cumulative results from Annual SHOT report 2013. Source: SHOT, The 2013 annual SHOT report, 2014. Reproduced with permission of SHOT.
introduced when the EU directive came into force, and some countries therefore have two parallel systems: one voluntary, often anonymous and comprehensive run by the transfusion medicine community, and one small official system ensuring that the directive requirements are fulfilled.

Traceability
In the event of a transfusion reaction, in many cases it is necessary to trace back to the donor and investigate (e.g., does the donor have HLA antibodies?) Conversely, if a donor is found to have seroconverted, the recipients of earlier donations (tested with negative results for blood-transmissible diseases) need to be traced and tested for possible infection, if this could be clinically relevant. Traceability from donor to patient and back, the storing of data necessary to link a particular donor and donation to a particular recipient, is a prerequisite for these hemovigilance activities and is laid down in the EU directive (Table 6.3).

Although only basic data need to be retained for the 30 years specified for EU member states, it remains challenging in the face of hospital or blood establishment progression of IT technology. Of note in the legislative framework, the recommendation is that confirmation of the transfusion or of final disposal of a blood component should be obtained and recorded. In many hospitals, this is achieved using a paper form that is returned to the blood transfusion laboratory. Ideally, the confirmation of transfusion should be added to the component issue information in the laboratory computer system, enabling it to be stored electronically with the other traceability data. In the future, as electronic bedside computer systems, enabling it to be stored electronically should be added to the component issue information in the

<table>
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<tr>
<th>Table 6.3 Data to Be Retained for 30 Years in EU Member States (2005/61/EU)</th>
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<tr>
<td><strong>By Blood Establishments</strong></td>
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<tr>
<td>Blood establishment identification</td>
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<tr>
<td>Blood donor identification</td>
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<tr>
<td>Blood unit identification</td>
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<tr>
<td>Individual blood component identification</td>
</tr>
<tr>
<td>Date of collection (year/month/day)</td>
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<tr>
<td>Facilities to which blood units or blood components were distributed, or subsequent disposition</td>
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donor’s next attendance. If the component is still in date, it should be retrieved. If it has already been transfused, a risk-based decision should be taken about whether it is necessary to counsel and/or test the recipient.28

**Donor hemovigilance**
Systematic surveillance of the first part of the transfusion chain—the collection of blood from the donor—is an essential element of hemovigilance, and it aims to secure and improve the safety of both the donor and the recipient. Blood establishments (including organizations that collect plasma for the production of plasma-derived medicines, often referred to as source plasma) should register adverse events in whole blood and component donors, actions taken as a result, and the outcomes. These events may be adverse reactions or complications resulting from donation, or adverse events—errors, incidents, and failures—related to the selection and management of donors, which may directly harm the donor or influence the quality of the product, thereby potentially harming the recipient.

Collection of blood from donors for the provision of components for clinical use is most frequently performed in the form of whole blood donation. Automated collection using apheresis technology is also used for the collection of plasma, platelets, and red blood cells, depending on local or national factors and policies. The less common donations of granulocytes, as well as of lymphocytes or peripheral blood stem cells, are also collected by apheresis; space does not permit detailed discussion of vigilance relating to these procedures.

Provision of information about the risks of donation based on evidence from surveillance, together with good clinical management of any complications, indicates a high professional standard of the blood collection facility and its care of the well-being of the donors. This, in turn, will improve donor confidence and satisfaction, making it more likely that the donor will return, thus benefiting the national supply of blood.29

Although awareness of the complications of blood donation is probably as old as blood banking,30,31 in the last 20–20 years this has strengthened. A joint working group from the ISBT and IHN (then, the EHN) was established in 2005, and this led to the first proposed classification with a set of definitions of complications related to blood donation32 to form the basis for surveillance and international comparisons. A revision was concluded in 2014.33 It is hoped that the use of this classification will enable comparisons and collaborative work to add to the available evidence to support improvements in donor care and selection.

**Complications related to blood donation**
Data on the occurrence of these complications were not at first included in the hemovigilance systems, but they have been reported by blood establishments. Large studies have been published by single blood centers in the United States and other countries; comprehensive national data have now also been published (for Denmark,30 France, New Zealand, and other countries), and data collected by the IHN with the use of the 2008 definitions have been presented at several meetings (Table 6.4).

The rate of reported donor complications varies according to the severity and range of reactions included. Preliminary data registered according to the ISBT classification suggest that the overall rate of complications in collection center practice is in the order of approximately 1 per 100 donations. The observed rate is known to be highly dependent on the method of ascertaining the reaction: A study where donors were contacted by telephone following their donation36 elicited an overall rate of 36%.

Postdonation information (PDI)
The quality system of a blood establishment requires that if it later becomes known that the donor could have had an infection at the time of donation, the blood establishment should have a procedure for contacting the hospital to which the components manufactured from that donation were distributed. This might, for instance, be an illness with fever within 24 hours of donation, or if a blood test performed several weeks after the donation because of symptoms reveals a diagnosis of hepatitis B. Postdonation information in other cases refers to cases where the screening failed to elicit a cause for deferral and this is found out, perhaps at the donor’s next attendance. If the component is still in date, it should...
### Table 6.4 Occurrence of Complications Related to Blood Donation (Examples)

<table>
<thead>
<tr>
<th>Study</th>
<th>Donations (Whole Blood Donations Unless Otherwise Specified; Comments)</th>
<th>Donor Complications (Reported Cases per 100,000 Donations)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Vasovagal Reaction</td>
</tr>
<tr>
<td>Newman(^{38})</td>
<td>1000 (interview 3 weeks after donation)</td>
<td>6400</td>
</tr>
<tr>
<td>Newman(^{18})</td>
<td>1000 (information obtained at donation)</td>
<td>20</td>
</tr>
<tr>
<td>Sorensen(^{35})</td>
<td>2,575,246 (national register of serious complications)</td>
<td>7</td>
</tr>
<tr>
<td>Sorensen(^{35})</td>
<td>41,274 (county register all complications)</td>
<td>478</td>
</tr>
<tr>
<td>Ounnougue(^{41})</td>
<td>2.6 million (national data, France 2011)</td>
<td>107</td>
</tr>
<tr>
<td>Eder (2008)(^{62})</td>
<td>6,014,472 whole blood donations</td>
<td>2721</td>
</tr>
<tr>
<td>New Zealand annual hemovigilance report 2013(^{43})</td>
<td>160,211, all blood collection (national data 2013)</td>
<td>1340</td>
</tr>
<tr>
<td>IHN (ISTARE database)(^{44})</td>
<td>18.8 million whole blood and apheresis donations (17 countries; 2012 data(^{4}))</td>
<td>487</td>
</tr>
</tbody>
</table>

\(^{a}\) Rates derived from figures in the publication.  
\(^{b}\) 2012 denominator supplied by ISTARE working group, chair C. Politis.  
\(^{c}\) Cases of “painful arm,” as defined in 2008 ISBT/IHN definitions.

Rates of reported complications are affected by differences in donor demographics—for instance, rates are higher in donors making their first donation. Studies of the occurrence of complications of blood donation have examined risk factors for their occurrence.\(^{45-47}\) Such factors need to be taken into account when analyzing the effects of differences or changes in procedures. The revised ISBT–IHN definitions are accompanied by a list of recommended parameters that should be recorded if possible.

The most common complications of donation are vasovagal reactions (approximately two-thirds), whereas the needle-related complications, hematomas and injuries of tissues including nerve injury or irritation, account for most of the remainder. In centers where apheresis is performed, additional types of reactions and complications are relevant—the most frequent are the consequences of infusion of citrate-containing anticoagulant solution when the donor’s blood constituents are reinfused following separation of the components that are being collected.

#### Vasovagal reactions

Vasovagal reaction is the most common donor complication (488 per 100,000 donations in the Danish study). The predominant symptoms are general discomfort, weakness, anxiety, dizziness, nausea, sweating, vomiting, pallor, and hyperventilation, associated with hypotension and bradycardia. The two last symptoms are essential for the diagnosis. Most vasovagal reactions are mild and transient, but some donors may lose consciousness (fainting or vasovagal syncope). In the more severe cases, this may be associated with convulsions and incontinence or may result in an accident if the donor falls. It is important to reassure the donor that these reactions do not indicate a predisposition to true epilepsy.

Vasovagal reactions are generated by the autonomic nervous system stimulated by psychologic factors and by the volume of blood removed relative to the donor’s total blood volume. An increasing number of studies have shown that young age, female sex, lower blood volume (estimated from weight and height), and first-donation status are significant risk factors.\(^{48}\) Based on these risk factors, a number of preventive measures have been evaluated (Table 6.5); some studies reported reductions of up to 20–25%.

Some vasovagal reactions (~10%)\(^{40,56}\) occur after the donor has left the donation area; these are so-called delayed reactions. These reactions are potentially dangerous, as the donor may be at risk of a serious accident. Female sex and a low estimated blood volume are risk factors for delayed vasovagal reactions.\(^{56}\)

### Table 6.5 Measures to Prevent Vasovagal Reactions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Study</th>
<th>Result and Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water drink shortly before donation</td>
<td>Newman (2007)(^{55}) (4312 high school students &lt;19 years of age)</td>
<td>21% reduction of vasovagal reactions</td>
</tr>
<tr>
<td>Applied muscle tension (AMT): The technique involves tensing the muscles in the legs and buttocks, which then raises the blood pressure.</td>
<td>France (2010)(^{51}) (RCT; total: 606)</td>
<td>Reduced presyncopal reactions in women (questionnaire studies)</td>
</tr>
<tr>
<td>Social support</td>
<td>Hanson (2009)(^{53}) (n = 65 completed study)</td>
<td>Possible improvement of return in male donors who adhered to instructions</td>
</tr>
<tr>
<td>Donor information addressing common donor concerns and giving tips for coping strategies</td>
<td>France (2010)(^{51}) (345 undergraduate donors assigned to intervention or control brochures; 67.5% had 1–4 previous donations)</td>
<td>Reduced presyncopal reactions (ascertained by questionnaire) and improved intent to donate again in inexperienced donors</td>
</tr>
<tr>
<td>Deferral of young donors with estimated blood volume &lt;3.5 L</td>
<td>Eder (2011)(^{62}) approximately 675,000 donations &lt;21 years annually (143,948 in 16-year-olds in 2009)</td>
<td>Improvements in donation attitude, confidence, and intention; more likely to volunteer to give blood</td>
</tr>
<tr>
<td>Combined intervention of water drink, deferral of donors with estimated blood volume &lt;3.5 L and encouragement to use AMT</td>
<td>Tommaso (2011)(^{55}) before-and-after study, total 213,031 donations by donors &lt;23 years of age.</td>
<td>VVR rate in 16-year-olds under modified selection criteria: 10.5% vs. 7.3%; odds ratio (OR), 0.67; 95% confidence interval [CI], 0.65–0.69 Overall reduction 24%; reduction of delayed reactions</td>
</tr>
</tbody>
</table>
In order to lower the risk of delayed reactions and of serious outcomes of these, it is essential to ensure that the donor feels completely well before leaving the donation area. Many facilities permanently defer donors following a severe delayed vasovagal reaction. Donors with hazardous occupations where they or others could be put at risk (e.g., pilots) should not return to work within 24 hours of donation.

Hematomas and other venepuncture-related or local complications

Hematoma is the second most common complication related to blood donation (275 per 100,000 donations). The symptoms are bruising, swelling, and pain at the venepuncture site.

A hematoma may occur if the needle punctures small vessels, or if blood leaks from the vein during or after venepuncture. Blood in the soft tissues behind the biceps tendon will initially spread behind the tendon and may not produce any visible swelling or pain. As the hematoma increases in size, it tracks along the blood vessels, nerves, and tendons to the forearm, and may cause paresthesia in the fingers because of compression or irritation of the median nerve.

Accidental puncture of a large artery in the antecubital fossa carries a high risk of a hematoma and of delayed bleeding, and can lead to other rare but very serious complications such as compartment syndrome of the forearm. Donor care staff should be trained to recognize and correctly manage arterial puncture, so as to avoid the potentially very serious sequelae.

Injury to the median nerve in the antecubital fossa accounts for only a small percentage of all immediate adverse reactions, but relatively often gives rise to serious long-term complications. In only a small percentage of all immediate adverse reactions, but the potentially very serious sequelae. To recognize and correctly manage arterial puncture, so as to avoid the potentially very serious complications.

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Anatomical studies have shown marked individual variation in the arrangement of nerves and blood vessels in the antecubital fossa, and injuries may occur despite good venepuncture technique. It is essential, however, that phlebotomists are familiar with normal anatomy of the region and are trained in correct techniques of needle insertion, together with prompt recognition and correct management of complications. To reduce the risk of direct nerve injury, the needle should be inserted only once and if the first attempt is unsuccessful, no further attempts should be made.

Hematoma should be managed by stopping the donation immediately if the donor complains of symptoms, applying pressure to the venepuncture site, and recommending that the donor rest the arm and avoid manual work with the donation arm for 24 hours. The donor should return to the blood center or seek medical treatment if there is persistent bleeding from the venepuncture site or if the swelling increases.

Complications associated with apheresis (automated) procedures

The return of donor blood, to which citrate solution has been added, causes a temporary reduction in ionized calcium in the circulation. In mild cases, this may give a tingling sensation in the mouth or extremities, a feeling of vibrations, or a metallic taste; usually, the symptoms resolve on reduction of the speed of return. Sometimes, a drink of milk or oral calcium supplement is administered. Intravenous calcium solutions are not usually necessary for the common types of collection, but are commonly administered in longer procedures (e.g., peripheral blood stem cells). In more serious citrate reactions, if untreated, symptoms may progress to carpopedal spasms, generalized muscle contractions (tetany), or cardiac arrhythmias, including cardiac arrest. Following a small number of reports of a mixup of saline and citrate bags that led to rapid infusion of citrate solution, blood operators are working together with manufacturers of disposables to modify the connectors, which in future could (once regulatory processes have been concluded) prevent this occurrence.

Long-term effects of regular whole blood donation and apheresis

A medium-term effect is fatigue in the days following a blood donation. Reported by 7.8% of donors in Newman’s interview study, it is, however, nonspecific and causality is difficult to assess. Fatigue is not currently included in the international classification system for complications of blood donation.

There has been patchy progress in monitoring and responding to longer term effects of regular whole blood donation. Most attention has been given to the iron depletion that is found in the majority of regular whole blood donors and can lead to iron-deficient erythropoiesis (with a hemoglobin level that is still normal) or to frank iron-deficiency anemia. Policies with regard to pre-donation screening of donors’ hemoglobin level differ between countries and blood establishments, as well as the response if iron deficiency is suspected. Some blood establishments conduct further investigations (e.g., performing a ferritin determination). In other settings, such donors are directly referred to their doctor for assessment and treatment. Some blood establishments supply oral iron supplements or advise potentially iron-deficient donors—even if not anemic—to see their family doctors to discuss the possibility of iron supplementation. In other countries, it is felt to be unacceptable to prescribe medication in order to obtain repeated donations—rather, the response is based on deferrals and sometimes preemptive adjustment of the interval between invitations for donation.

Frequent plasmapheresis

How innocuous is frequent plasma donation? In Europe, the maximum volume of plasma collected is limited to 15 L in a year, but donors in the United States (who are often paid or compensated) are less well protected. A study in 2010 found that concentrations of total protein, albumin, immunoglobulin G (IgG), and IgM were significantly lower in plasma pools from high-frequency donors (CI-inhibitor, pre-albumin, and C-reactive protein contents were higher). It is possible that the use of citrate-containing anticoagulant solution, which leads to calcium loss, might increase the likelihood of osteoporosis. A preliminary study using Dexa scans in Dutch donors gave reassuring results.

Use of growth factors, and monitoring safety of stem cell or granulocyte donors

Where donors are treated with growth factors such as granulocyte colony-stimulating factor, active follow-up is recommended for a year or longer for the ascertainment and care of conditions that could have an association with the growth factors or procedure.

Blood recipient hemovigilance

The different transfusion reactions are described in detail in other chapters in this book.
The definitions used by IHN\textsuperscript{64} and ISBT-WP\textsuperscript{65} can be found on their websites.

**Serious adverse events**
The EU directives require that serious adverse events be reported, but the legal scope is formally limited to adverse events at the blood establishment or in the blood transfusion laboratory. However, different hemovigilance systems have different scopes. Adverse events can have their origin at any stage of the transfusion chain. SHOT, the ISBT and IHN, and other hemovigilance systems have raised awareness of the risks of IBCT (i.e., all episodes where a patient was transfused with a blood component that did not meet the appropriate requirements or that was intended for another patient, including when the component was ABO compatible and/or if only a small quantity of blood was transfused and/or there was no adverse event). Some systems also capture and report on all episodes where a blood component that did not meet the appropriate requirements was wrongfully released from quarantine or issued, even if it was not transfused.

**What have we learned from hemovigilance systems?**
We now have a better understanding of the adverse reactions that occur in both blood donors and recipients of blood transfusion. The data from hemovigilance systems generally come from a broader base than data from scientific studies. This is valuable in several ways. It gives us a much better basis for informing donors and patients about risks. It has shown that it is generally safe to donate blood, but that significant donor complications do occur, maybe as often as one per 100 donations. Hemovigilance data also give information about the frequency and seriousness of recipient complications. This is important for directing further research to the most important areas. TRALI is such an example of a transfusion reaction that was seen in hemovigilance data to be more important than previously thought. Research directed to this problem led to effective preventive measures. Similarly, some other rare complications like GvHD and PTP seem to be quite rare. Hemovigilance data can say something about the main causes for the transfusion-related harm, and most significantly there are data showing that errors in pre-administration transfusion checks are the main cause of acute hemolytic transfusion reactions due to ABO incompatibility.\textsuperscript{66} This has led to preventive measures being identified such as computer-assisted pretransfusion bedside checking.

Hemovigilance has raised hopes that benchmarking should be possible. The European Union has already collected hemovigilance data from the member countries for several years. We have learned that benchmarking transfusion services in different countries is difficult, if not impossible. There are multiple reasons for this. The general healthcare systems in different countries vary. How the transfusion service is organized also varies, and so do the hemovigilance systems. The work done by IHN and ISBT on common definitions shows promising results in that agreement on definitions is possible, even if it takes time. Now the question is: What do we want to benchmark? When that question has been answered, the hemovigilance systems can start collecting the required data, including background data necessary to give the answers.

It is also doubtful whether hemovigilance data (e.g., the rate of reported transfusion reactions or IBCT) can be used for benchmarking hospitals or local transfusion services, because the complication rates are too low. Exceptions may be transfusion services in large countries, like the example from France mentioned in the next paragraph.

Hemovigilance data have made it possible to compare transfusion reactions to different products. The effect of introducing male-only plasma to reduce the incidence of TRALI is one such example.\textsuperscript{42,67} The effect on transfusion reactions by switching from fresh frozen plasma (FFP) to solvent-and-detergent (S/D)-treated pooled plasma in Finland is another example.\textsuperscript{68} In a recent health technology assessment (HTA) in Norway, comparing SD-plasma, single-donor pathogen-reduced plasma, quarantine FFP, and FFP, data from different hemovigilance systems proved to be valuable.\textsuperscript{69} In this HTA, the data from large countries that have different plasma products in use and a comprehensive hemovigilance system like France’s proved to be particularly useful in a field dominated by scientific studies too small to detect differences in infrequent complications.

**Donor**
Donor hemovigilance data showing the incidence of complications, together with the work\textsuperscript{70,71} showing that donors that experience complications tend not to donate again, have led to more focus on avoiding complications. Several preventive measures have been presented, such as giving donors water or isotonic drinks, with or without salty snacks, prior to donation; teaching donors to use muscle tension; and teaching the staff about social distraction to avoid vasovagal complications.

Work has started on incorporating estimation of blood volume as an acceptance criterion for blood donors. Tables for blood volume based on donor height and weight are now incorporated in the Council of Europe guide to preparation, use, and quality of blood components.\textsuperscript{72} One aim is to protect the donor; another is to be able to collect more from some donors.

Despite being an important complication related to whole blood donation, iron deficiency and iron deficiency anemia are frequently not reported in hemovigilance systems. There is a need for research and consensus development on the best way to capture information on this, so that this may provide background data and inform the discussion on measuring iron stores and on whether blood donors should be given iron supplementation routinely.

**Recipient**
Volume overload due to transfusion was not always regarded as a transfusion reaction, but since some hemovigilance systems started reporting this, it has received more attention. When the patients receive other IV fluids at the same time as blood, the volume overload was often ascribed to the other fluids, but the volume of blood components transfused should also be considered (Chapter 59).

In some cases, volume overload can result from unnecessary exposure to blood components. Both over- and undertransfusion are registered in some hemovigilance systems. These adverse events can result from (1) incorrect decision making; (2) prescribing errors, such as volume miscalculation; or (3) transfusion based on a spurious hemoglobin result from a sample diluted by intravenous infusion, from the wrong patient, or from a laboratory result that is incorrect or wrongly documented. These are relevant for a hemovigilance system, because the causes should be highlighted and preventive measures identified.

Reports to SHOT, when interpreted in the context of epidemiologic data, suggest that out of core hours, when staffing level are lower, transfusion carries an increased risk\textsuperscript{72} compared to those
administered during the day and that transfusion to pediatric patients is more likely to result in an adverse outcome than adult transfusion.\textsuperscript{75}

Overall, however, hemovigilance systems have demonstrated that blood transfusion is safe. An example from SHOT proves this while it still points at areas for further improvement. Over a 10-year period, during which time 30 million blood components were issued from UK blood services, SHOT received 3770 reports, of which 2717 (72\%) were of IBCT. Ninety-five percent of these patients survived with no serious effects, but 24 deaths were attributed wholly or in part to avoidable transfusion errors, and 100 patients suffered major morbidity.\textsuperscript{74}

**Discussion**

At the regional or national level, the hemovigilance system must be seen as impartial, independent, supportive, and professionally credible. Effective hemovigilance requires not only accurate and complete collection of data, but also interpretation within a predictable timeframe of the data in the context of what is known of transfusion epidemiology and practice, and use of the data to improve patient safety, both locally and nationally. The data and the analysis should be published in a format that can be used to support education and training. Reporting in itself is not a means of reducing errors or complications. Learning from the system may lead to improved safety awareness and better adherence to protocols. For maximal nationwide improvement, recommendations need to be incorporated in national guidelines or legislation, depending on the situation. Active involvement and “ownership” by professional bodies will help to ensure that recommendations are incorporated into clinical practice.

**Strengths of hemovigilance**

We now have transparency that was not available 20 years ago. Awareness of error-prone areas can lead to improved working procedures. Hemovigilance results combined with published research are leading to real improvements in transfusion safety. Both SHOT and the French hemovigilance systems have reported a lower rate of ABO-incompatible red blood cell transfusions in recent years.

A national hemovigilance system can give useful information on local, regional, national, and international levels. The data can be used in local improvement work as well as in making national and international guidelines and regulations.

**Limitations**

Hemovigilance systems do not register harm to patients because of failure to provide blood. This may be due to failure by the clinician to order blood, failure to transfuse the issued blood, or lack of available products in the transfusion service. The latter can be due to a general shortage of blood or more specific problems like lack of red cells with certain phenotypes or lack of HLA-compatible platelets.

The current systems are poorly suited to capture of complications due to repeated donations.

A hemovigilance system will be better at detecting immediate complications than complications occurring sometime after donation or transfusion. Delayed donor complications may be discovered if returning donors are asked about any complications after the previous donation, and donors should be reminded to inform the blood bank if they have complications after leaving the donation room. Delayed hemolytic transfusion reactions, typically occurring 10 days after transfusion, are probably underreported and probably often undiagnosed.

Passive reporting system can lead to underreporting, especially if you do not have a blame-free culture.

For good analysis, it is necessary to have denominator data. This can be data on units transfused, the underlying condition of the patients, patients not transfused, and so on. Highly automated transfusion services are usually at an advantage here, as are hospitals with comprehensive administrative computer systems.

**Further perspectives**

An important aspect of quality work is to reduce variation.\textsuperscript{75} At present, differences in system and in practice mean we are not properly able to investigate differences in reported incidences between countries. One must also expect that the safety culture and the reporting culture may vary a lot between countries. An example is the OECD’s attempt to include wrong blood transfused as a patient safety indicator. A never event such as this was thought to have the potential of a useful safety indicator. In practice, however, it had to be abandoned because the reporting countries showed too much variation for the rates to be credible.

For a system to work, one should not register more data than will be used for analysis. International agreement on a minimum set of data to include in hemovigilance systems would be useful. This could be the next step when agreement on definitions is reached.

**Conclusion**

Hemovigilance systems show that both blood donation and blood transfusion are safe. The data collected has been used to improve safety further by pointing research and improvement work in the right direction. Knowing the incidence and seriousness of complications is very valuable in this respect. Giving correct information on risks to donors and patients is necessary for donors and patients to trust the transfusion service. In the future international agreement on definitions and on recommended background data to collect may make benchmarking possible.

**Key references**

A full reference list for this chapter is available at: http://www.wiley.com/go/simon/